# DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

DIVISION OF RESEARCH RESOURCES
ANIMAL RESOURCES PROGRAM
PRIMATE RESEARCH CENTERS PROGRAM
ANNUAL PROGRESS REPORT

• 1.	PHS GRANT NUMBER: P 5 1 R R 0 0 1 6 5 - 2 6
2.	NAME OF RECIPIENT INSTITUTION: Yerkes Regional Primate Research Center
3.	HEALTH PROFESSIONAL SCHOOL (If applicable): Emory University  Woodruff Medical Center
4.	REPORTING PERIOD:
	a. FROM (Month, Day, Year): 0 1 - 0 1 - 8 6
	b. TO (Month, Day, Year): 12-31-86
5.	CENTER DIRECTOR:
	a. NAME: Frederick A. King, Ph.D.
	Director V. I. D.
	b. TITLE: Director, Yerkes Regional Primate Research Center;
	Professor, Department of Anatomy; Adjunct Professor, Department of Psychology; Associate Dean, Emory University School of Medicine c. SIGNATURE:
4	
6.	DATE SIGNED (Month, Day, Year):
7.	TELEPHONE (Include Area Code): 4 0 4 - 7 2 7 - 7 7 0 7

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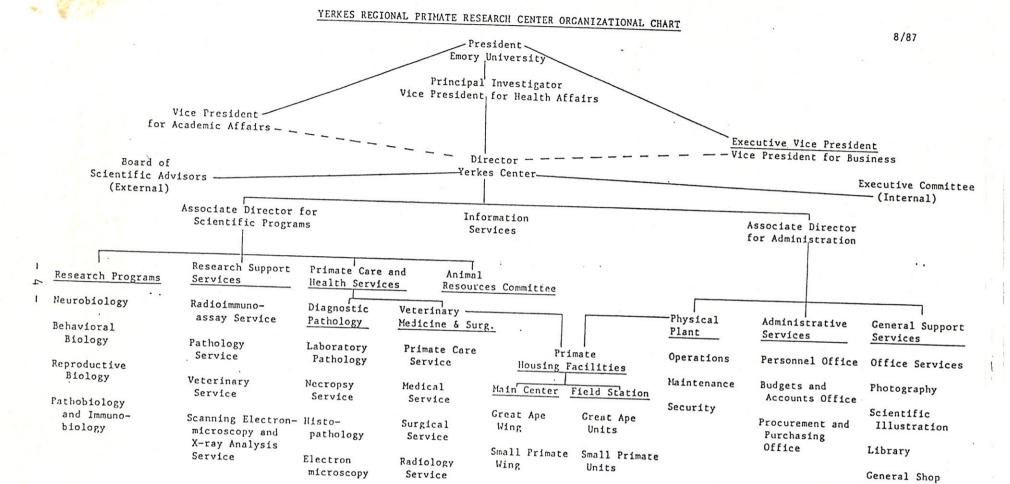
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#### Part I: NARRATIVE DESCRIPTION

#### A. SUMMARY OF ACCOMPLISHMENTS

#### 1) Strengths and Weaknesses of Current Program

Major strengths of the Yerkes Center during 1986 include the continued expansion of our research programs and interaction with investigators at the host institution as well as other local and regional universities and research institutions; further improvements in the physical plant and animal housing facilities; and the inhouse development of virology and immunology laboratories with a concomitant expansion of research programs related to the development of nonhuman primate models for the acquired immunodeficiency syndrome.

The continued increase in research programs at the Yerkes Center, particularly with reference to the increased numbers of affiliate and collaborative scientists who conduct their research with nonhuman primates at the Yerkes Center, continues to be one of our major strengths. The number of affiliate and collaborative scientists now numbers 107, as compared to 96 in 1985 and 84 in 1984. This function of the Yerkes Center provides a unique and valuable resource for research investigators at local and regional universities and research institutions, as well as institutions throughout the nation and in other parts of the world. As a result of these collaborative efforts, active and expanded research programs are currently underway in the areas of vision, development of AIDS animal models, aging, parasitic diseases and reproductive biology.

Major improvements were made in the physical plant and animal housing facilities during 1986. These improvements have strengthened our position as a research institution. The Yerkes Field Station waste water treatment and disposal plant was completed and placed into operation during 1986. The Field Station water is now provided by the Gwinnett County water system, rather than wells located on the premises. A number of Field Station compounds have also been renovated and terraced, with new indoor animal quarters added. The compound renovation has created a more aesthetically pleasing environment and has resulted in further improvement in animal care.

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Work was initiated in the latter part of 1986 on the renovation of two laboratories to provide inhouse virology and immunology capabilities. Recruitment for a virologist and an immunologist was also initiated. It is anticipated that these laboratories with the necessary personnel and equipment will be operational by early 1987, allowing for considerable expansion in our AIDS animal model development studies.

A weakness of the Center, which is becoming more critical with the passage of time, is our inability, due to fiscal constraints, to expand our physical plant and to add additional core faculty. Current facilities and major items of equipment are in need of renovation, modernization and/or replacement. Due to the increased research activities at the Center, there is a critical need for expansion of the physical plant for both research laboratories and animal housing, especially the latter.

### 2) Changes in Professional Personnel

Drs. Mark Wilson and Kim Wallen were both granted core scientist status during 1986. Both have been longtime productive, affiliate or collaborative scientists at the Center. Dr. Wilson is responsible for the operation of the Yerkes RIA laboratory, and has added a steroid component to this unit to complement the non-steroidal function. Dr. Wallen will continue to be active in his studies on the effects of hormones on behavior. Biographical sketches for Dr. Wilson and Dr. Wallen are included in the appendix.

#### 3) Major Problems Encountered or Anticipated

The harassment of the Yerkes Center by anti-research groups continues to be a problem that takes up a considerable amount of time of the Yerkes Center administration and faculty. The irresponsible, destructive and often unlawful activities of these misguided individuals also has necessitated the expenditure of considerable funds to provide for increased security.

An imminent problem faced by the Yerkes Center is the shortage of inhouse-produced nonhuman primates and lack of sufficient animal housing space to accommodate increasing numbers of research projects by core, affiliate and collaborative scientists. Our animal holding facilities are currently filled to capacity, with most of the animals assigned to specific research projects. Center breeding colonies have, within recent years, been producing sufficient numbers of animals to meet the needs of Center investigators. With increased research activities, we are rapidly reaching the point where our breeding colonies will no longer be able to provide for the needs of Center investigators. Consequently, unless we are able to expand our breeding colonies and provide for additional animal housing space, it will not be possible for the Center to accommodate new research projects in a timely manner.

### 4) Major Equipment Items Purchased

Base Grant					
1	Lab-Guard Hood	4,900.00			
1	Sysmex Cell Counter	13,990.00			
1	Chain Link Fence (2300 ft.)	34,473.00			
1	Cage Washer	43,399.00			
1	Evaporation w/Water Jet	4,378.00			
1	Intrusion Alarm (Add On)	2,083.00			
1	Programmable Freezer	10,800.00			
1	Portable Gas Welder	2,100.00			
1	DHV11 Board-8 Line	1,760.00			
3	Stainless Steel Stretchers	3,000.00			
2	Cushman Haulsters	14,408.00			
1	Configuration 3X Computer	4,270.00			
1	Six Pen Plotter	1,393.00			
1	Intrusion Alarm System	6,875.00			
2	Animal Housing Units	120,450.00			
1	Refrigerated Centrifuge	10,019.00			
1	Swinging Bucket Rotor	3,310.00			
1	Rack Rotor	2,967.00			
1	Upright Low Temperature Freezer	3,972.00			
2	Katolight Emergency Generators	78,525.00			
3	Primate Cages	10,511.00			
	0.1				
1	Other Grants				
1	Personal Computer	2,975.00			
1	Keratometer Microscope Printer	7,500.00			
1		1,316.00			
1	Infusion Pump Video Recorder	1,099.00			
2		2,576.00			
1	Zenith Computers Card Processor	2,100.00			
ì	RC-2 Camera	1,500.00			
1	Tall Grass Hard Disk	5,346.00			
î	Sonomed A-Scan	3,600.00			
1	IBM PC w/Monitor and Modem	6,368.00			
ì	Microscope with Camera	3,184.00			
î	Fortrax 4 x 4 Vehicle	11,838.00			
î	Freezing Unit Plate	3,000.00			
1		1,595.00			
1	Reflecting Tracking System Ocutome	13,037.00			
1	Paper Processor	3,073.00			
2	All-Talk Keyboards	7,743.00			
2	Zenith 256K Computer	8,000.00			
ī	23MB Cartridge Tape Backup	2,093.00			
2	Unix PC	1,212.00			
ī	CRT Image Synthesizer	1,250.00			
1	Wild Automatic Camera System	8,280.00			
1	MPS 51 Camora Rody Chicken Rd	1,644.00			
1	MPS 51 Camera Body Shutter Piece	1,044.00			
1	Semen Analysis Software Release System	36,083.00			
l	Interference Condensor	3,009.00			
1	Virgo Computer Operating System Taurus PC	6,500.00			
ì	Sliding Microtome	3,390.00			
•	orrarus arcrocome	3,890.00			

# 5) Improvements and Additions to Facilities

Alterations to Rooms 201 (Neuroanatomy Secretary 205 (Behavioral Biology), 243A (Primate Housing), and Cage Wash Area	11,794.00
Alterations to Room 242 (Small Primate Wing	,///100
Housing (Nursery))	11,728,00
Alterations to Rooms 141 (General Shop)	
and 144 (Instrumentation Shop)	12,190.00
Alterations to Building T-5 (Behavioral Biology/	
Neurobiology)	1,426.00
Three Cage Washer Enclosures	7,098.00
One 48' x 25' Storage Building	
and a partificing	20,434.00

### 6) Conferences and Workshops

During 1986, the Yerkes Center participated in the following conferences, workshops or meetings:

- a) The Directors of the NIH-sponsored Regional Primate Research Centers met at the Yerkes Center on February 27 March 1, 1986.
- b) A conference and working session of the American Psychological Association Committee on Animal Research and Experimentation met at the Yerkes Center on March 28-29, 1986. This group met with Yerkes faculty and administration to gain a better understanding of the purposes, facilities and studies of an NIH-sponsored Regional Primate Center.
- c) Atlanta University's "Minority Access to Careers" program met at the Yerkes Center on June 3-4, 1986.
- d) The Yerkes Center participated in an NIH-Emory University workshop on PHS Policy on Laboratory Animals on May 8-9, 1986.

### 7) Yerkes Visiting Speaker Series

January 30 Dr. Alan Walker, The Johns Hopkins University.
Topic: "Recent Discoveries of Homo erectus in East Africa."

Co-sponsored by the Department of Anthropology,  $\operatorname{\sf Emory}$  University.

February 22 Dr. Peter Marler, Rockefeller University.
Topic: "Behavioral Development: Dynamic
Antecedents and Neural Mechanisms."

Co-sponsored by the Emory Neurosciences Group.

- 6) Eight animals (3.6% of necropsies) were found to have neoplasms in 1986. Eleven tumors were found in these 8 animals. These included two carcinomas of the small intestine, two colon carcinomas, one carcinoma of the gallbladder, one salivary gland adenoma, one astrocytoma of the brain, one interstitial cell tumor of the testicle, one esophageal leiomyoma, one subcutaneous lipoma, and one chronic lymphocytic leukemia.
- 7) One additional case of listeriosis was diagnosed in 1986. This occurred in an aborted rhesus infant and represents the 19th case of listeriosis seen in our colony. Eight cases were diagnosed in 1982; single cases occurred in 1973, 1976, 1980, 1981, and 1983; 2 cases occurred in 1984; and 3 cases occurred in 1985. Animal species affected have included rhesus, stumptail macaques, Celebese black apes, squirrel monkeys, and a pig-tailed macaque. Most cases have been either abortuses, stillbirths or neonatal deaths.

Significant lesions observed in the 67 surgical pathology specimens examined in 1986 included neoplasms, amyloidosis, endometriosis, mycobacteriosis, lymph node hyperplasia, pulmonary acariasis, colitis, and a sperm granuloma. Neoplasms diagnosed by biopsy included a carcinoma of the colon, and a mast cell tumor of the skin.

Histopathology Service: During 1986 the histopathology laboratory processed 286 necropsy cases and/or biopsies. This entailed the production, and subsequent filing of 9,764 paraffin blocks. A total of 10,312 microslides were prepared from these blocks. Following microscopic review, all slides are maintained on file in the histopathology laboratory.

Clinical Pathology Service: During 1986, the clinical pathology laboratory received 6,429 specimens for evaluation. These determinations can be categorized as follows:

Hematology Examinations	3366
Bone Marrow Examinations	1166
Bacterial Culturas	3
Bacterial Cultures	2390
Fungal Cultures	6
nycopiasma cultures	5
Viral Cultures	_
Fecal Parasitology Examinations.	0
Serum Chemistrian	431
Serum Chemistries	837
Urine Chemistries	0
randulogy Examinations	745
rreguancy lests	42
Urine Analysis	
Imprint Smear Preparations.	130
Spinal Fluid Frances	505
Spinal Fluid Examinations	121
Count (retal/Brain Cells)	5
Miscellaneous Tests	43
	43

When compared with 1985, this number of laboratory specimens represents an increase of 715 specimens (12.5% increase). Increases were noted in the number of hematology examinations, bacterial cultures, spinal fluid examinations, fecal parasitology examinations, serum chemistries, imprint smears, urine analyses and pregnancy tests.

Selected pathogenic microorganisms isolated during the past year include:

Staphylococcus aureus Group B, Beta Streptococcus Shigella flexneri Klebsiella pneumoniae Pseudomonas aeruginosa Pasteurella multocida Listeria monocytogenes Campylobacter species Salmonella species

Aeromonas hydrophila Yersinia enterocolitica Yersinia pseudotuberculosis Yersinia fredericksenii Streptococcus pneumoniae Hemophilus influenzae Enteropath. E. coli

A total of 601 antibiograms were done on bacterial isolates during the year.

The most frequently encountered parasites continue to be Balantidium coli, Trichuris species, and Strongyloides species. A significant number of fecal smears contained Blastocystis hominis. The latter organism, generally considered a non-pathogenic yeast that inhabits the intestinal tract, has recently been reclassified as a protozoa. This organism has been incriminated as a cause of enteric disease and diarrhea in man and in experimentally infected guinea pigs. Our observations indicate that this organism may be causally related to some cases of diarrhea in nonhuman primates, and suggest that this organism should be considered a potential enteric pathogen in nonhuman primates. One case of giardiasis, one case of amebiasis ( $\underline{E}$ . histolytica) and one case of cryptosporidiosis were encountered during the year.

Electron Microscopy Laboratory: During 1986, the electron microscopy laboratory received 89 specimens for processing for ultrastructural evaluation. Specimens received included 3 tumors, 10 liver sections, 8 spleen sections, 9 lymph node sections, 7 GI tract specimens, 5 kidney specimens, 32 CNS specimens, I mouth lesion, 3 bone marrow specimens, I thymus specimen, 4 eye specimens, 1 testicular specimen, 1 peripheral blood specimen, 1 adrenal specimen, 1 heart specimen and 2 lung specimens.

Specimens Collected for Other Investigators: During 1986, 797 specimens were collected and shipped to 96 other investigators or laboratories. A partial listing of specimens provided includes serum, blood, tissue specimens, carcasses, skin, eyes, bone, and placenta. This includes 3,858 ml of whole blood, 6 ml of plasma, and 377 ml of serum from 8 nonhuman primate species.

# c) Primate Care and Housing---Main Station

#### 1) Great Ape Wing

Renovation of the Great Ape Wing caging was begun in 1986. This consisted of replacing or restretching the six guage chain link fencing on all 100 interior and exterior cages.

An epoxy aggregate floor was installed in the Infectious Diseases Building and the building was occupied in April 1986.

Continued emphasis was placed on the professional training of the primate care staff. As a result, seven primate care technicians received their AALAS Assistant Technician certificates in October 1986.

### 2) Small Primate Wing

During 1986 a replacement cage washer was purchased and installed. The area within which the replaced cage washer was located was converted into two primate housing rooms which will be used as nursery or critical care areas.

A utility vehicle was purchased to facilitate the moving of food and caging between outbuildings.

Five stainless steel racks and 20 cages were purchased to house animals over 10 kg. in order to comply with recent NIH primate caging guidelines.

Four doors within the Small Primate Wing were enlarged to accommodate the passage of the new larger cages as required by the aforementioned NIH guidelines.

### d) Primate Care and Housing---Field Station

During 1986, continued emphasis was placed on improving animal housing, methods of animal care, and the performance of animal care personnel. Items accomplished during the past year are summarized below:

Two (2) animal housing units (T-1 and S-1 and 2) were completely replaced with new units (Relocatable Exterior Primate Enclosures). Improvements in design and materials were incorporated into these new units to facilitate the routine care and enhance the research in these areas. Replacing these units has also decreased maintenance requirements, eliminated the need for air conditioning in the summer months and improved the living conditions of animals in these facilities.

Rehabilitation of the inside of compounds A-1, A-4, S-1 and S-2 was completed to prevent further erosion of the soil and damage to the structural integrity of compound walls. This was accomplished by grading the soil, installing retaining walls and drainage ditches and applying a layer of crushed rock to the surface.

A new cushman vehicle was purchased this year to provide for the distribution of food, supplies, cleaning equipment and research equipment.

To insure the safety and health of the Field Station colony a new temperature alarm system was installed to monitor all buildings that house animals. This system will allow around-the-clock monitoring of animal quarters for high and low temperatures and will provide fire/smoke detection in these areas.

#### e) Physical Plant

### 1) Main Station

During 1986 the following items were accomplished:

In order to accommodate the laboratory and office of the recently appointed Center virologist, Dr. Patricia Fultz, it was necessary to relocate and remodel several offices and laboratories on all three floors of the Center. This work included:

- a) Conversion of Dr. Larry Byrd's electronics shop into a secretarial office for the Division of Neurobiology.
- b) Relocation of all Veterinary Medicine personnel, Pharmacy and the Animal Records Registrar from the second floor to the third floor.
- c) Splitting of the Chief of Veterinary Medicine's former office on the second floor into two areas, a new electronics laboratory for Dr. Larry Byrd; the other an office for the soon-to-be-hired immunologist.
- d) The Instrumentation Shop was relocated to the General Shop area on the first floor with a concomitant increase of space for the latter in order to accommodate the requirements of both.
- e) The Center's Electronics Shop was relocated to another site on the third floor with all attendant alterations and renovations.

To meet with increasing demand for storage space at the Main Station, a block building was erected with 1080 sq.ft. of usable floor space.

An underground sprinkler system was installed in the front lawn of the Main Station so as to allow irrigation at non-peak use time.

### 2) Field Station

During 1986 the following items were accomplished:

Construction of the wastewater collection and treatment system was completed this year. The collection system, oxidation ponds and spray irrigation field are fully operational with all the buildings tied into the new system and all the septic tanks disconnected.

Installation of a water provision and distribution system was completed in 1986 to provide county water throughout the Field Station and replace the present well and pump system which was subject to failure during power outages.

Two (2) observation towers were built and installed in the T-1 and S-1 and 2 compounds to provide vantage points for observing animals in three (3) compounds. These towers significantly improved the safety of personnel and enhanced the research in these areas.

All buildings, compounds, observation towers and support structures were painted to prevent damage from rust and preserve the facilities at the Field Station.

A new emergency generator was purchased and installed to provide electricity for animal quarters during a power outage. This unit will provide emergency power for twenty-one (21) animal housing areas.

Installation of an additional 2,300 feet of perimeter fencing was necessary to protect the Field Station from intruders resulting from the development of adjacent property.

### f) Radioimmunoassay

The Radioimmunoassay (RIA) Laboratory provides assay services for Yerkes and non-Yerkes investigators for the analysis of protein ans steroid hormones. During the calendar year 1986, users of the RIA Laboratory and services provided were as follows:

Irwin S. Bernstein, Ph.D., principal investigator: This project is investigating how social variables may modulate sexual development in male rhesus monkeys. Analyses of serum testosterone and growth hormone (GH) were performed. This project is funded by NSF.

Thomas P. Gordon, M.S., principal investigator: These studies are investigating the role of the environment, particularly photoperiod in the seasonal occurrence of ovulation in rhesus monkeys. Analyses done in support of this NSF-funded project included estradiol (E2), progesterone (P4), luteinizing hormone (LH), testosterone, prolactin, and melatonin.

James Herndon, Ph.D., principal investigator: These studies examined the influence of social factors on reproductive function and behavior. Analyses of bioLH were performed for this NSF-supported project.

Ronald D. Nadler, Ph.D., principal investigator: This project describes how treatment with oral contraceptives influences sexual behavior in chimpanzees. Analyses of serum and urinary LH were performed. This project is supported by NIH.

Kim Wallen, Ph.D., principal investigator: The role of gonadal and adrenal hormones in the control of female and male sexual behavior is the focus of this project. Analyses performed included E2, P4, testosterone, LH, and cortisol. This project was supported by NSF.

Mark E. Wilson, Ph.D., principal investigator: This project is examining how endogenous factors and environmental cues influence growth and sexual maturation in female rhesus monkeys. Analyses included E2, P4, LH (bio and immuno-), follicle stimulating hormone (FSH), GH, somatomedin-C (Sm-C) and prolactin. This project is supported by NIH.

Another project is investigating the mechanisms controlling lactational infertility in rhesus monkeys and how it is prolonged in adolescent mothers. Analyses included E2, P4, LH, FSH, prolactin, GH and SmC. This project is funded by NIH.

Other: In addition to these projects, analyses were performed for these investigators: Dr. Kenneth Gould, Yerkes; Dr. Brent Swenson, Yerkes; Dr. Nancy Pope, Yerkes; Dr. David Mann, Morehouse School of Medicine; Dr. Daniel Barrow, Emory University School of Medicine; Dr. Danielle Blake, Emory Clinic; Dr. Carol Phillips, Emory University School of Medicine; Dr. Mario DiGirolamo, Emory University School of Medicine; Dr. Spencer Welch, Emory University School of Medicine; Dr. Edwin Dale, Emory University School of Medicine; Mr. Frank Sabitino, Emory University School of Medicine.

#### Number of determinations performed:

Compound	Number
hLH	292
hFSH	8
cynLH	1,184
cynFSH	315
bioLH	3,162
hGH	1,215
hPRL	1,496
Sm-C	1,857
Melatonin	782
Insulin	1,120
hCG	123
Creatinine	210
Prostaglandin F <sub>2</sub>	38
Estrone sulfate	57
Testosterone	1,300
Estradiol	2,014
Progesterone	2,196
Cortisol	1,345

Total: 18,714

The following hormonal assays were performed routinely by the RIA Laboratory during 1986:

Assay	Species
Human FSH Human LH	human, chimpanzee gorilla human, chimpanzee, gorilla,
Human PRL Human GH Monkey LH Bioassayable LH Monkey FSH Rat LH, FSH, and PRL GnRH Somatomedin-C Chorionic gonadotropin/LH	orangutan chimpanzee, gorilla, monkey chimpanzee, gorilla, monkey rhesus monkey all species monkey rodents all species all species
receptor assay Melatonin Beta-endorphin Estradiol Estrone Estrone sulfate Progesterone Testosterone Androstenedione Cortisol Insulin	great apes, rhesus monkey all species

The following analyses can be performed but are not presently being used: (1) ovine LH, (2) oxytocin, and (3) prostaglandin. In addition, creatinine and Lowry protein determination are also performed by the RIA Laboratory.

### g) General Office Services

This office is responsible for the following functions:

Verification and record keeping of time cards for bi-weekly employees;

Arrangements for travel and preparation of travel expense forms;

Processing and distribution of mail;

Maintenance of key inventory system;

Reception of Center visitors;

Maintenance and operation of photocopy equipment; and

Acquisition and distribution of office supplies.

#### h) Information Services

The Yerkes Information Services Office is responsible for developing and implementing internal and external communications programs. These programs encompass news media activities; employee orientation-information; the preparation and distribution of print and audiovisual materials; tours and presentations for scientific and educational groups; community relations; and a variety of special projects.

Through these programs, the Yerkes Center endeavors to inform its employees, the Emory University community, and the general public about the goals and accomplishments of the center's research and conservation programs.

The Information Services Manager/Assistant to the Director is responsible for these activities, key examples of which are described below:

Print and Audiovisual Materials: In 1986, the Yerkes Center's fact sheets, "The Conduct of Research and Animal Care at the Yerkes Primate Research Center" and "Conservation Oriented Research and Educational Activities," were updated. The Information Services Manager also revised the Yerkes Center's basic brochure, first published in 1981.

New print materials prepared by the Information Services
Manager include: "Yerkes Primate Research Center: Fact
Sheet" and "Research and Conservation Programs of the Yerkes
Primate Research Center with Zoo Atlanta." The latter fact
sheet, along with the Yerkes one-page publication, "Gorilla
Facts," were distributed to news media and dignitaries who
attended the groundbreaking for Zoo Atlanta's gorilla habitat
which will feature three family groups of gorillas on loan
from Yerkes.

The Information Services Manager, during 1986, initiated the production of a videotape about the center's research on Parkinson's disease. The videotape will be used in professional and public education. The Yerkes Center's collection of general and research slides which the Yerkes Director, Information Services Manager, scientists and students use in their speeches and publications and which are loaned to other individuals also was updated.

To publicize the Yerkes Visiting Speakers, the Information Services Office distributed 400 to 500 flyers about each Visiting Speaker to individuals and academic departments at Emory and other Atlanta scientific and educational institutions.

Employee Relations: Because of limited time and resources, only one issue of "Inside Yerkes," the center's employee newsletter, was published. In addition to employee orientation tours, the Information Services Manager organized briefings at which Yerkes scientists described their research studies. During 1986, employee briefings covered the Yerkes Center's studies on AIDS, Parkinson's Disease, the surgical treatment of urinary incontinence, and conservation studies in Borneo.

Local and National News Media Relations: The broadcast and print news media — particularly science—medical journalists — are responsible for informing the public about its investment in biomedical and behavioral research. The Yerkes Center administration regards news media activities as an obligation to the public whose tax dollars fund most of the biomedical research conducted in the U.S. Therefore, the Yerkes Information Services Manager informs appropriate news media about the status or accomplishments of Yerkes research projects that have inherent public concern or interest.

The news media's increasing focus on AIDS resulted in the Information Services Manager's devoting a great deal of time during 1986 to responding to journalists and informing reporters about the nature and accomplishments of the studies on AIDS which are conducted by Yerkes scientists in conjunction with the U.S. Centers for Disease Control. A wide range of news media reported on Yerkes-CDC research. Examples include the Atlanta Journal and Constitution, Newsday, Philadelphia Inquirer, Emory Magazine, Creative Loafing (Atlanta), Ft. Lauderdale Sun Sentinel (Florida), and numerous broadcast media which ranged from Atlanta radio station WGST to an Australian TV science series.

Numerous journalists and authors also have been provided with information and interviews regarding other Yerkes research studies. Examples include: Emory Voice and Emory Wheel student newspapers; Omni magazine; NOVA, a Public Broadcasting System television educational series; WTBS-TV "Between the Lines;" Emory Campus Report; National Geographic "Explorer" national TV program which is broadcast by WTBS-TV; and Research Resources Reporter.

For inclusion in an Emory University publication, Emory Experts: A Guide to Faculty Sources, extensive information about Yerkes scientists was provided by the Information Services Manager.

The selected proceedings of the IXth Congress of the International Primatological Society were published in two volumes by Van Nostrand Reinhold. The camera-ready text for these volumes was prepared by the Information Services Office.

Community Affairs: Presentations about the Yerkes Center were given by the Information Services Manager to several groups, which included: the Georgia Junior Academy of Sciences annual meeting, attended by over 200 high school students; the Georgia Science Teachers Association of metro Atlanta; Fernbank Science Center students; the southern regional meeting of the public affairs section of the Association of American Medical Colleges; and the Midtown Optimist Club.

Tours were provided to new employees as well as to various scientific and educational groups, including DeKalb County high school science teachers enrolled in a summer program at the Fernbank Science Center; Atlanta University students; and members of several Emory University Freshman Seminar Groups.

In addition, the Information Services Office responded to numerous letter and telephone inquiries from students, scientists and other individuals.

During 1986, the Information Services Manager was a trustee of the Atlanta Zoological Society and volunteer chair of the public relations task force of Zoo Atlanta's Public Marketing/Public Relations Committee. The Information Services Manager's volunteer activities complimented the Yerkes Center's involvement in the planning of Zoo Atlanta's first major exhibit: semi-naturalistic habitats of gorilla and orangutan families on loan from the Yerkes Center.

The Information Services Manager also participated in the Atlanta Chamber of Commmerce's communications advisory group and the Georgia Heart Association's public relations committee and chaired the public relations workshops at the association's annual meeting.

As program chair for the national American Medical Writers Association annual meeting, the Information Services Manager organized the conventions' major general session which focused on media coverage of AIDS. Several other meeting events were coordinated by the Information Services Manager.

The Information Services Manager also served on the editorial board for a new guidebook for scientists that will be published by the Foundation for Biomedical Research.

Special Projects: The Information Services Manager assisted the Yerkes Director with various special events and projects including the organization of speeches and the coordination of the biannual meeting of the directors and key staff of the seven regional primate research centers sponsored by the Division of Research Resources/National Institutes of Health. The meeting, which was held in Atlanta and hosted by the Yerkes Center, also was attended by NIH officials.

The Yerkes Center also hosted and the Information Officer helped to organize the biannual meeting of the American Psychological Associations' CARE (Committee on Animal Research and Experimentation) which was held in Atlanta.

# i) Bioelectronics and Instrumentation Shops

During 1986, the Bioelectronics and Instrumentation Shops carried out the following projects:

Neurobiology: A visual pattern generator was designed and constructed. This device permits presentation of precisely defined visual patterns under computer control. Troubleshooting and repairs were completed for computer monitoring system in visual development studies. A movable mirror carriage with 3' x 5' travel was constructed. Items of equipment were constructed for Dr. Boothe's vision studies, including face masks and test devices for baboon-sized animals, beam splitter for video camera, lens holders and shutters, head restraints, lighting system, and 10 to 15 other related items.

Reproductive Biology: A portable electroejaculation unit was designed, constructed and tested. An X-Y position locator was designed and built for osteoporosis studies. A sperm-freezing vessel was made. A behavioral data collection program was written and installed in a hand-held computer.

Behavioral Biology: Process control devices for several studies were built or programmed. Phase repeated (voice simulating) boxes were designed.

Computers and Word Processing: The PDP-11/73 which maintains budgets and accounts records was operated by Victor Speck during times when the Center was without a programmer. The components were ordered for the new Sun computer system which will replace the 11/73.

The computer and peripherals were ordered for a new computerized security system.

Support was provided for word processing in the Center. This support included computer to computer file transfer, as well as coordination of repairs and operator training for the Center's word processing computer.

Miscellaneous Projects and Repairs: Numerous repairs were made including dental scaler, cauterizer and vacuum pump. A telemetric fetal heartrate monitor was repaired. Several precision parts for the scanning electron microscope were constructed. Dozens of small or emergency repairs were made for all divisions.

Consultant Services Provided to the Center by Professor Harold Warner: During the past year, Professor Harold Warner (Emeritus), retired Chief of BME, continued to provide consultation to the Yerkes faculty. Specific consultation and assistance were provided in the following areas:

General Center Activities: Reviewed Therasonics Corporation published data regarding ultrasound stimulation for possible bone regeneration in osteoporosis. Therasonics was proposing that Yerkes join them in a study employing the great apes. Dr. McClure approved the joint venture in principle and furnished an application package for execution by Therasonics. The memo and application documents were mailed to Therasonics.

Subsequently, a meeting was held in Dr. McClure's office, attended by personnel of Therasonics, Dr. McClure, Dr. DeAndrade, and Professor Warner. It was agreed that the technique was worth a study effort and encouraged Therasonics to submit the formal application. Nothing further from Therasonics, regarding submission of a formal application detailing such a study has been forthcoming.

Reproductive Biology: Held discussion with Dr. Gould concerning waveform clipping when a high impedance animal load is stimulated with a sine wave in the absence of sufficient driving EMF.

Performed penile stimulation on 3 rhesus monkeys using a sine wave stimulating waveform; clipping occurred at 11 to 12 mA. Animals appeared to ejaculate after clipping occurred.

Three additional rhesus (2 control and 1 treatment) received penile stimulation 2 days later and ejaculated at about 5.5 mA employing a sine wave; clipping did not occur. The discrepancy was due to the use of an improper scale factor in the output current of the stimulator during the previous experiment.

Briefed Tom Buckner on the use of range switches to enable proper scale factor in the output current amplitude of the stimulator. Delivered a lengthy tutorial on tissue injury safety and general electric shock safety during electrical stimulation.

Advised Tom Buckner on repairing stimulating-probe connections and electrodes, and their safe use.

Neurobiology: Consultation for Philip Ho on fine, low-spring-constant coil springs for use with electrodes. Furnished him with some samples.

Veterinary Medicine: Consultation for Dr. Orkin on electrical grounding safety in O.R. Provided explanation with diagrams.

Yerkes General Shop: Advised on stabilizing rate of rise of velocity-controlled, animal-operated doors; suggested checking and eliminating frictional forces acting on doors and then adjusting counterweighting. This solved the problem.

### j) General Shop

The General Shop provides an important service for scientific and support personnel at the Center. This unit is responsible for the design, fabrication, maintenance and repair of all animal caging and related research equipment within the Center.

During 1986, the General Shop responded to 183 emergency repair calls. During the same period, the General Shop completed 310 work orders submitted by scientists and support personnel. These work orders included fabrication of caging, construction of research equipment and repair of existing equipment and caging.

#### k) Library

The Yerkes Library provides full library service for the research staff and administration.

During 1986, the circulation figures were approximately the same as during the previous year—6,000. Books and journals not available within the library were obtained on campus through daily trips to the campus, or through interlibrary loans from off-campus libraries. Reference, bibliographic information, and literature searches were obtained through the library or its online computer service, or with the help of the reference services at the larger campus libraries.

Unused books were decataloged and withdrawn from the shelves. Archival books were removed from the open shelves and placed in cabinets where they are still accessible and secure.

The reprints of faculty publications were added to the bound, indexed, reprint collection of Yerkes Publications. These reprints, beginning 1925 through 1986, now total approximately 2,400. Additional reprints were added to the special collection (dating back to 1866) of publications on primates, which now totals 3,900.

#### 1) Budget and Accounts

This office is responsible for grants management of the Center's base grant and faculty research grants and contracts.

Specific functions included within this department are:

Assistance to faculty in the preparation of grant and contract proposals; projection and monitoring of grant and contract expenditures and credits; and preparation of fiscal data and reports.

#### m) Purchasing

This office has responsibility, authority and accountability for the supervision and coordination of the purchasing functions of the Center.

Specific functions included within this office are:

Coordinates purchase of equipment, supplies and services with University Purchasing Department;

Verifies and approves payment of invoices for goods and services rendered by vendors;

Secures bids and quotations from vendors for equipment, supplies and services;

Monitors all contracts to insure Center and vender compliance;

Maintains purchase order records;

Processes reimbursement to faculty and staff for authorized out-of-pocket expenditures;

Processes accounts receivable transactions, prepares invoices and maintains records:

Prepares shipping documents and arranges transportation of shipments made by the Center:

Receives, verifies and distributes shipments of equipment and supplies;

Maintains inventory of equipment and arranges for needed repairs; and

Monitors Center telephone system to insure adequacy and arranges for needed repairs.

#### n) Photography

The Photography Department provides photographic services to the scientific and administrative staff.

During 1986, 536 requests for photographic services were received and processed. The types of photographic illustrations provided included black and white photographs and color slides of people, animals, caging, lesions, equipment, experimental procedures, electronic circuitry, buildings, surgery, necropsy, gross tissue specimens, and polaroid I.D. cards.

Other accomplishments included:

Black and white negative processing and darkroom sessions for printing was done in cooperation with investigators;

Slides were made from charts and graphs, radiographs, electron micrographs, book and magazine illustrations, and photographs;

Black and white negatives, prints and duplicate slides were produced for publication from charts and graphs;

Motion picture and slide projectors were operated for meetings and photographs of meeting sessions and speakers were taken;

Prints from file negatives were produced to fill requests from publishers of textbooks and magazines; and

Photographs, letters and certificates were framed for display.

### o) Scanning Electron Microscopy

The scanning electron microscopy/microanalysis facility provides two scanning electron microscopes (an ISI DS130 and an ISI Super III) and two energy dispersive x-ray analyzers (Tracor TN5500 and NS880) for use in training and support of research. The DS130 and TN5500 provide maximum resolution and the facility for element and image analysis. The Super III and NS880 are used for training purposes. Ancillary equipment and facilities for photography, specimen preparation and metal coating are also available. Research areas of the facility include high resolution imaging and development of methods for specimen coating with very thin films, especially chromium.

During 1986, this facility provided support to numerous research projects including: human fallopian tube mucosal attachment; human nasopharyngeal Hemophilus influenzae mucosa attachment; cultured endothelial cells; cultured pigment epithelial cells; damaged human fallopian tubes; sperm storage associated morphological changes; glycolipids on mycobacteria; deorganified bone; liposome morphology; structure of enamel crystals in humans; early myocyte-muscle development; and laser corneal surgery assessment.

#### B. HIGHLIGHTS

#### 1) Research Completed

# a) Recall and Recognition in Aged Rhesus Monkeys

The experimental analysis of memory has, historically, involved linguistically-competent human subjects. Memory processes, including recall and recognition, have therefore been confounded with linguistic ability. Animal subjects, however, permit the study of memory, independent of linguistic ability. Using rhesus monkeys as subjects, the behavioral biology laboratory has developed procedures that correspond in significant detail to those used in human memory research, yet are appropriate for studying memory processes in nonhuman primates.

The methodology developed is based on a touch-sensitive cathode ray tube (CRT) or computer terminal upon which a microcomputer displays visual stimuli that the subject must recall and reproduce correctly after an intervening period of time (delay). Characteristics of the visual stimulus, the size and location of the touch-sensitive area on the CRT, and the complexity of the visual pattern are determined by microcomputer software. With this visual-motor task, high accuracy levels of recall are

characteristic of the rhesus monkey after very short delays, and accuracy decreases as the delay increases. At delays approaching one minute, accuracy approaches chance levels.

Data obtained to date suggests that younger monkeys can maintain higher levels of accuracy on recall after longer delays than can aging monkeys, especially monkeys with ages greater than thirty years, but that differences due to age can be influenced by the amount of training and experience.

The methodology which has been developed provides an animal model for studying the relation between aging and memory in a way that can be useful for characterizing the neuropharmacology of aging and for identifying substances of potential therapeutic efficacy in treating memory deficits associated with aging.

# b) Intravesical Injection of Teflon for Vesicoureteral Reflux

The intravesical/subureteric injection of polytef paste has recently gained widespread acceptance and use in the treatment of vesicoureteral reflux in children (over 400 children have been treated). The limited animal studies which have been done have failed to demonstrate distant migration of the polytef particles from the intravesical/subureteric injection site. However, recent studies in nonrefluxing monkeys at the Yerkes Center have demonstrated both distant migration of polytef particles from the injection site and the presence of a large foreign body granulomatous reaction at the site of injection.

In these studies, 0.4 ml (1/2 of the amount used in humans) of polytef paste was injected transurethrally into the intravesical/subureteric space of eight monkeys. At six months, the injection sites, pelvic and paraaortic nodes, kidneys, liver, lungs and brain of five monkeys were studied by standard and polarized light microscopy. In addition, x-ray microanalysis directed by transmission electron microscopy was performed on tissues from selected sites. Distant migration of polytef particles from the injection site was demonstrated in all animals. A voluminous local granulomatous reaction was also found at all intravesical injection sites. This granulomatous reaction is being followed in the three remaining animals by both CT scanning and magnetic resonance imaging. These granulomas have been clearly imaged and appear to be actively growing.

Based on these observations, it is recommended that polytef paste not be used in children with normal life expectancies, until the long-term effects in humans are known.

### 2) Research in Progress

# a) AIDS Animal Model Development

As reported in our 1985 Annual Progress Report, a T-lymphotropic retrovirus (SIV/SMM) has been isolated from a high percentage of sooty mangabeys in the Yerkes mangabey breeding colony. Although

this virus appears to be, for the most part, nonpathogenic in the mangabey, inoculation of rhesus and pig-tailed macaques results in persistent infection with the development of a clinical AIDS-like disease in many of the infected animals. In initial experimental infection studies, 11 of 12 macaques became virus positive and seroconverted within 3 to 6 weeks of inoculation. Infected animals have shown variable degrees of peripheral lymphadenopathy, splenomegaly, diarrhea, weight loss and hematologic abnormalities, including lymphopenia, neutropenia and thrombocytopenia. Three of eight animals (37%) infected for 14 months or longer have died as the result of an AIDS-like disease. Two of the three animals which died showed generalized lymphoid depletion with prominent infiltrates of multinucleated syncytial giant cells throughout most tissues and organs. One of these animals had intestinal cryptosporidiosis and brain lesions that were comparable to AIDS encephalopathy of humans.

Blood transfusions from one of these cases, a pig-tailed macaque, to three other pig-tailed macaques resulted in acute clinical disease in all three recipients. Two of these died at 7 and 9 days post-transfusion and the third died at 10 weeks post-transfusion. All animals which died had generalized lymphadenopathy, splenomegaly and hyperplasia, hemorrhage and necrosis of lymphoid tissues of the intestine. Histologically, lymphoid tissues were reactive and contained foci of necrosis and multinucleated giant cells. Retrovirus, isolated from the acute fatal cases, resulted in acute clinical disease and death within 7 to 8 days of inoculation in three additional pig-tailed macaques. Lesions in all three animals were comparable to those seen in the transfusion recipients. Retrovirus was isolated from blood and multiple tissues of all acute deaths.

The susceptibility of rhesus and pig-tailed macaques to infection with this HIV-like virus and the subsequent development of clinical and fatal disease provides a model for studying the acquired immunodeficiency syndrome and for use in the evaluation of newly developed antiretroviral drugs or vaccines. Access to an animal model which develops acute, rapidly fatal disease following infection with an HIV-like retrovirus will provide a model system for the rapid assessment of the efficacy of antiretroviral drugs and vaccines.

# b) Establishment of a Chimpanzee Breeding and Research Program

A dedicated chimpanzee breeding colony has been established to insure the continued availability and productivity of this unique and valuable research animal. This colony is expected to produce 8 to 12 healthy and behaviorally normal offspring per year. These offspring will be used to establish a stable, self-sustaining breeding population of chimpanzees that will help guarantee the future availability of these animals for biomedical and behavioral research. The breeding program has been established with an existing, stable social group of chimpanzees, pair matings using known breeders, and artificial insemination. Infants will be managed in such a way as to maximize social experience, including extensive mother-rearing where possible,

peer group-rearing when nursery care is required, and fostering of nursery-reared infants onto competent mothers.

Research will also be conducted in areas that will promote improved reproductive success and efficiency and improved behavioral development. This will include investigations into the early detection of labor using telemetry to allow early and effective assistance when required to improve neonatal survival; investigation of hormonal manipulation to shorten interbirth intervals without separating infants from their mothers; methods of gamete preservation to improve artificial breeding techniques; and investigation of early rearing techniques in order to develop techniques that are conducive to subsequent successful reproduction and to identify behaviors that are predictive of future reproductive performance.

This program, as part of the national chimpanzee breeding plan, is expected to make significant contributions toward the maintenance and expansion of the nation's chimpanzee population. This will help insure the continued availability of this unique research subject that is critically needed for the study of important human disease problems.

# C. INSTITUTIONAL REVIEW COMMITTEES AND ALLOCATION OF RESOURCES

### 1) Executive Committee

The Yerkes Executive Committee is charged with the overall and general responsibilities in the areas of policy and program planning for the Center. This committee consists of the Center Director (Chair), Associate Director for Scientific Programs, Associate Director for Administration, Division Chiefs, and coordinators for the Field Station and Language Research Center. This committee meets monthly. Composition of the committee is as follows:

#### Executive Committee

Name	Degree	Academic Titles	Department or Division	Institution
F. King (Chair)	Ph.D.	Center Director	Administration	Yerkes
		Professor	Anatomy and Cell Biology	Emory Univ.
		Professor	Psychology	Emory Univ.
		Associate Dean	School of Medicine	Emory Univ
J. Magnotta	B • A •	Associate Director for Administration	Administration	Yerkes
H. McClure	D.V.M.	Associate Director for Scientific Programs, Research Professor and Chief, Division of Patho- biology and Immuno- biology	Pathobiology and Immunobiology	Yerkes
		Assistant Professor	Pathology	Emory Univ.
L. Byrd	Ph.D.	Research Professor and Chief, Division of Behavioral Biology	Behavioral Biology	Yerkes
		Associate Professor	Pharmacology	Emory Univ.
		Adjunct Professor	Psychology	Emory Univ.
		Adjunct Professor	Psychology	Ga. Tech.

### Executive Committee (Cont'd)

Name K. Gould	Degree D.V.M. Ph.D.	Academic Titles  Research Professor and Chief, Division of Reproductive Biology	Department or Division Reproductive Biology	Institution Yerkes
_		Adjunct Professor	Biology	Emory Univ.
B. Swenson	D.V.M.	Associate Research Professor and Chief, Division of Veterinary Medicine	Veterinary Medicine	Yerkes
J. Tigges	Ph.D.	Research Professor and Chief, Division of Neurobiology	Neurobiology	Yerkes
		Professor	Anatomy and Cell Biology	Emory Univ.
		Professor	Ophthalmology	Emory Univ.
T. Gordon	M.S.	Assistant Research Professor and Field Station Coordinator	Behavioral Biology	Yerkes
D. Rumbaugh	Ph.D.	Affiliate Scientist and Language Research Center Coordinator	Behavioral Biology	Yerkes
		Professor and Chairman	Psychology	Georgia State Univ.

# 2) Yerkes Animal Resources Committee

The Yerkes Animal Resources Committee (YARC) represents a combining of the previous Main Station Animal Resources Committee and the Field Station Animal Resources Committee in an effort to increase efficiency of operations. All members of both smaller committees continue to be members of the Yerkes Animal Resources Committee, with the exception of Dr. Kim Wallen, who is out of the country on leave of absense and has requested to be relieved of his duties on this committee, and Dr. Terry Maple who, as the Director of Zoo Atlanta, does not have the time available to serve on this committee.

The Yerkes Animal Resources Committee is responsible for the review,

evaluation and monitoring of research projects proposed to be conducted at all three Yerkes research sites: the Main Station, the Field Station and the Language Research Center. In addition, the committee is responsible for the review, evaluation and monitoring of research proposals involving Yerkes animals on loan to other institutions. The committee is specifically charged with the following responsibilities: a) evaluate and make recommendations to the Center Director regarding all proposed Center research projects; review of proposals taking into consideration scientific merit, relationship to the Center's mission, funding status, appropriateness of the primate species selected, and the provision of humane treatment to the experimental animals; b) make recommendations regarding the assignment of primates and housing space for research projects; c) make recommendations regarding the breeding of primates at the Center; and d) evaluate and make recommendations on any problems or conflicts that may arise in the area of animal care, housing, support services or research protocols. This committee serves as the primate subcommmittee for the Institutional Animal Care and Use Committee (IACUC). In this capacity, the Yerkes Animal Resources Committee has the responsibility for review of all Emory University proposals which involve the use of nonhuman primates. The composition of this committee is as follows:

### Yerkes Animal Resources Committee

Name	Degree	Academic Titles	Department or Division	Institution
H. McClure (Chair)	D.V.M.	Associate Director for Scientific Programs, Research Professor, and Chief Division of Pathobiology and Immunobiology	Pathobiology and Immunobiology	Yerkes
m		Assistant Professor	Pathology	Emory Univ.
T. Gordon (Co-Chair)	M.S.	Assistant Research Professor and Field Station Coordinator	Behavioral Biology	Yerkes
		Adjunct Asst. Professor	Psychology	Emory Univ.
L. Byrd	Ph.D.	Research Professor and Chief, Division of Behavioral Biology	Behavioral Biology	Yerkes
		Associate Professor	Pharmacology	Emory Univ.
		Adjunct Professor	Psychology	Emory Univ.
		Adjunct Professor - 34 -	Psychology	Ga. Tech.

# Yerkes Animal Resources Committee (Cont'd)

Name	Degree	Academic Titles	Department or Division	Institution
K. Gould	D.V.M. Ph.D.	Research Professor and Chief, Division of Reproductive Biology	Reproductive Biology	Yerkes
		Adjunct Professor	Biology	Emory Univ.
J. Herndon	Ph.D.	Associate Research Professor	Neurobiology	Yerkes
		Adjunct Assistant Professor	Biology	Emory Univ.
		Adjunct Assistant Professor	Psychology	Emory Univ.
J. Magnotta (ex officio		Associate Director for Administration	Administration	ı Yerkes
R. Nadler	Ph.D.	Research Professor	Reproductive Biology	Yerkes
		Adjunct Associate Professor	Psychology	Emory Univ.
J. Roberts (ex officio)	_ <del></del> )	Superintendent	Main Station Animal Care Unit	Yerkes
D. Rumbaugh	Ph.D.	Affiliate Scientist and Language Research Center Coordinator	Behavioral Biology	Yerkes
		Professor and Chairman	Psychology	Georgia State
S. Smith (ex officio)		Superintendent	Field Station Animal Care Unit	Yerkes
B. Swenson	D.V.M.	Associate Research Professor and Chief, Division of Veterinary Medicine	Veterinary Medicine	Yerkes

# Yerkes Animal Resources Committee (Cont'd)

Name	Degree	Academic Titles	Department or Division	Institution
J. Tigges	Ph.D.	Research Professor and Chief, Division of Neurobiology	Neurobiology	Yerkes
		Professor	Anatomy and Cell Biology	Emory Univ.
		Professor	Ophthalmology	Emory Univ.

# 3) Yerkes AAALAC Accreditation Committee

This committee was formally established to analyze the deficiencies and needs of the Center in order to obtain AAALAC accreditation, and to set a timetable and plan for the achievement of the required improvements. Although full AAALAC accreditation has been received, this committee will remain active. The committee will meet at least two times per year to review animal housing facilities and animal use to assure that full AAALAC accreditation is maintained. The composition of this committee is as follows:

### Yerkes AAALAC Accreditation Committee

Name  H. McClure (Chair)	Degree D.V.M.	Academic Titles  Associate Director for Scientific Programs; Research Professor and Chief, Division of Pathobiology and Immunobiology	Department or Division  Pathobiology and Immunobiology	Institution Yerkes
B. Swenson	n	Assistant Professor	Pathology	Emory Univ.
5. Swenson	D.V.M.	Associate Research Professor and Chief, Division of Veterinary Medicine	Veterinary Medicine	Yerkes
J. Roberts		Superintendent	Main Station Animal Care Unit	Yerkes

# Yerkes AAALAC Accreditation Committee (Cont'd)

<u>Name</u>	Degree	Academic Titles	Department or Division	Institution
S. Smith		Superintendent	Field Station Animal Care Unit	Yerkes
J. Magnotta	B.A.	Associate Director for Administration	Administration	Yerkes
T. Gordon	M.S.	Assistant Research Professor and Field Station Coordinator	Behavioral Biology	Yerkes

### 4) Committee on Aging Primates

This committee was established to insure the coordination of projects desiring to use aging nonhuman primates at Yerkes, and to develop a plan to derive the maximum scientific benefit from these valuable animals. All prospective studies on primate aging are reviewed by this committee. This committee works in close coordination with the Yerkes Animal Resources Committee. The composition of this committee is as follows:

### Committee on Aging Primates

Name	Degree	Academic Titles	Department or Division	Institution
J. Tigges (Chair)	Ph.D.	Research Professor and Chief, Division of Neurobiology	Neurobiology	Yerkes
		Professor	Anatomy and Cell Biology	Emory Univ.
		Professor	Ophthalmology	Emory Univ.
T. Gordon	M.S.	Assistant Research Professor and Field Station Coordinator	Behavioral Biology	Yerkes
H. McClure	D.V.M.	Associate Director for Scientific Programs; Research Professor and Chief, Division of Patho- biology and Immuno- biology	Pathobiology and Immunobiology	Yerkes
		Assistant Professor	Pathology	Emory Univ.

### Committee on Aging Primates (Cont'd)

Name	Degree	Academic Titles	Department or Division	Institution
L. Byrd	Ph.D.	Research Professor and Chief, Division of Behavioral Biology	Behavioral Biology	Yerkes
		Associate Professor	Pharmacology	Emory Univ.
		Adjunct Professor	Psychology	Emory Univ.
		Adjunct Professor	Psychology	Ga. Tech.
K. Gould	D.V.M. Ph.D.	Research Professor and Chief, Division of Reproductive Biology	Reproductive Biology	Yerkes
		Adjunct Professor	Biology	Emory Univ.

### 5) Computer Committee

This committee reviews all base grant computer purchases and coordinates computer use at the Yerkes Main Station and Field Station. The committee is also available as a resource to any investigator who needs information about computers. The composition of this committee is as follows:

#### Computer Committee

Name	Degree	Academic Titles	Department or Division	Institution
R. Boothe (Chair)	Ph.D.	Associate Research Professor	Neurobiology	Yerkes
		Associate Professor	Psychology	Emory Univ.
		Assistant Professor	Ophthalmology	Emory Univ.
J. Herndon	Ph.D.	Associate Research Professor	Neurobiology	Yerkes
		Adjunct Assistant Professor	Biology	Emory Univ.
		Adjunct Assistant Professor	Psychology	Emory Univ.

### Computer Committee (Cont'd)

Name	Degree	Academic Titles	Department or Division	Institution
V. Speck	B.A.	Electronics Shop Technician	Biomedical Engineering	Yerkes
E. Smith	Ph.D.	Associate Research Professor	Behavioral Biology	Yerkes
		Associate Professor	Anthropology	Emory Univ.
		Adjunct Associate Professor	Biology	Emory Univ.
J. Magnotta	B • A •	Associate Director for Administration	Administration	Yerkes

# 6) Library Committee

This committee provides guidance with regard to the library needs of the scientific and veterinary staff, and makes recommendations on journal and volume purchases, and library policies and procedures. The composition of this committee is as follows:

### Library Committee

Name E. Smith (Chair)	Degree Ph.D.	Academic Titles  Associate Research  Professor	Department or Division Behavioral Biology	Institution Yerkes
		Associate Professor	Anthropology	Emory Univ.
		Adjunct Associate Professor	Biology	Emory Univ.
B. Swenson	D.V.M.	Associate Research Professor and Chief, Division of Veterinary Medicine	Veterinary Medicine	Yerkes
J. Herndon	Ph.D.	Associate Research Professor	Neurobiology	Yerkes
		Adjunct Assistant Professor	Biology	Emory Univ.
		Adjunct Assistant Professor	Psychology	Emory Univ.
J. Magnotta	B.A.	Associate Director for Administration	Administration	Yerkes

### Library Committee (Cont'd)

N. Johns M. Wilson	Degree Ph.D.	Academic Tit Librarian Assistant Res Professor	Administration	Institution Yerkes Yerkes
		Associate in Medicine	Endocrinology	Emory Univ.

# 7) Affirmative Action Committee

The three main areas of responsibility of this committee include: (1) to serve as a vehicle for the proper disposition of complaints of grievances by employees concerning discrimination on the basis of race or sex; (2) to monitor the Center's implementation of Policies for Faculty Appointments and Promotions as approved by the Office of Equal Opportunity Programs; and (3) to provide for communication between the administration of the Center and the Office of Equal Opportunity Programs with regard to University policies on hiring, promotion and personnel matters. The composition of this committee is as follows:

# Affirmative Action Committee

Name J. Herndon (Chair)	Degree Ph.D.	Academic Titles  Associate Research Professor	Department or Division Neurobiology	Institution Yerkes
		Adjunct Assistant Professor	Biology	Emory Univ.
		Adjunct Assistant Professor	Psychology	Emory Univ.
K.Pralinsky	B.A.	Assistant Super- intendent, Main Station	Animal Care	Yerkes
F. Jewell		Receptionist	Administration	Yerkes
J. Magnotta (ex officio)	В.А.	Associate Director for Administration	Administration	

### 8) Primate Habitat Committee

This committee has the responsibility of making recommendations to the Yerkes Center and Zoo Atlanta on the following issues and related matters:

- a) Nature and duration of Yerkes primate loans to Zoo Atlanta.
- b) Assignment of Zoo and/or Yerkes responsibilities for primate husbandry, care, veterinary services and breeding of Yerkes primates assigned to the Zoo.
- c) Ownership and disposition of resulting offspring.
- d) Research policies and accessibility of Yerkes primates at the Zoo to scientists on the staff of Yerkes, the Zoo, or other institutions.
- e) Facility design with regard to habitat type, breeding, research and display.
- f) Routine facilities operation responsibilities.
- g) Assignment of specific species and individual animals from the Yerkes Center.
- h) Financial arrangements between Yerkes and the Zoo.
- i) Coordination of public relations activities and announcements.
- j) Other matters that the Committee considers relevant.

The composition of this committee is as follows:

### Primate Habitat Committee

Name  K. Gould (Chair)	Degree D.V.M. Ph.D.	Academic Titles  Research Professor and Chief, Division of Reproductive Biology	Department or Division Reproductive Biology	Institution Yerkes
		Adjunct Professor	Biology	Emory Univ.
B. Swenson	D.V.M.	Associate Research Professor and Chief, Division of Veterinary Medicine	Veterinary Medicine	Yerkes
H. McClure	D.V.M.	Associate Director for Scientific Programs; Research Professor and Chief, Division of Patho- biology and Immuno- biology	Pathobiology and Immunobiology	Yerkes
		Assistant Professor	Pathology	Emory Univ.

#### Primate Habitat Committee (Cont'd)

Name	Degree	Academic Titles	Department or Division	Institution
T. Gordon	M.S.	Assistant Research Professor and Field Station Coordinator	Behavioral Biology	Yerkes
J. Magnotta	B.A.	Associate Director for Administration	Administration	Yerkes
T. Maple (Co-Chair)	Ph.D.	Affiliate Scientist	Behavioral Biology	Yerkes
		Professor	Psychology	Ga. Tech.
·		Director	Zoo Atlanta	City of Atlanta
R.McManamon	D.V.M.	Veterinarian	Zoo Atlanta	City of Atlanta
S. Hood	M.A.	Assistant Director of Operations	Zoo Atlanta	City of Atlanta

### 9) Main Station Space Utilization Task Force

This task force was established to survey, evaluate and make recommendations to the Director's office regarding space utilization at the Yerkes Main Station. The need for such a committee was necessitated by a substantial increase in animal housing space and number of research projects during the past few years, with no increase in laboratory, office and support services space. The task force was charged with the responsibility of assessing the utilization of all areas of the Main Station and formulation of recommendations regarding any changes needed to maximize and more efficiently use the presently available space. The composition of this task force is as follows:

#### Main Station Space Utilization Task Force

Name	Degree	Academic Titles	Department or Division	Institution
J. Tigges (Chair)	Ph.D.	Research Professor and Chief, Division of Neurobiology	Neurobiology	Yerkes
		Professor	Anatomy and Cell Biology	Emory Univ.
		Professor	Ophthalmology	Emory Univ.

# Main Station Space Utilization Task Force (Cont'd)

Name L. Byrd (Co-Chair)	Degree Ph.D.	Academic Titles  Research Professor and Chief, Division of Behavioral	Department or Division Behavioral Biology	Institution Yerkes
		Biology  Associate Professor  Adjunct Professor	Pharmacology	Emory Univ.
		Adjunct Professor	Psychology Psychology	Emory Univ Ga. Tech.
K. Gould	D.V.M. Ph.D.	Research Professor and Chief, Division of Reproductive Biology	Reproductive Biology	Yerkes
		Adjunct Professor	Biology	Emory Univ.
J. Magnotta	B.A.	Associate Director for Administration	Administration	Yerkes
H. McClure	D.V.M.	Associate Director for Scientific Programs; Research Professor and Chief, Division of Patho- biology and Immuno- biology	Pathobiology and Immunobiology	Yerkes
		Assistant Professor	Pathology	Emory Univ.
B. Swenson		Associate Research Professor and Chief, Division of Veterinary Medicine	Veterinary Medicine	Yerkes

# 10) Task Force on 1986 Budget

Due to projected changes for FY 1986-87 in the Center's Base Grant budget, this task force was charged with the responsibility of critically and thoroughly evaluating all aspects of the Center's operating costs. Following this evaluation, recommendations were made to the Director concerning the allocation of funds in the most efficient manner. The composition of this task force is as follows:

### 1986 Budget Task Force

Name	Degree	Academic Titles	Department or Division	Institution
J. Magnotta (Chair)	B.A.	Associate Director for Administration	Administration	Yerkes
T. Gordon	M.S.	Assistant Research Professor and Field Station Coordinator	Behavioral Biology	Yerkes
H. McClure	D.V.M.	Associate Director for Scientific Programs; Research Professor and Chief, Division of Patho- biology and Immuno- biology	Pathobiology and Immunobiology	Yerkes
B. Swenson	D.V.M.	Assistant Professor  Associate Research Professor and Chief, Division of Veterinary Medicine	Pathology Veterinary Medicine	Emory Univ. Yerkes

### 11) Animal Records Committee

The committee's charge is to develop an animal records system that can be adapted for computer use to facilitate storage, retrieval and processing of animal records relating to husbandry and management, medical history and research utilization. The composition of this committee is as follows:

### Animal Records Committee

Name	Degree	Academic Titles	Department or Division	Institution
B. Swenson (Chair)	D.V.M.	Associate Research Professor and Chief, Division of Veterinary Medicine	Veterinary Medicine	Yerkes
T. Gordon	M.S.	Assistant Research Professor and Field Station Coordinator	Behavioral Biology	Yerkes

# Animal Records Committee (Cont'd)

Name R. Boothe	Degree Ph.D.	Academic Titles  Associate Research	Department or Division Neurobiology	Institution Yerkes
		Associate Professor	Psychology	Emory Univ.
H MaCl	77. **	Assistant Professor	Ophthalmology	Emory Univ.
H. McClure	D.V.M.	Associate Director for Scientific Programs, Research Professor and Chief, Division of Patho- biology and Immuno- biology	Pathobiology and Immunobiology	Yerkes
0 0		Assistant Professor	Pathology	Emory Univ.
G. Cannon	B.S.	Animal Records Registrar	Veterinary Medicine	Yerkes
Biohazard Ca	Easter O.	•		

# 12) Biohazard Safety Committee

The Biohazard Safety Committee was formed in 1986 to monitor the use, storage and disposal of hazardous materials at the Primate Center to insure that all Yerkes laboratories are in full compliance with OSHA and EPA regulations governing safety in the laboratory. The composition of this committee is as follows:

## Biohazard Safety Committee

Name M. Wilson (Chair)	Degree Ph.D.	Academic Titles Assistant Research Professor	Department or Division  Behavioral Biology and Reproductive Biology	Institution Yerkes
		Associate in Medicine	Endocrinology	Emory Univ.
D. Anderson	D.V.M.	Assistant Research Professor	Pathobiology and Immuno- biology	Yerkes

## Biohazard Safety Committee (Cont'd)

<u>Name</u>	Degree	Academic Titles	Department or Division	Institution
K.Pralinsky	B.A.	Assistant Super- intendent, Main Station	Animal Care	Yerkes
J. Magnotta	B.A.	Associate Director for Administration	Administration	Yerkes

# 13) Ophthalmology Research Laboratory Building Use Committee

The responsibility of this committee is to consider and make assignments of space in the Ophthalmology Research Laboratory Building on the Yerkes premises to assure cooperation and smooth coordination of scientific projects conducted by Yerkes core faculty and members of the Emory University Department of Ophthalmology. In matters in which the committee cannot reach agreements among the members, these are taken to the Director of the Yerkes Center and the Chairman of the Department of Ophthalmology for adjudication. The composition of this committee is as follows:

# Ophthalmology Building Use Committee

Name H. McClure	Degree D.V.M.	Academic Titles  Associate Director for Scientific Programs, Research Professor and Chief, Division of Pathobiology and Immunobiology	Department or Division  Pathobiology and Immunobiology	Institution Yerkes
		Assistant Professor	Pathology	Emory Univ.
J. Magnotta	B.A.	Associate Director for Administration	Administration	Yerkes
B. McCarey	Ph.D.	Affiliate Scientist	Pathobiology and Immunobiology	Yerkes
		Associate Professor	Ophthalmology	Emory Univ.
D.Broussard	·	Department Administrator	Ophthalmology	Emory Univ.

## 14) Summer Internship Committee

This committee is charged with the responsibility of evaluating applicants for the Yerkes summer internship program; selection of the most outstanding applicants for which positions are available and making recommendations to the Director concerning the selected applicants and the Yerkes Division or investigator to whom the applicants could most apporpriately be assigned. The composition of this committee is as follows:

### Summer Internship Committee

Name L. Byrd (Chair)	Degree Ph.D.	Academic Titles  Research Professor and Chief, Division of Behavioral Biolog	Department or Division  Behavioral Biology	Institution Yerkes
		Associate Professor	Pharmacology	Emory Univ.
		Adjunct Professor	Psychology	Emory Univ.
		Adjunct Professor	Psychology	Ga. Tech.
D. Anderson	D.V.M.	Assistant Research Professor	Pathobiology and Immuno- biology	Yerkes
M. Tigges	Ph.D.	Associate Research Professor	Neurobiology	Yerkes
		Associate Professor	Anatomy and Cell Biology	Emory Univ.

## D. DISSEMINATION OF INFORMATION

As in past years, the Center has continued to use the following mechanisms for the dissemination of information:

- 1) Brochures and literature are distributed to Yerkes staff, all officers and departments of Emory University, other universities, institutions, public mailing list, legislators, professional societes and associates.
- 2) Articles are published in NIH and Emory University publications and in newspapers and magazines.
- 3) Lectures and videotape and slide presentations are given at other institutions and to the public, as well as at scientific and professional meetings.

4) Seminar programs on behavioral biology of primates and the Yerkes visiting speaker series are scheduled throughout the year.

Additional documents on Center research programs, the conduct of research and animal care at the Center, the importance and benefits of animals to human health, and primate contributions to human health have been developed for distribution to faculty and staff, the news media and the general public, as needed.

A detailed "Application to Conduct Research at the Yerkes Center" has been developed and distributed to all Center faculty; this document is also distributed to departmental chairmen at Emory and other regional universitites, and is provided to all investigators interested in initiating research projects at the Center. This application includes information on research opportunities at the Center, criteria for the use of primates in research, Center access policy, standards and procedures for working with nonhuman primates, guidelines for experimental surgery and procedures and guidelines for the preparation and submission of research proposals.

# APPENDIX TO INSTRUCTIONS DRR SCIENTIFIC CLASSIFICATION

OPPE:DRR 06/01/85

<del></del>	AXIS I		AXIS II
Code	RESOURCE MATERIAL/RESEARCH AREA	Cod	ie RESEARCH AREAS
Nos.	(Maximum 6 Codes)	Nos	(Maximum 6 Codes)
1 .	Animals		Aging
	a. Vertebrates, Mammal	32	Anesthesiology
	b. Vertebrates, Non-Mammal	34	
	c. Invertebrates	36	Behavioral Sci/Psychology/Social Sci
2	Biological/Chemical Compounds	38	Bioethics
	Biomaterials	39	Biotechnology (rDNA, CDNA, hybridoma)
	Cells & Subcellular Material	40	Communication Science
	Human Subjects	42	Computer Science
	Membrane/Tissue/Isolated Organ	44	Congenital Defects or Malformations
7 1	Microorganisms	46	Degenerative Disorders
	a. Bacteria	48	Device, Protheses, Intra/Extracorporeal
•	<pre>b. Viruses</pre>	50	Drug Studies
	c. Parasites		a. Toxic b. Other c. Orphan Drugs
	d. Other	52	Engineering/Bioengineering
8 1	Plants/Fungi	54	Environmental Sciences
9 7	rechnology/Technique Development		a. Toxic b. Other
10 (	Other (SPECIFY)	56	Epidemiology
	Clinical Trials		Genetics, Including Metabolic Errors
	a. Multicenter b. Single Center	60	Growth and Development
		62	Health Care Applications
	NATOMICAL SYSTEM/RESEARCH AREAS	64	Immunology and Allergy
	ده الله الله الله الله الله الله الله ال	66	Infectious Diseases
13 (	Cardiovascular System	68	Information Science
	Connective Tissue	70	
	Endocrine System	-	Mental Disorders/Psychiatry
	Gastrointestinal System		Metabolism and Transport
	a. Esophagus		a. Carbohydrate
	b. Gallbladder		b. Electrolyte, Mineral, Water Balance
	c. Intestine		c. Enzymes
	d. Liver		d. Gases
	e. Pancreas		e. Hormone
	f. Stomach		f. Lipid
.7 H	dematologic System		g. Nucleic Acid
_	Integumentary System		-
	Lymphatic and Recticulo-	76	h. Protein and Amino Acid
	Endothelial System	76	Neoplasms/Oncology
0 M	Suscular System	70	a. Benign b. Malignant
	Rervous System	78	Nutrition
	ral/Dental	80	Radiology/Radiation Nuclear Medicine
	· ·		a. Ionizing (Xray, Nuclear Reactor)
	Reproductive System		b. Non-ionizing (Microwave, Radar)
	Respiratory System	82	Rehabilitation
.5 S	Sensory System	84	Statistics/Mathematics
	a. Ear	86	Surgery
	b. Eye	88	Transplantation
	c. Taste/Smell/Touch	90	Trauma/Burns
	keletal System	92	Other (SPECIFY)
7 U	rinary System		·
	ther (SPECIFY)		

# DIVISION OF BEHAVIORAL BIOLOGY

Larry D. Byrd, Ph.D., Chief

Core Faculty: L. Byrd I. Bernstein

T. Gordon

E. Savage-Rumbaugh
E. Smith
K. Wallen

M. Wilson

# Associate, Affiliate and Collaborative Faculty:

Affiliate and Co	ollaborative Faculty:
R. Barr	
G. Berntson	Department of Pediatrics, McGill University Departments of Psychology and Pediatrics, Ohio State University
B. Blount	Department of Anthropology, University of Georgia
S. Boysen	
J. Branch	
K. Bruce	Wilmington Wilmington
C. Busse	NCR Corporation of San Juan Buonto Bio
J. Dahl	Terkes Regional Primate Secessor Contain the
F. de Waal	Wisconsin Wisconsin
C. Ehardt	Department of Anthropology and Linguistics, University of Georgia
D. Estep	Department of Psychology, University of Georgia
H. Gouzoules	TOPAL SINCIPLO OF ENVIRONMENT EMANOR PROFILE :
S. Gouzoules	191893 NEUTUNGI PRIMATA PARANAN CALL
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· · · · · · · · · · · · · · · · · · ·	School of Psychology, Georgia Institute of Technology, and Zoo Atlanta
M. Marr	
<pre>E. Menzel</pre>	School of Psychology, Georgia Institute of Technology
	Stony Brook State University of New York at
H. Miles	Department of Anthropology, University of Tennessee at
N. Pope	Yerkes Regional Primate Possanch Contact
M. Romski	Department of Psychology, Georgia State University Department of Psychology Georgia State University
D. Rumbaugh	
S. Schwartz	TEN TO THE SECRET CHILDREN HAT CONSIDER AS A CONSTRUCTION OF THE SECRET SECRETARY OF THE SE
A. Smith	
S. Smith	School of Psychology, Georgia Institute of Technology
H. Terrace	
W. Tomasello	POPUL GREETE THE POVERNIARY CATUMET IN TO THE
R. Tuttle	A SERI CHICKLY OF EVACIOUS ONLY FROM MINERAL ST
	College. University of Chicago
M. Walker	Maryland School of Medicine
P. Whitten	School of Medicine School of Medicine
I. Wundram	Department of Anthropology, Oxford College of Emory University
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1a 16c	36 60 74a 78	<ul> <li>(a) Barr, Ronald G. Smith, Euclid O. Konner, Melvin J.</li> <li>(b) MDCM, FRCP(C) (RGB); Ph.D. (EOS); M.D., Ph.D. (MJK)</li> <li>(c) Division of Behavioral Biology</li> <li>(d) McGill University (RGB)</li> </ul>	X	X	4	Pan troglodytes	

Lactose Absorption and Behavior in Infant Chimpanzees (Pan troglodytes)

Abstract:

This project is designed to test the hypothesis that incomplete lactose absorption can cause distress behavior in infant chimpanzees (Pan troglodytes). The hypothesis is being tested by means of controlled feeding trials in which either the quantity of lactose or the feeding pattern has been changed. In addition, measures of hydrogen excretion taken during control periods will be used to provide new data on whether and for how long incomplete lactose absorption occurs under standard, nursery feeding conditions. Each subject is tested at 2, 4, 6 and 8 weeks of age under three feeding conditions: control; added lactose; and frequent feeding. Outcome measures include behavioral events and states and incomplete lactose absorption as determined by breath-hydrogen analysis. the past year, research assistants were trained in the observational techniques to be used and in the collection of breath-hydrogen samples. Initially, pilot tests were conducted in one infant chimpanzee to assure feasibility of the methodology. Based on results of these tests, minor modifications were made to the protocol. Subsequently, three additional infant chimpanzees served as subjects for the collection of behavioral data and breath-hydrogen samples. Only the breath-hydrogen measures have been systematically examined. Although there are insufficient data for statistical analysis, the individual response profiles indicate that (1) incomplete lactose absorption does occur under standard nursery feeding conditions, (2) there is a diurnal rhythm of incomplete lactose absorption with more incomplete absorption in the afternoon than in the morning, and (3) there is an age-related tendency toward less incomplete absorption with increasing age. These findings are similar to previous reports for normal human infants under similar feeding conditions, and are consistent with the expectation that infant chimpanzees may be an appropriate model for studying the relationship between incomplete carbohydrate absorption and distress behavior. on this project will continue until ten infant chimpanzees have been tested. If the results are positive and encouraging, additional funding will be requested.

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		(c) Division of Behavioral Biology				<u>mulatta</u>			
		(d) University of Georgia							
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. Modification of Aggression in Adolescent Males

#### Abstract:

Focal and instantaneous scan-sampling data, as well as male testosterone measures, have been collected on male rhesus monkeys (Macaca mulatta) ranging in age from two to four years and on females ranging in age from three to four years. All subjects have been maintained in two normally-constituted groups from which all older males have been absent since August of 1985 (Group 1) and August of 1986 (Group 2). Significant kinship, age, sex, group and seasonal differences have been found. In addition, a strong interaction among age, sex whether these experimental subjects are developing agonistic or other social matured in the presence of adult males.

The agonistic patterns of the male and female subjects developed similarly until puberty. Following puberty, however, the male subjects exhibited significantly less aggressive behavior toward females and immmatures as compared to age-matched female controls. In addition, male subjects began to show dissociation from their matrilines and to exhibit a strong preference for the company of similarly-aged males, a pattern which emphasizes the preference for male play partners observed in juvenile males. In addition, postpubertal natal males exhibited significantly less sexual behavior than younger natal males or adult neonatal males, but they could and did impregnate most of the available females in the absence of adult natal males. A serendipitous finding was the development of sharp seasonal weight gain and loss patterns as males matured; females (that did not become pregnant) did not exhibit a similar pattern.

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		(c) Division of Behavioral Biology			90					
	4	(d) Ohio State University (GGB, STB)								
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Descriptive Title (80 characters):
 Psychophysiological and Electrophysiological Indices of Cognitive Processes in Great Apes

#### Abstract:

DADT II

During 1986, the Primate Cognition Project incorporated heart-rate response measures in the quantitative evaluation of information processing in the chimpanzee. Heart rate (HR) was recorded noninvasively and without restraint in a chimpanzee in response to photographs of three categories of humans (caregivers, familiar individuals and strangers). The results showed differentiation of cardiac patterns based on the social relationship of the particular humans and the The paradigm was extended to include photographs of chimpanzees with which the subject, a 4-1/2 year-old female chimpanzee, shared different social interactions (aggressive, friendly, and stranger). Again, cardiac reactivity patterns reflected the different psychosocial relationships between the subject and the specific animals depicted in the photographs. These objective indices support the hypothesis that the chimpanzee can recognize individual animals from photographs and that HR measures can serve as a quantitative correlate of such recognition. Psychophysiological measures (HR) designed to evaluate the functional basis of attention in the chimpanzee were also incorporated into a vigilance task with the same animal. These data are being compared to similar data from children with congenital heart defects who have undergone open-heart surgery (and who may later suffer Attention Deficit Disorder [ADD]), a group of learning-disabled ADD children and a normal group. The studies of attention and information-processing in the chimpanzee will provide an important comparative perspective for understanding the complexities of attentional processes in normal and compromised children. In collaboration with the Columbus Zoological Gardens and Ohio State University, plans are underway for a \$1.2 million research and outdoor-display facility to move beyond the interactive research setting and provide for natural chimpanzee behaviors, to establish a social group that will accommodate older animals as they mature, to provide the opportunity to extend the chimpanzee-cognition study, and to provide for direct public access to ongoing primate studies which enhance our understanding of chimpanzee and human information processing.

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#### Abstract:

This study was designed to investigate the social interactions which are typically described as competition and cooperation. The first objective was to develop and test a procedure for studying competition and cooperation in rhesus monkeys (Macaca mulatta). The second objective was to conduct a finer analysis of the effects of three elements of reinforcement on the choice of whether to compete or to cooperate: (1) magnitude of reinforcement; (2) probability of reinforcement; and (3) immediacy of reinforcement. It was hypothesized that, with respect to each independent variable, the subject should choose the alternative (individual vs. competitive task or individual vs. cooperative task) with the highest probability or amount of reinforcement. The computer system and apparatus being used in this study consist of a Southwest Tech microcomputer, two touch-information display (TID) units, various computer-controlled auxilliary devices, and a two-compartment test apparatus with ample room for testing two monkeys simultaneously. Four female rhesus monkeys, each approximately ten years of age, are currently being studied on the choice between competitive and individual task completion. Following completion of this phase of the study, the animals will be trained to make a choice between cooperative and individual task completion. If successful, this experimental analysis of social behavior will provide a novel procedure for studying other types of social behavior. Furthermore, the results of this study can be compared with results obtained from other species, including humans, using similar tasks and, perhaps, distinct characteristics of human social behavior and/or general social behavioral principles common to a larger number of species will begin to

Choice among Competitive, Cooperative and Individual Task Completion

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Spatial Localization by Chimpanzees after Changes in Position

#### Abstract:

The objective of this study was to examine the ability of chimpanzees (Pan troglodytes), ranging in age from 6 to 55 years, to retrieve a food item hidden in a covered food cup following a change in its location via rotation of the experimental apparatus. In the first set of conditions, the subject was able to observe the apparatus being rotated either 0, 90, 180, 270 or 360 degrees. In the second set of conditions, the subject could not see the apparatus while it was being rotated, and was required to determine the location of the baited food cup via the position of an auditory stimulus (a small clicker) attached to the experimental apparatus. The position of the clicker could either predict the location of the baited food cup or provide no cue concerning its location. The results of this study revealed two important findings: (1) a subject's ability to locate the hidden food item varied as a function of the clicker's ability to provide information concerning the correct location of the hidden item; and (2) there were no age differences in performance as measured by accuracy of responding and response times. Comparative data from humans of five different ages were also collected. This study comprised a doctoral dissertation research project; the Ph.D. degree was awarded by the Georgia Institute of Technology in June, 1986.

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la	36	(a) Branch, Jane E. Gust, Deborah A.		X	16	Pan				
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		(c) Division of Behavioral Biology								
		(d) Georgia Institute of Technology (JEB, DAG)								
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1. Descriptive Title (80 characters):
Effect of Solar Eclipse on the Behavior of a Captive Group of Chimpanzees

#### Abstract:

Data were analyzed and the results published on a study to examine changes in the behavior of a group of captive chimpanzees (Pan troglodytes) during an annular solar eclipse. The study capitalized on the fact that the group was maintained in an outdoor compound at the Yerkes Regional Primate Research Center Field Station in Lawrenceville, Georgia, and that the study site was located in the path of the annular solar eclipse of May 30, 1984. each animal was recorded using an instantaneous scan-sampling technique. Beginning two days prior to the eclipse and continuing through the day following the eclipse, data were collected from 1100 to 1300 hours daily. At 1214 hours on the day of the eclipse, when the sky began to darken and the temperature began to decrease, solitary females and females with infants moved to the top of a climbing structure. As the eclipse progressed, additional chimpanzees began to congregate on the climbing structure and to orient their bodies in the direction of the sun and moon. At 1223 hours, during the period of maximum eclipse, the animals continued to orient their bodies in the direction of the sun and moon and to turn their faces upward. One juvenile stood upright and gestured in the direction of the sun and moon. Sunlight began to increase at 1225 hours, and the animals began to descend from the climbing structure as the brightness increased. The behaviors exhibited by the group during the period of maximum eclipse were not observed prior to or following the eclipse nor as darkness approached at normal, daily sunset. These data indicate that a solar eclipse, a rare and uncommon environmental event, can influence and modulate the behavior

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Language, Mentally-Retarded Children and Family Correlates

#### Abstract:

The primary goal of this project is to examine the impact of the home and school-based language interventions with mentally-retarded human children on the families of these children. The subjects of this study are the children described in the Georgia State University Mental Retardation Project are designed to compare the effects of these two child-focused language interventions on (1) the retarded child's interaction with his/her siblings and parents, (2) the siblings' and parents' perception of their retarded retarded child, and (4) the way in which the family as a whole organizes of extended family members, friends, neighbors, community agencies and seranalysis of the data can be initiated for purposes of addressing major questions.

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Interactions following Copulatory Harassment by Stumptail Macaques

#### Abstract:

Harassment of a copulating pair by group members has been described in a variety of nonhuman primate species, particularly stumptail macaques (Macaca arctoides). To elucidate the functions served by this type of harassment, a social group comprising 33 stumptail macaques was observed over a three-month period. A total of 126 harassed copulations involving six mating males and lating pair were observed during 58% of the five-minute periods immediately rather than the mating female. Rates for affiliative or submissive responses received by the mating male from the harassers and rates for aggressive acts baseline rates for these behaviors. These data indicate that harassers and copulating males re-establish social and dominance relationships following anism for harassers to test these relationships.

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 Descriptive Title (80 characters): Contexts for the Hindquarters Presentation Posture in Stumptail Macaques

#### Abstract:

Behavioral responses which are typically observed within the context of heterosexual copulation, but which may also occur within other social contexts, have been termed 'sociosexual' behavior. The hindquarters-presentation posture is one of several sociosexual responses exhibited by stumptail macaques (Macaca arctoides). Qualitative observations suggest that this posture serves a variety of functions, social, sexual and dominance-related, depending upon the participants and context. To describe quantitatively the hindquarters-presentation posture, a factor analysis was conducted of the immediate (within 30 seconds) responses to 2,531 presentations observed in a stable social group of 23 stumptail macaques over a seven-month period. The following six distinct contexts for presentations were quantitatively apparent and the factors identified: genital/hip contact, copulation, affiliative pattern, subordinate female pattern, male pattern, and submission. Moreover, although responses to presentations varied with the age, sex and dominance relationships of the participants, the first response to a presentation which was observed most often was genital investigation of the presenter. These quantitative analyses have confirmed some of the presumed social functions of hindquarters presentation and have suggested others not suspected previously. Therefore, factor analysis appears to be a viable method for organizing and describing sociosexual behavior.

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Behavioral and Physiological Concomitants of Drug Abuse

#### Abstract:

The long-range objective of this project is to characterize the behavioral, cardiovascular and thermoregulatory effects of various drugs that may have abuse liability or that may have therapeutic value in treating drug abuse. Experiments have been conducted to determine the effects selected drugs can have on the central nervous system of conscious nonhuman primates by studying the effects of these drugs on learned behavior in squirrel monkeys and chimpanzees, to determine the effects the drugs can have on heart rate, arterial blood pressure and core temperature in squirrel monkeys at doses that have effects on behavior mediated via the central nervous system, and to determine whether the behavioral, cardiovascular or thermoregulatory effects are enhanced, diminished or blocked by other drugs or by behavioral procedures. Methods used to study the effects of drugs have included the direct measurement of arterial blood pressure and heart rate as indices of cardiovascular activity, the direct measurement of colonic temperature as an index of thermoregulatory activity, and learned, psychomotor behavior as an index of central nervous system activity. Experiments have confirmed similarities in the behavioral effects of caffeine, cocaine, nicotine and d-amphetamine even though each is from a different pharmacological class, and there have been pronounced similarities in the physiological effects at doses that act behaviorally. Research is now beginning to identify drugs that can block or attenuate the effects of these prototypical In addition to developing appropriate animal models for studying the effects of drugs, the project also uses the animal models to generate a better understanding of the effects certain types of drugs can have in humans and in animals, and to identify ways in which undesirable effects of the drugs can be attenuated. The research is supported primarily by a grant from the National Institute on Drug Abuse.

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Behavioral Modulation of Cardiovascular Activity

#### Abstract:

The major objective of this research is to study and characterize the modulation of cardiovascular activity by ongoing behavioral processes. The central nervous system (CNS) has long been recognized as being significantly involved in the regulation of cardiovascular activity, especially the regulation of blood pressure and heart rate. The CNS is also known to be the source of control of learned behavior, especially as differentiated from spinal or reflexive behavior. How the modulation of cardiovascular activity becomes integrated with or influenced by ongoing, centrally-mediated behavior is not well understood. Research in the laboratory has now identified behavioral procedures that can induce increases and decreases in arterial blood pressure and heart rate during daily periods in a controlled environment. Experiments are underway to describe the course of development of decreased cardiovascular activity in the squirrel monkey, to identify factors determining its development, and to identify conditions under which decreases can be maximized. The research is supported, in part, by funds from the Eagles' Max Baer Heart Fund.

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Recall and Recognition in Aged Rhesus Monkeys

#### Abstract:

Historically, the experimental analysis of memory has involved linguistically-competent human subjects. As a result, memory processes, including recall and recognition, have been confounded with linguistic ability. Animal subjects, however, permit the study of memory independent of linguistic ability. Using rhesus monkeys as subjects, this laboratory has developed procedures that correspond in significant detail to those used in human memory research, yet are appropriate for studying memory processes in nonhuman primates. The methodology is based on a touch-sensitive cathode-ray tube (CRT) or computer terminal upon which a microcomputer displays visual stimuli that the subject must recall and reproduce correctly after an intervening period of time (delay). Characteristics of the visual stimulus, the size and location of the touch-sensitive area on the CRT, and the complexity of the visual pattern are determined by microcomputer software. With this visual-motor task, high accuracy levels of recall are characteristic of the rhesus monkey after very short delays, and accuracy decreases as the delay increases. At delays approaching one minute, accuracy approaches chance levels. Moreover, the data suggest that younger monkeys can maintain higher levels of accuracy on recall after longer delays than can aging monkeys, especially monkeys with ages greater than thirty years, but that differences due to age can be influenced by amount of training and experience. The methodology provides an animal model for studying the relation between aging and memory in a way that can be useful for characterizing the neuropharmacology of aging and for identifying substances of potential therapeutic efficacy in treating memory deficits associated with aging. The objective of this research, supported by G. D. Searle and Company, is to develop a nonhuman primate model of memory performance that can demonstrate changes in behavior typical of aging in humans.

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Reproductive Biology and Behavior of Chimpanzees

#### Abstract:

Work continued as part of a study of the effects of oral contraceptives on sexual behavior (Dr. R.D. Nadler, Principal Investigator), and two foci subsidiary to the main program were addressed. Firstly, a new technique for the detection of ovulation in chimpanzees was verified. A commercially-available detection strip, the Ovustick, developed for use in humans to detect the periovulatory surge of luteinizing hormone (LH) in urine, was applied to common chimpanzees (Pan troglodytes). In conjunction with daily, detailed scoring of the perineal swelling cycle and radioimmunoassay (RIA) of urine for LH, it was possible to show a close correspondence among three phenomena: the first sign of detumescence of the females' genital swelling; a doubling or tripling of LH (measured by RIA in mIU/ml); and graded responses of the Ovustick. periovulatory LH peaks were detected by RIA and Ovustick. The correspondence between the first LH peak and detumescence, for 23 cycles from six females, was the closest recorded to date and yielded a highly invariable luteal phase of 15.9 days (SEM = 0.52 days). Secondly, behavioral data were collected from female common chimpanzees having a premenstrual abnormality in their sexual swelling that supplemented data obtained from animals in the main study. data collected from the common chimpanzees were compared to data derived from pygmy chimpanzees during a previous study, and analyzed with respect to structure in order to refine our ability to distinguish the communicatory functions of structurally-similar gestures and postures. that: (i) iconic aspects of affect or 'feeling state' are structural elements of nonverbal communication; (ii) female proceptivity is more clearly distinguishable from hierarchical and affiliative interactions; (iii) behaviors which are analogous to 'negative symptoms' in humans are recognizeable; (iv) some captive female chimpanzees exhibit a premenstrual syndrome-like phenomenon; and (v) design components of human language are incorporated into chimpanzee non-

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Reproduction and Thermoregulation of Gibbons

#### Abstract:

Pilot research on the reproductive characteristics of the monogamous lesser apes was extended by: (1) continuing to monitor one adult female and a two-year-old infant comprising a small family group of gibbons (Hylobates lar) in order to document the relationship among weaning, the resumption of ovarian cyclicity and the interbirth interval; (2) conducting an anatomical investigation of female external genitalia by examination of postmortem material; and, as a supplement to this main program, (3) studying thermoregulation in the gibbon with a focus on determining the thermal significance of variation in coat color. Two undergraduate students were directed in the collection of behavioral and environmental data relating to microhabitat preferences (use of sun, shade and the environmentally-regulated interior, ambient temperature, relative humidity and windspeed). The students simultaneously monitored the mother-infant interactions and sexual behavior between the adult male/female Data on variation in the appearance of the female external genitalia were collected by personnel in the Division of Reproductive Biology (Dr. K.G. Gould, Division Chief). The principal results were: (1) the infant was initially weaned at 54-56 months of age, sexual activity resumed during postpartum amenorrhea, but suckling then resumed and sexual activity and genital swelling. were held in abeyance for an additional eight months; (2) detailed postmorten examination of a single female clarified the structure of the external genitalia which was found to be complex with reflexed labia minora associated with prominent folds flanking the urethral meatus; and (3) distinctions were found in the use of shade and the interior by the black-coated and blonde-coated individuals over an ambient temperature range of 45-105° r. The black-coated gibbon remained outdoors more on cool, sunny days, but used more shade on hot, sunny days; it can be inferred that dark coats are thermally beneficial at low temperatures and light coats are advantageous at higher temperatures.

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Descriptive Title (80 characters):
 Daily Activity Patterns and Reproduction of Howler Monkeys

#### Abstract:

PART II

SECTION A

A 30-day field study was conducted near the winter solstice in Belize, Central America, with the objective of verifying that the mantled howler monkey of Belize (Alouatta pigra luctuosa) exhibits an unusual activity pattern. Previous survey work on nonhuman primates conducted in Belize during 1982, 1983 and 1984 yielded evidence suggesting that howler monkeys were active both day and night, and that the amount of time these monkeys were active during these two times varied with environmental conditions, i.e. that this platyrrhine monkey exhibits a polytypic activity pattern like that of the strepsirrhine genus Lemur. Three groups of howler monkeys were located between 200 and 480 m elevation, and vocalizations from all three groups were continuously monitored 24 hours per day for a period of ten days. One group was contacted visually and followed through four 24-hour periods and during three additional, briefer periods. Ambient temperatures were monitored at 30-minute intervals throughout the 21 days spent in the forest. The focal group was found to be active through sunset and resumed feeding activity between 0230 and 0430 hrs, four hours and two hours prior to sunrise. It is hypothesized that the relatively cool conditions, with minimum temperatures as low as 54°F, placed energetic loads on the animals that required them to resume activity and feeding over intervals which were shorter than the winter night length. These findings and those of other workers require re-evaluation of the notion that the Ceboidea are fundamentally diurnal (with the night monkey being 'secondarily' nocturnal). In addition, female howler monkeys were observed with conspicuous perineal sexual swellings not unlike those of chimpanzees; adult males had relatively large testicles, also like chimpanzees. These howler monkeys exhibit reproductive characteristics similar to those of chimpanzees and have the potential to provide a productive subject for expanding our understanding of the making systems of the hominoids.

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1. Descriptive Title (80 characters):
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The Role of Tension Regulation and Reciprocity in Food Sharing among Chimpanzees

#### Abstract:

From March 1 through May 31, 1986, observations were conducted on the social behavior of a group of chimpanzees (Pan troglodytes) maintained in a large outdoor compound at the Yerkes Regional Primate Research Center Field Station. The purpose of this study was to further our understanding of the proximate mechanisms of food-sharing behavior and social tolerance.

Sharing must depend on some effective means of tension regulation. The chimpanzee, the species that is taxonomically closest to humans, is known to exhibit an extensive use of calming body contact during periods of tension and following aggressive episodes. This study investigated how reassurance behaviors during feeding sessions, or sharing and/or other helpful behaviors part with possessed food, e.g. if chimpanzee A grooms chimpanzees to extended period of time in the morning, will this early prolonged grooming affect B's willingness to share with A later in the day? Such questions have widely studied but for which data are currently scarce.

Fifty-four feeding sessions were conducted, and approximately 175 hours of observation were made. Most of the data collected were entered directly into a computer, but observations of the feeding sessions were recorded verbally via tape recorder. By the end of calendar year 1986, all data were processed and ready for analysis.

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Sex and Aggression in Stumptail Macaques

#### Abstract:

The effects of the removal of high-ranking males on the sexual and aggressive behavior of lower-ranking males were examined in a captive group of stumptail macaques (Macaca arctoides). The group consisted of six adult males, 14 adult females and 13 juveniles and infants. Three experiments were conducted, each of which contained two primary conditions: (1) all males present in the group (Condition AM); and (2) high-ranking male(s) removed from the group (Condition HR). Data were collected for 30 minutes on each male under both conditions using the focal-animal sampling technique. In all three experiments, the levels of sexual behavior exhibited by the lower-ranking males were significantly higher for Condition HR (p  $\leq$  .05). Moreover, the levels of aggressive behavior exhibited by lower-ranking males were significantly higher ( $p \leq .05$ ) for Condition HR in two of the three experiments. Data collected under control conditions indicated that these increases were not simply the result of animal handling and/or removal. Furthermore, additional analysis revealed that the highest rates of sexual and aggressive behavior were directed almost exclusively toward adult females. For nine out of 15 trials conducted under Condition HR, the female that received the highest rate of sexual behavior was also the recipient of the highest rate of aggressive behavior. These results suggest that the presence of high-ranking males in a group can inhibit or suppress sexual and aggressive behavior in lower-ranking males. Further analysis is needed, however, to elucidate the precise relationship between the sexual and aggressive behavior of the males.

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Social Stimulation and the Resumption of Copulation in Macaques

#### Abstract:

Copulatory data derived from observations of social groups of rhesus macaques (Macaca mulatta) and stumptail macaques (Macaca arctoides) were analyzed to test the hypotheses that male/female pairs would resume copulation significantly sooner if a second male copulated with the female shortly after ejaculation by the first male. Data collected from both groups supported this hypothesis. These results, obtained as an extension of studies conducted previously on Macaca nemestrina, suggest that an abbreviation of copulatory intervals due to social stimuli occurs in several species of nonhuman primates, both in social groups and in experimentally-created triads. These findings are also consistent with the hypothesis that socially-mediated resumption of mating is related to intrasexual competition among males.

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Endocrine Control of Seasonal Reproduction

#### Abstract:

Work in this laboratory has been directed toward testing the hypothesis that photoperiod is the variable producing a seasonal mating cycle in rhesus monkeys, and toward elucidating further the neuroendocrine mechanisms which result in annual intervals of anovulation. Two approaches have been used to attain these goals: longitudinal studies of subjects maintained on either a natural photoperiod or an experimentally-defined light/dark schedule; and specific evaluation of particular neuroendocrine systems at various times during the annual cycle. Adult rhesus monkeys, housed socially in outdoor compounds with attached indoor quarters, were subjects for the collection of behavioral data to monitor sexual activity and for radioimmunoassay of blood samples to characterize ovarian, pituitary or other hormone secretion as primary dependent variables. tained on short days exhibited a pattern of sexual behavior and ovulations nondistinguishable from other groups, a result consistent with the interpretation that the end of the annual mating season results from a refractoriness to shortday stimulation and not from active inhibition due to increasing day length. However, timing of the resumption of mating behavior and ovulations during the subsequent season was also similar among study groups. This analysis also provided several additional results. Timing of the onset of ovulation occurred consistently in a narrow range across subjects and, conversely, the final ovulation of the season occurred over a period typically exceeding three months. produce long days with a combination of natural and artificial light (of ordinary intensity) have not been effective, evidently because subjects exposed to intense natural light may be less sensitive to artificial light stimulation. The average interval of seasonal anovulation in nonpregnant, nonlactating female rhesus monkeys (185  $\pm$  4 days) was not altered significantly in subjects maintained on a continuous short-day schedule nor by abrupt shifts to short days either in the mid-mating or mid-nonmating season. Male testosterone levels showed a clear seasonal rhythm on both a natural photoperiod and on short-day schedules.

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Kin Recognition in Primates

#### Abstract:

Research is being conducted on the patterns and mechanisms of kin recognition in primates. Modern evolutionary theory recognizes the selective advantage that may be accrued by animals through behaviors which increase the fitness of kin-related conspecifics. Little is known, however, about how individuals come to distinguish their kin from other, nonrelated conspecifics, especially in primates. Although it has been known for many years that matrilineal kin relationships are important in the social organization of most species of Old World monkeys, the extent to which patrilineal kin are also discriminated is not known. Techniques for paternity determination, such as immunogenetic blood typing, are now sufficiently developed to enable the documentation of paternal kin lines in some primate species, such as the rhesus monkey. In collaboration with Dr. W. Stone of Trinity University, this laboratory is using such blood-typing techniques to establish paternal kin lines in one of the rhesus monkey groups housed at the Yerkes Primate Center Field Station. Focal-animal sampling will be used to collect behavioral data needed to assess whether these paternal kin are discriminated by the monkeys. The critical component of this project, one which distinguishes it from several other attempts to address this question in rhesus monkeys, is the collection of extensive data on social behavior of individuals of known paternity while the subjects mature in an undisturbed social group. Previous investigations, which have yielded controversial and contradictory results, have attempted to study the question of paternal kin recognition under highly-artificial conditions and have considered only a few behaviors. By considering the full range of behaviors that occur in a naturally-composed group, a more sensitive test of the issue of paternal kin recognition can be made. Data collection began in December, 1986, and will continue through April, 1987. Additional paternity tests using a second, companion group will be conducted in April, 1987. Preliminary analyses of the behavioral data should be completed by mid-summer, 1987.

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Ontogeny of Semantic Communication in Primate Aggression

Abstract:

Research on the ontogeny and functions of scream vocalizations emitted during aggressive interactions by rhesus monkeys living in social groups at the Yerkes Primate Center Field Station has continued. Behavioral observations, tape recordings, playback experiments and computer-aided acoustic analyses are used to study five discrete types of screams employed by victims of an attack in the recruitment of agonistic aid. These calls function in a rudimentarily representational manner in that they index external features of an opponent and the agonistic episode, thereby providing allies, usually matrilineal relatives, information crucial to making 'decisions' concerning tactics to be used during Agonistic alliances are important in the development and maininterventions. tenance of the dominance relationships that regulate aggression in many primate species, and the vocal signals used in the recruitment of allies have been a neglected component in studies of this system. Research during the past year has concentrated on acoustical analyses of the distress calls recorded previously from infant rhesus monkeys born into the study group during 1985 and These analyses, which are still ongoing, suggest that the origins of scream vocalizations used by juveniles within the context of agonistic recruitment can be traced to the distress vocalizations which neonates are able to produce from the first days of life. Kidnapping by juvenile females appears to be one important context for the production of these distress calls. mother's responses to these early distress vocalizations influence the development of the infant's vocal behavior during agonistic situations will be the focus of the next set of analyses conducted. All analyses will be completed and final reports will be written in time for submission of a renewal application in July, 1987. The overall objective of this and future research on macaque agonist vocal behavior is to understand the mechanisms that account for individual variation in the ability to communicate effectively during aggressive encounters with social companions.

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Project Chantek: Communication and Cognition

#### Abstract:

Project Chantek is a research program designed to investigate the early stages of language development by identifying the communicative and cognitive processes that underlie the emergence of the ability to use symbols. The submacus) that is being taught to communicate via gestural signs based on the ated at the University of Tennessee at Chattanooga in 1978, and was transferred to the Yerkes Regional Primate Research Center in March of 1986. Continuing setting, concentrating on the analysis of existing data and on the continuation tive caging now required due to his larger size.

Progress was achieved in several areas during 1986. The relocation of Chantek from a housetrailer on the University of Tennessee campus to the new adjustment to his new living conditions. With the recent additions of BARREL, continue to comprise the largest category of signs in his vocabulary. Significant results include evidence of spontaneous gestural signing and use of the POINT sign (an ability that has not been reported previously in apes). Future research efforts will concentrate on data analysis, sign relention and generalization studies, and on Chantek's resocialization with other orang-utans and its effect on his cognitive and communicative development.

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		(d) Georgia State University									

CECTION A

Neuropsychological Foundations Project

Abstract:

The first-handedness studies conducted with the common chimpanzees (Pan troglodytes), Sherman, Austin and Lana, utilized archival videotapes taken at different ages. These animals' uses of objects, gestures, tools, free play and lexigram keyboards were encoded for each hand's status during the execution of an action, the activity being performed, and the orientations of both the goal and the subject. Sherman showed a general right-hand bias for most tasks and, depending upon the task, Austin exhibited greater variability in unimanual hand use. The primary goal of the project was to study the relationship between hand use and communication activities in comparison with non-communication activi-In a second series of studies using traditional laboratory handedness assessment measures, Sherman, Austin and Lana were given a series of unimanual tests and bimanual tests. The results revealed individual differences among the animals in hand use depending on the specific type of task being performed (fine motor vs. ballistic, etc.). Fifty mentally-retarded human subjects were evaluated twice using the UCLA Handedness Paradigm, and the results showed little relationship between language competence and handedness. During the past year, Sherman and Austin have been involved in training on the various lateralization paradigms. Both Sherman and Austin have achieved 90% correct trials at the fastest (100 milliseconds) presentation rates in either hemifield. Lana had achieved approximately 75% correct trials on the next fastest presentation rate when she was dropped from the study due to pregnancy. Moreover, a pilot study using a dichotic-listening paradigm was conducted with Kanzi, a pygmy chimpanzee (Pan paniscus). Human words which he had previously appeared to comprehend were developed into 20 unique pairs based on number of syllables and specific phonemes (clay-clover, head-bread, etc.). Three out of four tapes showed better left-ear recall, but only one tape revealed a statistically-significant difference between ears using the strictest criteria. The results of this pilot study suggest a left-ear advantage in language processing for Kanzi.

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Georgia State University Mental Retardation Project

#### Abstract:

This laboratory has now completed the studies designed to determine the extent to which social communicative interactions are influenced by three settings (home, school and institution) and by different communicative partners. The results revealed differences among the three settings with the greatest communication occurring in the home, followed by the school and then by the Thirteen moderately- or severely-retarded young children (mean age = 12.8 years) have begun an intervention phase of this study in either the home or the school setting. Using a portable, battery-operated, electronic communication system, the subject touches a symbol and the system 'talks' for Parents and teachers are also using the system with the subjects. Communication probes (CUPs) and structured language-assessment probes (LAPs) have been conducted at systematic intervals. Preliminary review of the CUPs indicates that the children are successfully using the communication system and are learning the meanings of the symbols. An unexpected development was that four of the seven original, first-year subjects recognize the printed English word that appears above the lexigram symbol, and three of these subjects are now able to approximate more closely than during the baseline probe the conventional spoken word which corresponds to the symbol. In addition, some of the subjects are now involved in an advanced intervention phase in which the communicative system is available in both the home and the school settings.

Three non-speaking, retarded adults, who reside in an institutional setting and participated in a previous laboratory-intervention project, have also completed the baseline assessment phase of the study. Computer-based communication systems have been installed in the residential units, and the direct-care staff personnel are using the systems with the residents. The residents have transferred the use of the system from the laboratory to the residential unit and are now successfully using the system.

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Cognitive Studies in Pan troglodytes

#### Abstract:

The cognitive studies project has been very successful during the past year in teaching Lana, a female common chimpanzee (Pan troglodytes), some important aspects of numbers. Through the use of a computer prorgram, color monitor and joystick, Lana is presented a series of trials in which a target number (either 1, 2 or 3) appears on the screen of the monitor in a random location at one elevation. As Lana 'touches' that number with a cursor controlled by the joystick, several boxes appear on the bottom half of the screen in random number and placement. Again using the joystick to control the cursor, Lana touches the boxes, hopefully in agreement with the target number. Thus, if the number is 3 on the screen, Lana should touch three boxes before returning with her cursor to touch the target number once again. As each box is touched in turn, a box of random size, color and location appears at the top of the screen, i.e. if, once again, the target number is 3, then three boxes of random size would appear in random placement at the top of the screen. Lana is now performing this task with approximately 85-90% effectiveness. Additional numbers will be used and further tests will be conducted in order to teach Lana other aspects of the meanings of specific Arabic numerals. Moreover, Drs. Emil W. Menzel and Herbert S. Terrace have made significant progress during the past year in teaching Sherman and Austin, two common chimpanzees, how to use a 'map' depicted on a color monitor so as to know which of six buttons to touch on a keyboard. Tests conducted to date have involved moving the television screen distally and from right to left. These animals have demonstrated that they are able to determine which key needs to be pressed on a keyboard placed in front of them. Work on spelling has progressed, but results have not been satisfactory; Lana has learned how to spell four words. Nevertheless, the amount of effort involved suggests that we have yet to learn how to teach her to spell words efficiently. Time permitting, this question might be pursued next year, but the main focus of this project will be on map reading and learning Arabic numerals.

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	82	MAR, RM); Univ. of GA (GHB)				1, 1	٠			

 Descriptive Title (80 characters): Biobehavioral Studies of Language and Cognition: A Program Project

#### Abstract:

This program project consists of five separate projects ranging from basic research with chimpanzees to individual and social studies with mentally-retarded human subjects. The project entitled "Language Acquisition in Pan paniscus" focuses on this relatively unstudied species' capacity for learning symbols and using the symbols in referential communication. Data derived from this project are germane to our understanding of the acquisition of language skills in both normal and mentally-retarded children. The project entitled "Cognitive Studies in Pan troglodytes" includes studies to (1) determine the ability of chimpanzees to use maps in order to obtain rewards, (2) to explore this species' capacities for learning the specific values of Arabic numerals, and (3) to explore this species' ability to draw inferences which lead to prompt and appropriate alterations of previously-learned behaviors. This project involves scientists from the State University of New York and Columbia University. The "Georgia State University Mental Retardation Project" has been studying language acquisition by both severely and profoundly mentally-retarded children who live at home and attend public school. The principles and methods used in this project have been derived from the "Language Acquisition in Pan paniscus" project. The "Neuropsychological Foundations Project" is directed toward the definition of cerebral lateralization of function in all subjects comprising this program project, and is conducted with the goal of improving our understanding of brain-behavior relationships in symbol learning and language acquisition. Finally, the "Language, Mentally-Retarded Children and Family Correlates Project" is designed to study the structure and function of families in association with symbol learning and language acquisition by their mentally-retarded children who are being studied in the "Georgia State University Mental Retardation Project".

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Language Acquisition in Pan paniscus

# Abstract:

The pygmy chimpanzee (Pan paniscus) project has been very productive during the past year in that Panbanisha, a pygmy chimpanzee, has now been reared successfully with Panzee, a common chimpanzee (Pan troglodytes), for 15 months. The successful co-rearing of these two species has contributed to this laboratory's efforts to sort out the degree to which perceived species differences are a reflection of genetic determination or environmental rearing. To date, only the Pan paniscus have learned to comprehend human speech with precision (Kanzi now understands about 200 words) and have spontaneously learned lexigram symbols in a representational way to provide for two-way referential communication. The animals are only now beginning to provide evidence that they have learned something about spoken words and symbols. Both subjects are prime and ideal for this study. Lana's infant (Pan troglodytes), born last November with Sherman as the male breeder, and the anticipated offspring of Matata (Pan paniscus) will serve as controls for the study of Panzee and Panbanisha.

Another major analysis, conducted in collaboration with Dr. Patricia M. Greenfield of the University of California at Los Angeles, has defined a set of rules that Kanzi (Pan paniscus) uses reliably when making combinations of lexigrams and gestures in 'strings' of 2, 3 and 4. Some of these rules have been use of lexigrams and gestures in combination. (Interestingly, the research technicians have also been influenced by the way Kanzi has, on his own, come to form these strings.) This work is significant and is believed to have considerable relevance for our understanding of the roots of syntax. Dr. Greenfield believes that there is great similarity between Kanzi and normal children concerning their use of lexigrams and gestures in combination. Work on the topics described above will be continued throughout the coming year.

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Tana River Reserve

#### Abstract:

The Tana River Primate Reserve in Kenya, East Africa, is inhabited by two highly-endangered nonhuman primate species, the Tana River red colobus monkey (Colobus badius refomitratus) and the crested mangabey (Cercocebus galleritas galleritas), as well as five less-endangered species including the Syke's monkey (Cercopithecus mitis albotorquatus), the vervet or green monkey (Cercopithecus aethiops johnstoni), the yellow baboon (Papio cynocephalus), the greater galago (Galago crassicaudatus) and the lesser galago (Galago senegalensis braccatus). Initial reconnaissance of the Tana River was conducted during the past year, and proposals have been submitted to various agencies requesting support for the establishment of a permanent field site to conduct long-term behavioral/ecological studies on several of these endangered primate species.

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Effects of Drugs on Group Behavior

### Abstract:

During the final months of support for this project, major data-analysis summaries were completed. The goal of this project was to investigate the effects of commonly-abused drugs on the behavior of individual animals living were made to study a variety of stumptail macaques (Macaca arctoides). Efforts as well as morphine and its antagonist, naltrexone. Comparative data on the behavioral effects of these drugs in group-living nonhuman primates should be useful in elucidating the properties of these substances as mediated through the animals' social environment.

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Behavioral Ecology of the Tana River Red Colobus

# Abstract:

This project has been funded, in part, by a dissertation improvement grant to conduct a field study of the highly-endangered Tana River red colobus monkey (Colobus badius refomitratus) in Kenya, East Africa. The initial study site was chosen during the past year, and efforts were made to select, among the groups of this species that inhabit the 150-km² area comprising the Tana River Primate Reserve, those groups which would be most appropriate for long-term study. Two groups have been identified, and the collection of behavioral and ecological data has begun. In addition, a census of the red colobus monkey as well as the similarly-endangered crested mangabey (Cercocebus galleritas galleritas) was also conducted. Work on this long-term field project will continue through 1988.

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Descriptive Title (80 characters):
 Acute Effects of a GnRH Agonist on Male Sexual Behavior

## Abstract:

The major objective of this project was to investigate the effect of 35 days of administration of a GnRH agonist (WY-40972) to four intact, adult male rhesus monkeys (Macaca mulatta) tested with a group of eight intact female rhesus monkeys. Each male received either GnRH agonist or saline (control) via osmotic minipump (Alza Corp. No. 2ML4). The male subjects were treated in a counterbalanced design, with two males first receiving agonist and two receiving saline. Five days per week, 30-minute test sessions were conducted with male subjects in the presence of the female, and at least one female was within three days of her estradiol peak on every test day. results showed that agonist treatment suppressed testosterone levels to the 200-400 pg range and decreased male sexual behavior. Two of the four males displayed almost complete inhibition of sexual behavior, and two exhibited a less pronounced reduction of sexual behavior. The degree of behavioral suppression produced by the agonist treatment was unrelated to testosterone level, male age or order of treatment. These results demonstrate that the acute chemical suppression of testosterone reduces, but does not eliminate, male sexual behavior.

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		(c) Division of Behavioral Biology				F				
		(d) N/A								

Social and Androgenic Influences on Male Sexual Behavior

## Abstract:

Studies are now in progress to investigate nine intact, adult male rhesus monkeys (Macaca mulatta) serving as subjects for each of three treatments: (1) GnRH agonist (Wy-40972) administered via osmotic minipump plus daily injections of oil; (2) GnRH agonist administered via osmotic minipump plus daily injections of testosterone; and (3) water (control) administered via osmotic minipump plus daily injections of oil. The nine subjects have been divided into three social groups containing three males per group. At all times, each group contains one male that has been subjected to each treatment. During a given week, each male is tested (a) on a pair-test with an ovariectomized, estradiol-treated female, (b) in a group situation with the female and the two other males in his group (3:1 test), and (c) in a second group situation with three estrogen-treated females and the other two males in his group (3:3 test). Using this procedure, this study can investigate the effects of both testosterone suppression and social context on male sexual behavior.

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Descriptive Title (80 characters):
 Adrenal Function and Female Sexuality

## Abstract:

Eight intact, female rhesus monkeys (Macaca mulatta) were observed with each of two vasectomized adult male rhesus monkeys (a) during an untreated ovarian cycle and (b) during treatment with dexamethasone administered via osmotic minipump. This study utilized a counterbalanced design such that four females received dexamethasone first and the remaining four received water first as a control. On every day of each cycle, 30-minute observation sessions were conducted, and the behaviors of each female in the presence of each male within a  $15.3 \times 15.3 \text{ m}$  outdoor compound were noted. All female subjects displayed clear cyclic patterns of approach and solicition toward the males under the control and dexamethasone-treatment cycles. equally often with females under both conditions. Dexamethasone treatment suppressed serum cortisol by more than 90 percent but did not suppress estradiol or progesterone. All females appeared to ovulate during dexamethosone treatment. Androgen levels are currently being assayed. These results suggest that normal adrenal function is not necessary for a full display of female sexual interest, and they contradict the suggestion that female rhesus monkeys are fundamentally different from other mammalian females in that they depend upon adrenal secretions for female sexual motivation.

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Progesterone Inhibition of Female Sexuality

## Abstract:

Six ovariectomized female rhesus monkeys (Macaca mulatta) were treated with crystalline estradiol via silastic implant. After ten days of estradiol treatment, the subjects received an injection of either 75  $\mu g/kg$  progesterone dissolved in oil or oil alone (control treatment) once per day for five days. Following each day's injection, females were tested in a 15.x x 15.3 m compound with each of three males for 30 minutes per male. Results revealed no statistically-reliable differences in any measure of male or female behavior during the period of progesterone treatment in comparison to the period of oil treatment. The females under both treatment conditions continued to approach, solicit and copulate with males. Serum progesterone levels were elevated to the mid-luteal range (5-10 ng/ml) during the first day of injections. These results suggest that the dramatic decrease in sexual behavior observed in intact females during the first five days following the ovarian estradiol peak is probably not the result of the increases in luteal progesterone levels which occur at this time but, rahter, is more likely the result of declining levels of estradiol.

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Postpartum Effects of Adolescent Pregnancy

# Abstract:

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CECTION A

Since female primates are capable of reproducing prior to the completion of physical maturation, the effects of pregnancy and lactation on interbirth intervals may be more pronounced in young mothers. This laboratory has demonstrated that a significant proportion of primiparous mothers exhibit an extended period of lactational infertility due to a continuation of a more intense pattern of nursing compared to agemates which ovulate within a normal interbirth interval. Moreover, young primiparous females may be more sensitive to the effects of the suckling stimulus on the secretion of gonadotropins. This effect of primiparity is restricted to very young mothers, since older primiparous mothers exhibit an adult-like pattern. Based on these data, it was hypothesized that the effects of suckling on gonadotropin secretion, whether mediated through enhanced estradiol negative feedback or through non-gonadal restraint, synergizes with the 'adolescent' neuroendocrine capacity of young females to prolong lactational infertility in adolescent mothers. In order to investigate this hypothesis, studies were initiated to examine episodic gonadotropin secretion and how it is influenced by suckling and estradiol. Initial studies have indicated that, during the breeding season, estradiol significantly reduces luteinizing hormone pulse amplitude but not frequency.

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26		(c) Division of Behavioral									
		Biology (d) Genetech, Inc. (CR); Inst. of Child Health (JT									

Hormonal and Seasonal Regulation of Puberty in Females

## Abstract:

PART II. SECTION A

This laboratory continued to examine how environmental factors influence the neuroendocrine control of puberty and the timing of first ovulation. In order to examine the role of growth hormone (GH) in the tempo of sexual maturation, GH (Genetech, Inc.) was administered to immature, gonadally-intact (n = 6) and estradiol-treated, ovariectomized (E2ovx) females (n = 5) and the results compared to untreated intact (n = 7) and E2ovx controls (n = 4). Bone ages were higher at an earlier chronological age in the GH-treated monkeys. Furthermore, a precocious first ovulation occurred in 50% of the GH-treated intact monkeys as compared to 0% of the controls. Although maturational increases in luteinizing hormone (LH) occurred at the same age in both groups of E2ovx subjects, higher LH levels were achieved in the GH-treated animals. These changes occurred independently of differences in increases in body weight. These data suggest that elevations in GH may be involved in the final stages of puberty, possibly acting to decrease the negative feedback efficacy of estradiol on LH release.

Environmental factors may override these endogenous changes, thus restricting first ovulation to the fall months. Spring-born monkeys housed outdoors (SBO: n = 7) and winter-born monkeys housed outdoors (WBO: n = 9) were compared to spring-born monkeys housed indoors (SBI: n = 9). For the SBI females, menarche occurred during the summer months and at a significantly younger age (26 months). Menarche occurred at a similar age (30 months) for WBO and SBO females, but at different times during the fall months (September and November, respectively). Moreover, 78% of the SBI females exhibited a precocious first ovulation compared to 0% for SBO and 56% for WBO females. These ovulations occurred at approximately 32 months for SBI females, but at approximately 36 months for WBO females. These data suggest that seasonal factors can override endogenous changes to restrict pubertal events to the fall months in outdoor-housed monkeys.

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J. G. Herndon

J. W. Tigges M. H. Tigges

J. R. Wilson

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D. L. Barrow	Department	of	Neurological Surgery, Emory University
A. W. English	Department (	of	Anatomy and Cell Biology, Emory University
M. L. Feldman	Department (	of	Anatomy, Boston University
A. Fernandes	Department (	of	Ophthalmology, Emory University
M. S. Fiandaca	Department of	of	Neurosurgery, Emory University
J. A. Gammon	Department of	of	Ophthalmology, Emory University
P. M. Iuvone	Department of	of	Pharmacology, Emory University
R. T. Jackson	Department of	of	Surgery, Emory University
J. B. Justice	Department (	o f	Chemistry, Emory University
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R. L. Susman	Department of	) f	Anatomical Sciences, State University of
	New York		
J. Sutin	Department c	)f	Anatomy and Cell Biology, Emory Universi
K. M. Sweeney	Department c	)f	Neurosurgery, Emory University
	-		5 . 5 , 5

# Visiting Scientist:

Department of Ophthalmology, Emory University R. J. Epstein

### Consultants:

H. M. Eggers Department of Clinical Ophthalmology, Columbia University

H. Warner Consultant in Biomedical Engineering

J. P. Wilmeth Anderson Eye and Ear Associates, Anderson, South

Carolina

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Plasticity of the Neocortex and the Development of Epilepsy

# Abstract:

The anatomical substrate that allows for the clinical development of epilepsy is unknown. In order to investigate this, we are employing the alumina model in nonhuman primates. This is a chronic model which produces spontaneous specific alterations in the neocortex as the maturation of the epileptic focus develops, we are hoping to elucidate the sequence of events surrounding the the initial injury results predominantly in the loss of inhibitory synapse and result is an aberrant linkage in the local synaptic circuitry resulting in an excitatory and lacking of recurrent inhibition.

Preliminary data clearly demonstrate GABAergic cell loss in the developing epileptic focus which becomes statistically significant when seizure activity of neurotransmitter receptor binding sites observed in autoradiographs is epileptiform activity begins to be observed, the number of GABAergic receptors markedly decreases in the epileptic focus. Surrounding the epileptic focus is an significant loss of other neurotransmitter receptors within the epileptic focus, GABAergic-chloride ion receptor complex. Similar changes are not observed in the contralateral homogeneous cortex or in surgical or non-surgical controls.

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Transplantation of Fetal Tissue in the MPTP Primate Model of Parkinsonism

# Abstract:

The purpose of this project is to produce a Parkinson-like syndrome in non-human primates and then attempt to reverse the syndrome through transplantation of fetal mesencephalic tissue. The model uses chronic administration of the N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) to selectively destroy the dopaminergic cells in the nigrostriatal pathway which results in a movement disorder with many characteristics of Parkinsonism. The tissue transplant technique has been developed in rats, but whether the primate brain has the same potential for behavioral plasticity and same degree of immunologic privilege remains to be determined.

After baseline is obtained, serial intravenous injections of MPTP are administered until the animal demonstrates stable gross Parkinsonism-like characteristics. Behavioral alterations are monitored by clinical examinations, performance on learned tasks and analysis of video recording of spontaneous caged activity. Biochemical alterations are monitored by CSF spontaneous caged activity. After documentation of deficit, transplantation of cell suspension of fetal mesencephalic tissue is stereotactly implanted in multiple areas of the caudate and putamen.

We have successfully transplanted 5 animals from which preliminary data is available supporting the hypothesis that transplantation of neurohormonally active tissue in the brain is effective in reversing abnormalities and biochemical abnormalities in primates. Three of the experimental transplantation animals have been sacrificed, and are being extensively studied for pathological alterations using standard light microscopic, electron microscopic, immunocytochemical and cathecholamine-fluorescent technique. The graft appears to have taken, and catecholamine containing cells have been identified within. Long-term evaluations of transplanted subjects are essential to determine the ultimate potential for transplantation in the treatment of Parkinson's disease.

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Transplantation of Adult Homologous and Fetal Pituitary Tissue in Primates

#### Abstract:

The major purpose of this study is to determine the feasibility of homologous pituitary transplantation in a primate model. In doing so, we plan to also determine the advantages or disadvantages of adult vs. fetal donor tissue in transplantation and evaluate whether such a transplant can maintain trophic hormone levels, maintain hypothalamic-pituitary feedback, and demonstrate reserve capability during stimulation of the implanted tissue.

Initially, baseline endocrine data is obtained by measuring pituitary hormones before and after the administration of the available hypothalamic releasing hormones. The animals then undergo a transcranial hypophysectomy. These pituitary cells are dispersed by an enzymatic technique and stereotactically transplanted into the median eminence of a second hypophysectomized rhesus monkey. After a recovery period of approximately one month, the endocrine studies are repeated to determine if there is recovery of baseline hormonal function and response to the hypothalamic releasing factor stimulation test. These tests are repeated again at 2 months prior to sacrifice of the animals. Following sacrifice, the brains are studied anatomically by light microscopy, immunocytochemical techniques, and electron microscopy to study the anatomy of the donor-host relationship of neural transplantation.

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Strabismus in Monkeys

## Abstract:

Subjects in these experiments are monkeys that have a naturally occurring strabismus. All were located, initially, through screening of the new births at the University of Washington Primate Center. The naturally strabismic monkeys were moved from the University of Washington to Yerkes during 1986. They are now being tested behaviorally in the Neuropsychophysics laboratory to determine the nature of their strabismic amblyopia.

PART II, SECTION A

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Descriptive Title (80 characters):
 Behavioral Studies of Aphakic Amblyopia

#### Abstract:

The Neuropsychophysics laboratory is conducting behavioral tests of acuity and contrast sensitivity in monkeys that have been made aphakic soon after birth. Following the lensectomy, animals are assigned to one of several treatment groups: 1) an untreated control group, 2) a group in which the aphakic eye wears a contact lens that provides optical correction to a nearpoint, and 3) a group whose aphakic eye receives the same treatment as group #2, and in addition the opposite eye is occluded. Our findings to date reveal that group 1 animals develop severe aphakic amblyopia, group 2 animals a moderate amblyopia, and group 3 animals near normal acuity in their aphakic eyes. However, in group 3 animals, the occluded eye develops a severe amblyopia. The animals used in this study have been shared with Dr. M. Tigges for neuroanatomical studies.

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Effects of Contact Lens Wear on the Cornea of Infant Primates

#### Abstract:

Extended-wear contact lenses (EWCL) are being used increasingly for the correction of aphakia in infants, but there is a lack of data documenting their effects on the corneas of young children. Therefore, corneal studies were performed on infant monkeys wearing EWCL for the correction of surgical aphakia. Nine newborn monkeys underwent unilateral lensectomy and anterior vitrectomy. Seven eyes were fitted with aphakic EWCL postoperatively and two wore no lenses. After at least six months, corneas were studied with slit-lamp and specular microscopy, and with light microscopy (LM) and electron microscopy (EM). Small central corneal opacities developed in two aphakic eyes corrected with EWCL after episodes of keratoconjunctivitis. One of these corneas was found to have a mildly increased coefficient of variation (CV) of endothelial cell size (polymegathism). Although EWCL are well tolerated by the corneas of aphakic infant primates, their association with endothelial polymegathism, which may indicate physiologic compromise, mandates careful long-term follow-up.

These monkeys are part of the amblyopia project and therefore were shared by all investigators involved in that project.

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Anatomical Studies of the Aging Macaque Auditory System

#### Abstract:

The anatomical studies of the auditory system conducted during 1986 were carried out at Boston University School of Medicine using fixed tissue samples obtained from Macaca mulatta which has been maintained at Yerkes. The tissues of interest are middle ear structures, cochlea, VIII nerve, cochlear nucleus, and superior olivary samples. Analysis of these tissues has been carried out using light microscopy. Since the primary focus of the work is cytological change accompanying advancing age, the material studied has come from animals ranging in age from young adulthood (5 years old) to very advanced age (34 years old), with particular attention being paid to structural features which are characteristic of old individuals but which are not found, or are found at a very reduced level, in young individuals. Examples of age-related phenomena of interest in the study are cell and axon loss, lipofuscin accumulation, and alterations in vascular morphology. For several specific structures, normative data are lacking. This is true, for example, of the cytology of the normal young adult medial superior olivary nucleus. In such cases, initial efforts are being directed towards providing quantitative and qualitative cytological descriptions for the young adult, in order to have available baseline data against which to judge aging changes.

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Descriptive Title (80 characters):
 Ambient Noise Exposure of Cage-reared Macaques

#### Abstract:

Current studies by the present investigators are focused on the auditory system of aged Macaca mulatta. The work seeks to determine the nature and extent of auditory changes associated with advancing age, and uses both functional and anatomical methods. Functional assessment of the auditory system uses operant conditioning techniques to examine changes in behavioral responsiveness to auditory stimuli. Anatomical assessment of the auditory system is being carried out in the same population using light and electron microscopy. Proper interpretation of the findings from these studies requires knowledge of the environmental factors which impinge upon the biology of the animals. Among these environmental factors which are of particular relevance are the long-term ambient cage environments at Yerkes. Accordingly, the principal goal of this project is to ascertain whether the typical noise levels are such as to significantly alter the auditory system independently of other changes occurring as a result of aging processes. To carry out this work, ambient noise levels are being studied using high-speed recording with a precision tape recorder. The data are analyzed using spectrum analysis and waveform digitization techniques. Preliminary analysis of the pilot data suggests that the chronic prevailing noise levels are not hazardous to the animals and do not constitute a confounding variable in the study of age-related auditory changes. Further recording sessions at Yerkes are required to obtain definitive records. This information should be a useful contribution to the general characterization of animal maintenance conditions at

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 Descriptive Title (80 characters): Methods for New Contact Lens Design

## Abstract:

The members of our research team involved in the production of contact lens are currently investigating methods to develop new lens designs. Mr. Charles Chandler, who is an expert in optics and contact lens design, has been instrumental in this effort teaching the principles and complex mathematical calculations and formulas applied in the programs for the production of these lenses.

Our recent interest is to improve one of the most important lens features, that is, the lens diameter. As animals grow older, there is a tendency to lose more lenses as the eyes also grow. Therefore, larger lenses are needed.

Due to the increasing number of animals in the various ongoing projects, our demand for lenses has also substantially increased. A large inventory of contact lenses of powers that vary from -15 to +50 diopters is available, so lenses are replaced as soon as they are detected to be missing.

Lenses are cut on a lathe which is preset on different programs for the various powers. The new programs will not only allow us to produce larger lenses, but also improve other lens parameters, like the edge design and base curve which play critical roles in the fitting process.

With these new lenses, we will be able to provide the animals with a more comfortable fit and we believe, also, that the rate of lens loss will decrease.

The animals used in this study have been shared with Dr. R. Boothe for the amblyopia project and with Dr. M. Tigges for neuroanatomical studies.

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 Descriptive Title (80 characters): Effects of a GnRH Agonist Upon Testosterone Levels and Male Sexual Behavior in Rhesus Macaques

# Abstract:

Male rhesus monkeys were paired with estrogen-treated females and tested for sexual behavior before, during and after treatment with Wy40972, a gonadotrophin agonist. This drug was administered via an osmotic minipump at the rate of 2 ul/hr. Treatment resulted in a decline in testosterone levels and in an associated decline in male sexual behavior. Declines in behavior were varied in that some animals cease copulating completely while some still ejaculated occasionally. Prior to the cessation of ejaculation, the white coagulated plug becomes clear and watery, but sperm are still present in vaginal lavage. Behavioral and physiological effects of treatment are reversed when the GnRH agonist is removed after 8 weeks of continuous treatment.

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 Descriptive Title (80 characters): Reproductive Function of Primates: Influence of the Behavioral Environment

#### Abstract:

Ovarian hormone levels were monitored in rhesus monkeys during the breeding and non-breeding seasons. Ovulation (as inferred from progesterone levels in blood serum in excess of 1.5 ng/ml) was most frequent in the breeding season but was completely absent only during the month of August. Summer (non-breeding season) ovulations were more frequently "silent," or without heterosexual behavior, than were winter ovulations. This suggested that estradiol stimulation may cause different behavioral responses at different times of the year. To test this hypothesis, ovariectomized females were treated with subcutaneously implanted estradiol pellets at different times within and outside the normal breeding season. In either season, treatment with estradiol resulted in increased female-to-female sexual behavior. Only during the breeding season, however, did the estradiol-treated, ovariectomized females interact sexually with males. Although males copulated with both estradiol-treated and gonadally intact, untreated females during the breeding season, their rates of copulation with the intact females were higher.

In other studies, the influence of estrogen treatment of some females upon the frequency of summer ovulation in other group members was examined. We found that the frequency of summer ovulation is greater when some female group members are treated with estradiol. We are evaluating this finding in light of our surprising observation that some females ovulate "silently" even when other group members remain untreated.

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Rapid Endocrine Changes During Social Behavior in Rhesus Monkeys

# Abstract:

Work continues in the third year of this three year study designed to examine behavioral changes during behavior in male rhesus monkeys. The design of the study calls for a complete sequence of tests to be conducted in individual animals and for these tests to be repeated until enough data has been gathered to permit statistical evaluation of the results. In each animal, tests are conducted in which the animal is exposed to normal social tension. These situations are constructed by employing known characteristics of the social behavior of this species.

One type of test involves placing male monkeys in the presence of other males so that mutual threatening is likely. Test situations are monitored by an observer who notes submissive and threat responses in both animals. During tests, blood samples are automatically collected from one of the animals by means of an animal-worn backpack which was developed at Yerkes. This system is designed to permit determination of blood hormone values in samples collected without interfering with ongoing behavior. Resultant blood samples are compared with samples from sessions involving mild non-social stress produced by noise or from control sessions in which the animal remains alone for the test session.

We expect that blood samples and behavioral data already in hand will enable us to evaluate the hypothesis that social stress produces greater endocrine responses than does non-social stress, and that the nature of the endocrine response to non-contact aggression is related to dominance status.

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Descriptive Title (80 characters):
 Development and Aging Dopamine Systems in Rhesus Monkey Retina and Effects of Monocular Occlusion

# Abstract:

Experiments were conducted to determine the influence of age and of visual deprivation on the retinal dopamine system, a neuronal system that has previously been implicated in the processing of visual stimuli and in the homeostatic regulation of the photoreceptor-pigment epithelial complex of non-primate vertebrates. Reginal dopamine levels were relatively low at birth, but increased rapidly during the postnatal period. By 3-4 weeks of age, dopamine levels more than doubled, reaching levels seen in adults. The levels of dopamine in retina remained relatively constant during the normal life span of the animals, and did not decline in retinas of old monkeys (20-34 years old).

Monocular occlusion with opaque contact lenses appeared to decrease the synthesis and metabolism of retina dopamine. The concentrations of dopamine and of 3,4-dihydroxyphenylacetic acid, the primary metabolite of dopamine, were consistently lower in retinas of occluded eyes, compared to matched controls. Occlusion also resulted in lower activity of tyrosine hydroxylase, the rate-limiting enzyme in the dopamine biosynthetic pathway. These studies suggest that dopamine synthesis in rhesus monkey retinas is stimulated by light, as it is in retinas of lower mammalian and non-mammalian vertebrates.

The animals used in these studies have been shared with Dr. M. Tigges for the development of the geniculostriate system, with Dr. R. Boothe and his collaborators for behavioral studies, and with Dr. J. Tigges for the aging project. This study was supported in part by EY06001.

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Descriptive Title (80 characters):
 Neuropeptide Y in Developing Hypothalamus and Pituitary

# Abstract:

Neuropeptide Y (NPY) has been shown to be present throughout the nervous and endocrine systems in several species including rats and humans. NPY affects the secretion of reproductive and growth hormones from the rat pituitary and may be a major regulator of peptide release from the hypothalamus. We have examined the distribution of NPY-immunoreactivity in the hypothalamus, pituitary and in some cases the ovaries and pineal gland of nonhuman primates. These studies were performed to enhance our understanding of NPY in these species and gain insight into the function of NPY in humans. These animals were perfused and the tissues described above were removed and processed for immunohistochemical analysis of the distribution of NPY at the light microscopic level. Some of the results of these studies have been presented in abstract form at the annual meeting of the Society for Neuroscience (Tigges et al. 1986) and are now being prepared for publication in manuscript form. The remainder of the research is being analyzed and portions of it will be presented at the Neuroscience Meeting this year. Significant new observations have been made which have broadened our concept of NPY in the neural lobe of the primate pituitary and also in relationship to the pituitary portal vasculature. These results have important implications regarding the function of NPY and open new directions for future research. orangutans, the 2 chimpanzees, and most of the rhesus monkeys are the same animals used in the studies of M. Tigges.

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Descriptive Title (80 characters):
 Age Changes in Neurons and Neuroglia in Cerebral Cortex

## Abstract:

The purpose of the study is to determine if the cerebral cortex of the monkey provides a useful model for some of the aging changes encountered in humans. The main questions being asked are:

- 1. Are neurons lost from the aging cerebral cortex?
- 2. What kinds of cytological changes occur in aging in cerebral cortex?
- 3. Do senile plaques occur in aging monkey cerebral cortex?
- 4. If plaques do occur, what is the nature of the neuronal processes which enter them?

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CO staining in Area 17: Differences Between Monkeys and Apes

# Abstract:

In a variety of Old and New World monkey species, staining for the mitochondrial enzyme cytochrome oxidase (CO) in striate cortex has revealed a distinct laminar-specific pattern of CO reactivity. Over a period of several years we studied the striate cortex of 2 chimpanzees, 2 orangutans and 1 gibbon. All of these apes were sacrificed because they showed a rapid deterioration of their health which made it apparent that they were terminally ill. The laminar staining pattern for CO in area 17 varied from that of monkeys. The most conspicuous difference occurs in layer 4. Instead of a 3-banded tier of differential CO staining in the sublayers of layer 4, in all 3 ape species a single, densely reactive band, about 400-500 um thick, is situated approximately halfway through the striate gray. The ventral border of the CO band is sharp; the dorsal border is less distinct. A system of "dots" rests on this band, extending at least into superficial layers 3 and 2. These "dots" are slightly wider and seem to form a less regularly arranged geometric pattern compared to monkeys. Ventral to the dark CO band is a lightly reactive layer, followed by a slightly more reactive layer adjacent to the white matter. This staining pattern in apes resembles that found in human striate cortex (Horton and Hedley-White, Phil. Trans. R. Soc. B. 304, 255-272, 1984). In monkeys, it has been shown that the CO staining pattern in striate cortex demarcates those layers which receive direct input from neurons of the lateral geniculate nucleus. The results in apes and humans raise the question of a possible species difference in the geniculostriate circuitry between monkeys, and apes and humans. In support of this possibility is our earlier autoradiographic result in chimpanzee showing only one single tier of silver grains about halfway down the cortical gray, after intravitreous injection of tritiated proline (Brain Res. 166, 386-390, 1979). The 2 orangutans and the 2 chimpanzees are the same animals used in the NPY

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NPY in Area 17 of Normal and Visually Deprived Infant Rhesus Monkeys

# Abstract:

In area 17 of newborn rhesus monkeys, neurons and axons immunoreactive for NPY (NPY+) exhibit a laminar-specific distribution. The majority of NPY+ neurons is found in layer 6 and in the white matter, fewer NPY+ neurons occur in the supragranular layers. This distribution is similar to that seen in adults. The NPY+ neurons exhibit various morphologies based on soma shape and size, and on dendritic arborization patterns. In contrast to Hendry et al. (J. Neurosci., 1984), we find that NPY+ neurons give rise to typical axons arising from a prominent axon hillock. Commonly these axons become beaded within a short distance from the parent soma. They frequently course over adjacent NPY+ somata and/or wrap around NPY+ dendrites. Whether this close spatial proximity indicates a functional interaction within the NPY+ network must be resolved with other methods. At birth, NPY+ axons are less abundant compared to adult monkeys, but their laminar distribution pattern resembles the adult pattern. NPY+ axons are most heavily concentrated in the lower half of layer 1 and in layers 4A, 4B and upper 4C; in contrast, lower 4C is only sparsely labeled. Visual deprivation beginning at birth either via monocular eyelid suture or with an occluder lens on one eye does not seem to interfere with the normal postnatal development of the NPY system. Monocular enucleation at birth, however, causes a reduction of NPY+ cells and fibers in area 17. These results suggest that during development the NPY network in area 17 is resistant to monocular form deprivation and occlusion, but vulnerable to the interruption of the connections arising from one eye.

The animals used in this study have been shared with Dr. M. Iuvone for retinal studies and with Dr. Boothe and his collaborators for behavioral studies. These studies have been supported exclusively by funds from EY06001.

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Descriptive Title (80 characters):
 Observations on an Interneuron in the Primate Lateral Geniculate Nucleus

## Abstract:

Because the lateral geniculate nucleus is not simply a visual thalamic relay station, its connections beyond those from the retina probably determine its functional role in visual information processing. A major factor in such processing is believed to be the local circuit neuron (interneuron), but the response properties of such a neuron have not been characterized in a primate. As part of a more comprehensive study, a neuron in parvocellular lamina 6 was first extracellularly recorded, then impaled and injected with horseradish peroxidase. Its receptive field properties were similar to those of other parvocellular neurons (OFF center response, 2.4 msec latency to optic chiasm stimulation, etc.). Subsequent histological processing revealed at the light microscopic level a small soma with four primary dendrites having branches coming off at unusual angles ( $^{1}90^{\circ}$ ). All of the dendrites stayed within lamina 6 and the two long ones were oriented almost perpendicular to the laminar borders. The soma and parts of the dendrites were embedded in plastic for electron microscopy. At the EM level, the dendrites received retinal and presumed cortical synapses, but were unusual in having synaptic vesicles and presynaptic contacts with unlabeled dendrites, somata, and flattened vesicle-containing terminals. No axon was observed for this neuron. These observations indicate that this neuron is an interneuron. Thus, at least some interneurons in the primate LGN have response properties which are similar to relay neurons and probably function in antagonistic or synergistic feed-forward inhibition.

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Visual Field Losses in Naturally Strabismic Macaque Monkeys

# Abstract:

We have measured the visual fields of 3 naturally strabismic monkeys, both binocularly and monocularly for each eye separately. The method is similar to that used previously in cats and dogs (Sherman '73, Sherman and Wilson '75). Briefly, we determined the horizontal extent of the monkey's visual field by way of observation of the monkey's responses to food stimuli (raisins).

Strabismic monkey T81008 has a left esotropia, with a larger angle of deviation at near fixation than at far fixation. When tested under binocular conditions, the right visual field extended to 90° but the left field to only that the left eye turns in during near binocular fixation. When tested monocularly, the visual fields of each eye of this animal extend from 45° contralaterally to 90° ipsilaterally.

Strabismic monkey F82366 has a right esotropia. This animal shows a right visual field loss when tested binocularly, and this loss persists even when the right eye is tested under monocular conditions. The field of the right eye extends from  $45^\circ$  contralaterally to  $67^\circ$  ipsilaterally, whereas the left eye field extends from  $45^\circ$  to  $90^\circ$ .

Strabismic monkey M75038 has an alternating esotropia with preference for OD. This animal also shows an asymmetry in the monocular fields. The right eye field extends from  $45^{\circ}$  contralaterally to  $90^{\circ}$  ipsilaterally. The left eye field extends to  $45^{\circ}$  contralaterally but this animal does not respond consistently beyond  $45^{\circ}$  ipsilaterally and is totally unresponsive beyond  $67^{\circ}$ .

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Descriptive Title (80 characters):
 Difference Between Lateral Geniculate Neurons (cat) With and Without
 Appendages: Retinal Input Patterns

Abstract: Many neurons in the DLGN of cat have complex clusters of appendages while others have relatively sparse, spiny processes or smooth dendrites. In this report we describe variations in the synaptic input to DLGN neurons that are distinguished from each other by appendage morphology. We have three classes of neurons: First, those cells which have smooth dendrites or periodic occurrence of small spiny processes. Second, those neurons with clusters of grape-like appendages which tend to appear at or beyond primary branch points (Guillery's Class 2 cells), and third those neurons that show multi-lobed appendages connected to stem dendrites by relatively long and thin stalks (> 2 microns). We have found that specific patterns of synaptic input are associated with neurons with relatively smooth dendrites. In all of these neurons input from retinal terminals was heavy on the primary dendritic shaft up to the first branch point. (15 to 25 microns from the cell body). Retinal input virtually disappeared a few microns beyond the primary branch point and was replaced by synaptic contacts from profiles containing either round or pleomorphic vesicles. About 30% of the synaptic contacts made by retinal terminals with these neurons were involved in triadic arrangements. We have studied two neurons that bear grape-like appendages (gold toned). In both cases virtually all the retinal input was to the appendages (15 to 60 microns from soma) and not to the dendritic stem. Nearly all the synaptic contacts (95-98%) made with these neurons were involved in triadic arrangements. We have also studied 5 neurons with stalked, multilobed appendages. The bulk of the retinal input to all 5 of these cells was to the appendages with only a few retinal synaptic contacts on dendritic stems or the soma. The appendages of the three GAD positive cells and the gold toned neuron contained synaptic vesicles and were presynaptic to dendritic processes in triadic arrangements. The appendages of the intracellularly filled X-neuron did not contain vesicles and were postsynaptic to retinal terminals and vesicle containing profiles in triadic arrangements.

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Descriptive Title (80 characters):
 Ocular Dominance in Striate Cortex of Aphakic Monkeys

## Abstract:

The use of long-wear soft contact lenses offers an excellent technique for correcting the visual input to an aphakic eye or to block the input to a normal eye. Using this technique, we are studying the behavioral, electrophysiological and anatomical results of various conditions of monocular aphakia in rhesus monkeys. All monkeys had the experimental procedures (e.g., natural lens removal, corrective lens fitting, occluder lens, etc.) initiated within a few weeks after birth. Following at least a one year period of postnatal rearing, the monkeys were set up for electrophysiological recordings from the striate cortex, usually contralateral to the aphakic eye. Multi-unit cortical activity was sampled in all layers at intervals of 100 um with the main target being layer IV. Normally reared control monkeys had 61 to 74% of the multi-unit activity in striate cortex driven equally, mostly or entirely by the contralateral eye. In contrast, a monocularly lid-sutured monkey had only 10% of cortical activity driven by the deprived eye. One uncorrected aphabic monkey had 23% of the cortical activity driven by the aphakic eye. For another monkey with a lenscorrected aphakic eye, 36% of the cortical activity was driven by the aphakic eye. Finally, a monkey with an occluded normal eye and a lens-corrected aphakic eye showed 70% of the cortical activity driven by the aphakic eye. We conclude from these results that the amount of cortical activity correlates well with the degree of normal vision provided to a developing monkey, and that given a relatively normal input, free from competition from the normal eye, an aphakic eye can retain physiological cortical connections.

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 Descriptive Title (80 characters): Geniculostriate System of Aphakic Monkeys

## Abstract:

Rhesus monkeys had the natural lens removed surgically from one eye shortly after birth. Subsequently the aphakic eyes of most of these monkeys were optically corrected to a nearpoint with extended-wear soft contact lenses. In addition, mosst monkeys wore opaque contact lenses to occlude the fellow, unoperated eye. The effects of these treatments on the visual system were assessed with anatomical, electrophysiological, and behavioral methods. The major finding was that the effects of the various treatments on the aphakic eye varied in degree depending uponn the relative amount of patterned input received by the aphakic eye compared to its fellow eye. Best results for aphakic eyes were obtained under conditions in which the aphakia was optically corrected to a nearpoint and the fellow eye was continuously occluded. The poorest results for the aphakic eye were obtained when no post-surgical treatment was provided to either eye. The behavioral, electrophysiological, and anatomical assessments of the treatment effects on the aphakic eyes correlated closely with each other. These results are consistent with a binocular competition model of visual development. Results obtained from the continuously occluded eyes that were opposite an aphakic eye are not easily explained with a binocular competition model, and the measured parameters of these occluded eyes were not always consistent. It is suggested that these latter results may reflect an effect of deprivation per se as opposed to a binocular competition effect. Some of our treatment conditions are similar to current clinical treatments for human infantile monocular cataracts, and for this reason our methods provide a nonhuman primate model for studying aphakia.

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 Descriptive Title (80 characters): Necrotizing Gingivitis (Noma) in an SIV/SMM Infected Infant Mangabey

### Abstract:

A T-lymphotropic retrovirus has been isolated from sooty mangabey monkeys in the Yerkes Center breeding colony. This virus, SIV/SMM, is morphologically identical to and serologically related to HIV. Although virus-infected mangabey monkeys are usually clinically normal, the virus does cause an AIDS-like disease in experimentally-infected macaque monkeys. Approximately 67% of the mangabeys checked to date have been seropositive and virus positive. In these initial studies, all virus-positive animals were sexually mature adults (90% of adults checked). More recently, SIV/SMM was isolated from a 5-month-old, female mangabey that was found dead in the outdoor breeding colony. At autopsy, the infant was emaciated and dehydrated and had an extensive necrotizing gingivitis that involved the upper gums and lips; the maxillae were exposed and the lesion had eroded through the hard palate. There was also a mild lymphadenopathy of the submandibular, cervical and mesenteric nodes. The lesions in this animal were compatible with a diagnosis of noma, a form of severe necrotizing gingivitis that has been associated with immunodeficiency, malnutrition, leukemia or AIDS in man and a retrovirus-induced immunodeficiency in nonhuman primates. The affected infant had antibodies to SIV/SMM and the virus was isolated from peripheral blood, spleen, mesenteric lymph nodes, liver and brain, suggesting an etiologic relationship to the occurrence of noma. The high incidence of infection in sexually mature animals in this colony and the recent documentation of infection in and infant suggests that the epidemiology of this HIV-like retrovirus infection in mangabeys may be comparable to HIV infection in humans (i.e. transmitted by sexual contact or perinatally).

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CECTION A

Chronic Fatal Disease in Gorillas Seropositive for STLV-I Antibodies

#### Abstract:

Sera from ten gorillas were tested by indirect immunofluorescent antibody assay, Western blotting and ELISA to human T-lymphotropic viruses for cross-regorilas were found to be antibody positive. Of the four seropositive gorillas, one is currently alive in the colony, whereas the other three have died with diarrhea, gastroenteritis, weight loss, shigellosis, and periodic episodes of anemia and lymphopenia. One of the three animals had severe oroesophageal candidiasis. The three deaths occurred over a period of 6 years, 8 months.

The second and third gorillas which died had contact with the first gorilla that died of a chronic, progressively debilitating condition. All three deaths occurred in gorillas that were seropositive to members of the simian and human retrovirus families. With the exception of one animal, other members of the gorilla colony are seronegative. Efforts are currently underway to attempt to isolate virus from the one seropositive animal that is currently in the colony. The relationship between STLV-I infection and disease in these gorillas is unknown at present.

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1a 3 4 7c 17	. 64 66	a) Collins, William E. b) B.Sc., M.S., Ph.D. c) Pathobiology and Immunobiology d) Centers for Disease Control, USPHS		X	11	Pan troglodytes				

 Descriptive Title (80 characters): Adaptation of <u>Plasmodium</u> sp. to Chimpanzees for Malaria Vaccine Studies

## Abstract:

Animals are inoculated and parasites obtained for (1) development of monoclonal antibodies to blood stages, (2) preparation of genomic libraries, (3) extraction of m-RNA for genetic engineering studies with E. coli, (4) antigen for serologic for (a) infection of mosquitoes through membrane feeding to produce sporozoites (c) to infect Aotus and Saimiri monkeys for the study of hypnozoites, and production of immune sera. The following parasites and animals have been inoculated during the past year: P. ovale - (Ellie, Lucy, Ossabaw, Augusta), P. vivax-Merv, Augusta, Heppie).

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Transplacental Active Immunization in Rhesus Monkeys

# Abstract:

Since it is known that the human neonate is deficient in its response to the antigenic stimulus of either protein or polysaccharide antigens during the first months of life, this study was designed to determine if vaccination of the mother can be used to enhance the antigenic response in infants. Eight pregnant rhesus monkeys have been immunized at various stages of gestation with commercially available diphtheria-tetanus vaccine. Following parturition, their infants will be checked within five days of birth for IgG, IgM and IgA antibodies to diphtheria and tetanus toxoid antigens. These eight infants together with four additional control infants will be bled at 2, 4 and 6 months of age and immunized with DT and PRP-D vaccine. Sera from the 12 infants will be tested for IgG, IgM and IgA antibodies against tetanus, diphtheria and PRP. Antibody titers and isotype class will then be compared between the three experimental groups. These studies will allow a determination of whether immunization strategies and techniques can be developed which will prime the fetus in utero to selected antigens. If such can be done, the administration of a booster dose at the time of birth should increase the infant's immune response and thereby prevent or decrease the severity of in-

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Intravesical Injection of Teflon for Vesicoureteral Reflux

# Abstract:

Recently intravesical/subureteric injection of polytef paste has been used to treat vesicoureteral reflux in over 400 children. Limited animal studies have reported no distant migration of polytef particles from the intravesical/subureteric injection site. In contrast this study in nonrefluxing monkeys demonstrates not only distant migration of polytef particles from the injection site but also a huge local foreign body granulomatous reaction has been identified.

We injected 0.4 cc (1/2 of human dosage) of polytef paste transurethrally into the intravesical/subureteric space of eight monkeys. At six months, five monkeys were sacrificed. The injection sites, pelvic and paraortic nodes, kidneys, liver, lungs, and brain of each animal were studied by standard and polarized light microscopy. In addition, x-ray microanalysis directed by transision electron microscopy was performed at selected sites. Distant migration of polytef particles from the injection site was confirmed in all animals. A voluminous local granulomatous reaction was found at all intravesical injection sites. In three living animals this granulomatous reaction is being followed lomas are clearly imaged and are actively growing. We believe that until the long term effects in humans are known, polytef paste should not be used in children with normal life expectancy.

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Refractive Keratoplasty: A Laboratory Investigation

## Abstract:

The purpose of our previous year's research has been to continue to develop and assess new refractive keratoplasty procedures as well as harvest basic science data on the cornea that will help understand and control the principles of refractive keratoplasty. The investigations on plus powered hydrogel intracorneal lenses implanted via a microkeratome lamellar keratectomy have been encouraging. The biocompatibility and accuracy of the refractive corrections have demonstrated the clinical safety and efficacy. The refraction data are less convincing for the minus powered hydrogel intracorneal lenses. This group will be expanded with improved lens design. Specifically, the research conducted during the past year involving nonhuman primates has been to:

- initiate longterm (3 year) postoperative histology and specular microscopy of monkey corneas with hydrogel intracorneal lenses;
- 2) initiate postoperative (greater than one year) histology and histochemistry of monkey corneas with polysulfone (unfenestrated) intracorneal lenses;
- 3) expand the efficacy evaluation of hyperopic and myopic hydrogel intracorneal lenses in the monkey model.

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 Descriptive Title (80 characters): Evaluation of the Long Term Effects of Irradiation in Rhesus Monkeys

## Abstract:

A group of 76 rhesus monkeys (55 irradiation-exposed and 21 non-exposed controls of comparable age) has been studied from year 10 to year 30 post-irradiation. Studies were designed primarily to document the incidence and characterize the types of tumors which occurred in this unique population. During this period, 68 of the initial group of animals died. Thirty-three of the 68 (48.5%) animals which died had one or more neoplasms at the time of death. Tumors occurred in 28 of 50 (56.0%) irradiation-exposed animals which died, and in 5 of 18 (27.7%) non-exposed controls which died. Consequently, 28 of 33 (84.8%) tumor cases occurred in irradiation-exposed animals.

Tumors were diagnosed in 16 of 24 (66.6%) bomb-exposed animals which died; 6 of 15 (40.0%) Co<sup>60</sup> exposed animals; and in 4 of 5 (80%) animals exposed to pure neutron irradiation. During this same time period, a tumor incidence of 4% (7 of 172) was encountered in other rhesus monkeys in our colony that were 10 years of age or older at the time of death.

The most frequently encountered tumors involved the intestinal tract (12 adeno-carcinomas and 1 leiomyosarcoma), and the second most frequently involved organ was the pancreas (2 acinar cell carcinomas, 1 acinar cell adenoma, and 4 islet cell adenomas). Other tumor types, in decreasing order of frequency, included adrenal adenomas or pheochromocytomas (4), soft tissue sarcomas (3), basal cell carcinomas of the skin (3), kidney carcinomas or adenomas (3), pituitary adenomas (2), thyroid carcinoma and adenoma (2), uterine leiomyoma (2), splenic hemangioma (2), lymphoma (2), 2 esophageal leiomyomas, and one each of glioblastoma of the brain, leukemia, seminoma, subcutaneous fibroma, subcutaneous lipoma, liver cell carcinoma, cholangiocarcinoma, salivary gland adenoma, squamous cell carcinoma of the mouth, and breast carcinoma. These observations suggest that irradiation exposure is cancerogenic in the rhesus monkey.

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1. Descriptive Title (80 characters): Amyloidosis in Nonhuman Primates

Abstract:

The occurrence of a high incidence of spontaneous amyloidosis (95 cases in 12 years) in the Yerkes colony (primarily in outdoor-housed animals) has presented a unique opportunity to evaluate the epidemiology, pathogenesis, etiology, immunologic features and possible modes of treatment or prevention of this increasingly important human and animal disease problem. The tissue distribution of amyloid, pathologic features, and clinical features of this disease in nonhuman primates are comparable to that seen in man. The disease in both man and nonhuman primates, as well as other animal species, is usually a progressive fatal disease, with no satisfactory method of treatment.

Amyloidosis has been observed in 7 species of nonhuman primates (74 rhesus, 11 pig-tails, 3 black apes, 3 macaque hybrids, 2 squirrel monkeys, 1 mangabey monkey and 1 stumptail macaque) housed in 22 different outdoor compounds. The disease has been diagnosed throughout the year and has occurred in animals from 9 months to more than 15 years of age. A significant number of the animals with amyloidosis have a history of arthritis.

Initial treatment trials with DMSO gave encouraging results. Three of 12 treated animals showed clinical improvement and significant reduction in the amount of tissue amyloid on repeat biopsies. Two of these animals continue to appear clinically normal (5 and 7 years after diagnosis) and low serum protein and albumin values returned to, and continue to be maintained at normal levels. One of the three animals died recently from hemorrhagic pancreatitis and did have recurrent amyloid in the spleen and intestine. Three of four other animals treated with DMSO are currently alive 5 years post-diagnosis; the other animal died 4 years after diagnosis. One of four animals treated with high doses of vitamin C is currently alive five years post-diagnosis. Three other vitamin C treated animals died at 3 and 6 years post-diagnosis. One untreated control died at 5 years post-diagnosis; a second untreated control is currently alive at 3 years post-diagnosis.

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 Descriptive Title (80 characters): SIV/SMM: Prevalence and Association with Disease in a Breeding Colony of Mangabey Monkeys

#### Abstract:

PART IT SECTION A

The mangabey breeding colony at the Yerkes Center has a high incidence of infection with SIV/SMM, a T-lymphotropic retrovirus that is morphologically identical to and serologically related to HIV. This mangabey colony, established in 1969 with wildborn mangabeys, currently consists primarily of lab-born animals. Overall, there has been no difference in the incidence of clinical disease in the mangabeys as compared to other species at the Yerkes Center. During the past 17 years, 26 of 76 deaths (34%) in the colony were due to clinical diseases, including enterocolitis, pneumonia, amyloidosis, septicemia and meningitis. Candidiasis, lymphadenopathy and splenomegaly were rarely encountered. Two neonates were found to have a herpetic (CMV) glomerulitis. Two recently encountered diseases in mangabeys, amebiasis and necrotizing gingivitis (noma), suggest that the virus infection may, on occasion, be associated with clinical disease and death. Amebiasis occurred in an 11-year-old female; noma occurred in a 5-monthold infant. Both animals were seropositive for SIV/SMM and virus was isolated from blood and multiple tissues from both cases, including the brain from the noma case. Although 90% of the adult mangabeys checked have been virus positive, this represents the first SIV/SMM isolation from an infant. The high infection rate in mature animals and the occurrence of infection in an infant suggests that transmission of SIV/SMM may be comparable to the transmission of HIV (i.e. by sexual contact or perinatally). These observations suggest the use of this colony of naturally infected mangabeys as a model system for study of the epidemiology and pathogenesis of an HIV-like retrovirus, and for identification of cofactors that may be associated with the occurrence of AIDS.

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1a 7b 19	56 64 66	a) McClure, Harold M. Anderson, Daniel C. Fultz, Patricia N. b) D.V.M.; D.V.M.; Ph.D. c) Pathobiology and Immunobiology d) CDC (P.N.F.)	X	X	7	Macaca nemestrina				

 Descriptive Title (80 characters): Response of Pig-tailed Macaques to SIV/SMM Infection

# Abstract:

A pig-tailed macaque, inoculated intravenously with SIV/SMM, developed a viremia that persisted until death 14 months post-inoculation. The animal had chronic diarrhea, lymphadenopathy, lymphopenia and thrombocytopenia and terminally was anemic and ataxic. At autopsy, there was generalized lymphadenopathy, splenomegaly and a 26% weight loss. Histology revealed lymphoid depletion and a diffuse infiltrate of multinucleated giant cells in lymph nodes, spleen, intestine, brain and most other tissues. The animal also had intestinal cryptosporidiosis, and retrovirus was isolated from multiple tissues, including the brain. Blood transfusions from this animal to 3 other pig-tailed macaques resulted in acute clinical disease in all 3 recipients. Two of these died at 7 and 9 days post-transfusion and the third recovered from the acute episode that was characterized by diarrhea, weight loss, thrombocytopenia and oral candidiasis. This animal subsequently died at 10 weeks post-transfusion. All animals which died had generalized lymphadenopathy, splenomegaly and hyperplasia, hemorrhage and necrosis of lymphoid tissue of the intestine. Histologically, lymphoid tissues were reactive and contained foci of necrosis and multinucleated giant cells. Bacterial organisms were not isolated or demonstrated by special stains in tissue sections. Three additional pig-tailed macaques were inoculated intravenously with a retrovirus isolated from either the initial case or a transfusion recipient. All 3 virus recipients developed acute clinical disease within 5 days and died within 7-8 days post-infection. Lesions in all 3 animals were comparable to those seen in the transfusion recipients. Our observations indicate that SIV/ SMM is either more pathogenic in the pig-tailed macaque or that the virus has become more virulent after passage in one animal.

PART II, SECTION A DRR SCIENTIFIC SUBPROJECT FORM GRANT NUMBER P 5 1 R R O O 1 6 5 - 26 REPORT PERIOD: January 1, 1986 to December 31, 1986 INSTITUTION: Yerkes Regional Primate Research Center 5 Science Code (a) Investigator(s) C T Usage Factor AXIS I AXIS II (b) Degree(s) 0 Н ARB Funds (c) PRC Division/Unit R Ε Number Species Used Allocated (d) Non-Host Institution la 56 a) McClure, Harold M. Χ 12 Macaca 7b 64 Anderson, Daniel C. mulatta 19 66 Fultz, Patricia N. χ b) D.V.M.; D.V.M.; Ph.D. c) Pathobiology and

 Descriptive Title (80 characters): SIV/SMM Infected Rhesus Macaques as Models for HIV Infection

Immunobiology

d) CDC (P.N.F.)

#### Abstract:

In order to determine the pathogenicity of an AIDS-like virus (SIV/SMM) isolated from sooty mangabey monkeys for rhesus macaques, 12 young rhesus ranging from 1 to 15 months of age were inoculated intravenously with approximately 104 TCID of the virus. Eleven of the 12 animals became virus positive and seroconverted within 3 to 6 weeks of inoculation; most of these have remained virus positive for periods of 7 to 20 months post-inoculation. Infected animals have shown variable degrees of peripheral lymphadenopathy, splenomegaly, diarrhea, weight loss and hematologic abnormalities, including lymphopenia, neutropenia and thrombocytopenia. Two deaths have occurred in this group of animals. One animal died at 15 months post-inoculation following a one month history of progressively worsening pneumonia that failed to respond to antibiotic therapy. At autopsy, the animal was found to have extensive pneumonia, generalized lymphadenopathy and massive splenomegaly. Histologic examination revealed diffuse infiltrates of multinucleated giant cells in the lungs, lymph nodes, spleen and other tissues. The second animal was found dead at 19.5 months post-infection without having shown any clinical signs of disease. This animal also had extensive non-bacterial pneumonia, generalized lymphadenopathy and splenomegaly

The susceptibility of rhesus macaques to infection with this HIV-like virus and the subsequent development of clinical and fatal disease provides a model for studying the acquired immunodeficiency syndrome and for use in the evaluation of newly developed anti-retroviral drugs or vaccines.

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Descriptive Title (80 characters):
 Retrovirus Serology and Virus Isolation Attempts in Selected Nonhuman Primate
 Populations

## Abstract:

In order to obtain additional information on the occurrence and distribution of retrovirus infections in various nonhuman primate populations, we have conducted serologic surveys on selected groups of nonhuman primates at the Yerkes Center, another U.S. primate facility and on animals maintained in Kenya. Peripheral blood cells from seropositive animals were cultured for retrovirus.

A total of 213 great apes (139 chimpanzees, 8 pygmy chimpanzees, 20 gorillas, 37 orangutans, and 9 gibbons) in the Yerkes colony were checked for antibodies to HTLV-I, HTLV-III and SIV/SMM. All great apes were seronegative for antibodies to HTLV-III and SIV/SMM; five chimpanzees were positive by EIA and IFA for antibodies to HTLV-I. Ten mangabeys and 23 African green monkeys maintained in Kenya were surveyed for the presence of antibodies to SIV/SMM; all mangabeys were seronegative but 7 of the 23 African green monkeys were found to be seropositive. A retrovirus was subsequently recovered from peripheral blood cells of one of the seropositive African green monkeys. Three of eight mangabeys maintained at another U.S. facility were found to be seropositive to SIV/SMM; a retrovirus was isolated from two of the three seropositive animals. Other monkeys in the Yerkes colony which have been screened for antibodies to SIV/SMM include 34 rhesus macaques, 23 pig-tailed macaques and 20 stumptail macaques. These were all seronegative except for one stumptail macaque. Despite the fact that this one stumptail macaque has repeatedly been seropositive, repeated attempts to isolate virus from peripheral blood cells of this animal have been negative.

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1a 2 7b	50b 64 66	a) McClure, Harold M. Anderson, Daniel C. Nahmias, Andre J. Schinazi, Raymond F. b) D.V.M.; D.V.M.; M.D.; Ph.D. c) Pathobiology and Immunobiology	X	X X	12	Macaca mulatta	·					

AIDS Drug Development

#### Abstract:

The objectives of this study, which is one part of a large program project grant concerning the development of new drugs for the treatment of HIV infections, are to utilize the rhesus monkey model to evaluate the toxicity and efficacy of compounds that are developed for the treatment of HIV infections. Newly developed drugs will initially be tested in vitro for anti-retroviral activity. Those which show promising anti-retroviral activity in vitro will be tested for toxicity in mice prior to testing for toxicity in nonhuman primates. Non-toxic drugs which show in vitro anti-retroviral activity will then be tested for efficacy in either the prevention or treatment of SIV/SMM infections in the rhesus monkey model.

Preliminary toxicity studies have been done in rhesus monkeys with three newly developed drugs which show promising in vitro anti-retroviral activity. Two of these drugs appeared non-toxic in rhesus monkeys, whereas one showed excessive toxicity. Since the latter appeared quite promising with regards to its in vitro anti-retroviral activity, this drug is being reformulated into another, hopefully, less-toxic form. The in vivo anti-retroviral activity of these agents will be evaluated in the near future in the SIV/SMM infected rhesus monkey model system.

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		d) Univ. of Conn.(R.J.C.)								

Treatment of Paratuberculosis in Stumptail Macaques

Abstract:

Naturally occurring Mycobacterium paratuberculosis infection in a colony of stumptail macaques has provided an opportunity to evaluate the efficacy of an experimental drug (LM-427; Rifabutine) in the treatment of this non-tuberculous mycobacterial infection.

Seven infected stumptail macaques have been treated for one year or more with Rifabutine. Two additional infected animals that were placed on treatment showed rapid deterioration of clinical condition and died within 5 to 6 weeks of the time treatment was initiated. At the time treatment was initiated, all animals were showing chronic diarrhea and marked weight loss; infection was confirmed in all animals by biopsy and/or culture prior to the initiation of treatment.

Five of the 7 animals treated for one year or more have shown dramatic improvement in their clinical condition. This includes improvement in general clinical appearance and marked weight gain. Repeat biopsies of the intestine and mesenteric lymph nodes of these 5 animals also showed dramatic improvement following treatment. This included a decrease or disappearance of the histio-cytic infiltrate in the lamina propria of the intestine and a decrease in the number or absence of acid-fast bacilli. Two of the seven treated animals did not respond to treatment, continued to show chronic diarrhea and progressive weight loss, and subsequently died of the infection. Treatment was discontinued after was sacrificed due to degenerative joint disease of the spine. The latter animal was negative for AFB at the time of autopsy. The remaining animals have been monitored for periods of 6 to 20 months after treatment was discontinued. These animals continue to appear clinically normal and have shown progressive weight gains.

PART II, SECTION A DRR SCIENTIFIC SUBPROJECT FORM GRANT NUMBER P 5 1 R R 0 0 1 6 5 - 26 REPORT PERIOD: January 1, 1986 to December 31, 1986 INSTITUTION: Yerkes Regional Primate Research Center 3 0 5 Science Code (a) Investigator(s) C T Usage Factor AXIS II AXIS II (b) Degree(s) 0 Н ARB Funds (c) PRC Division/Unit R Number Species Used Allocated (d) Non-Host Institution E R 1a 56 a) McClure, Harold M. Χ 38 Macaca 7a 66 Anderson, Daniel C. Χ arctoides 16c Swenson, R. Brent Χ Chiodini, Roderick J. Χ b) D.V.M.; D.V.M.; D.V.M. 9 Macaca Ph.D. mulatta c) Pathobiology and Immunobiology d) Univ. of Conn. (R.J.C.)

Descriptive Title (80 characters):

Paratuberculosis in Stumptail and Rhesus Macaques

# Abstract:

Until recently, paratuberculosis had not been reported in either humans or nonhuman primates. We have documented endemic infection with <u>Mycobacterium paratuberculosis</u> in a colony of stumptail macaques and a <u>M. paratuberculosis</u>-like agent has been recovered from humans with Crohn's disease.

Fourteen fatal cases of paratuberculosis have occurred in the stumptail colony within the past 6 years, and fecal cultures of 76% of the colony of 38 monkeys were positive for  $\underline{M}$ . paratuberculosis. Infected animals without obvious clinical disease were shedding as many as  $2 \times 10^6$  colony forming units of the organism per forming units of the organism per forming units of the organism per gram of tissue. Clinical signs in infected animals include chronic diarrhea and weight loss.

In order to determine the susceptibility of rhesus monkeys to  $\underline{\mathsf{M}}.$  paratuberculosis infection and to determine the infectivity of feces from animals that had been on treatment, experimental infection studies were initiated in young rhesus monkeys. Fecal material from an infected, non-treated animal and from an infected, treated animal, was administered by nasogastric intubation to three young rhesus, respectively. These animals have been monitored for two years for clinical signs of disease and feces have been cultured monthly for  $\underline{\mathsf{M}}.$  paratubercudiarrhea in recent months, fecal cultures from all animals have remained negative for  $\underline{\mathsf{M}}.$  paratuberculosis, and histologic examination of biopsies from the lower small intestine has not revealed acid-fast organisms or lesions.

These observations extend the natural host range of  $\underline{\mathsf{M}}$ . paratuberculosis to include nonhuman primates and add support to current suggestions that  $\underline{\mathsf{M}}$ . paratuberculosis may be pathogenic for humans.

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 Descriptive Title (80 characters): Chimpanzees Exposed to Human AIDS

# Abstract:

PART II. SECTION A

The objective of this study, done in collaboration with and funded by CDC, is to develop the chimpanzee as a model for the acquired immunodeficiency syndrome (AIDS). The availability of such a model will permit more detailed investigations of the pathogenesis, modes of transmission and immunologic features of AIDS, and will provide an animal model in which anti-retroviral drugs and vaccines can be tested.

To date, 13 chimpanzees have been either directly or indirectly exposed to either LAV-1, LAV-2 or ARV prototypes of the human AIDS virus (HIV). As a result of these studies, the chimpanzee has been established as a model for infection with the human AIDS virus. Although infected animals have remained clinically normal, they have shown variable degrees of mild, transient lymphadenopathy and some hematologic and immunologic changes. We have demonstrated their susceptibility to infection by way of intravenous inoculation of HIV, by way of blood transfusion from an infected chimpanzee, and by exposure of the vaginal mucosa to a solution of LAV. Infection has not occurred following long term cage contact with infected chimpanzees or by exposure to HIV by way of the oral mucosa.

Although LAV infected chimpanzees have not, to date, developed an AIDS-like disease, they are susceptible to infection with the human AIDS virus, and thus should be adequate models for the evaluation of promising anti-retroviral drugs or vaccines.

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1a 7a 17 18 19	64 66	a) McClure, Harold M. Gordon, Thomas P. King, Frederick A. Olkowski, Zbigniew b) D.V.M.; M.S.; Ph.D.; M.D. c) Pathobiology and Immunobiology	XXX	X	54	Cercocebus atys					

Characterization of Experimental Leprosy in the Mangabey

## Abstract:

This study, done in collaboration with the Delta Primate Center, was initiated following the occurrence of a spontaneous case of lepromatous leprosy in a mangabey monkey, and the subsequent transmission of the disease to mangabeys from the Yerkes colony. Experimental infection studies were done at the Delta Center; pathologic evaluations to compare mangabey leprosy with that seen in man was done at the American Registry of Pathology; and the Yerkes Center was primarily responsible for development of the mangabey breeding colony to provide mangabeys for the infection studies, and the documentation of baseline hematologic, blood chemistry, and immunologic parameters for the mangabey.

During past years, the mangabey breeding program has been very successful; we have averaged 18 surviving progeny per year for a net annual reproductive success rate of 60% (18 surviving infants/30 mature female breeders). The stillbirth rate has averaged 7% and the neonatal death rate has averaged 5%. There has been a net increase in colony size, despite the fact that we have shipped 8-10 mangabeys/year to the Delta Center for experimental leprosy infection studies. During the past four years, 40 mangabeys have been shipped to the Delta Center. Baseline hematologic, blood chemistry and immunologic values have been documented on all of the animals shipped. Despite the success in experimental transmission of leprosy to the mangabey monkey and in the maintenance of a breeding colony which was providing more than adequate numbers of mangabeys for the experimental infection studies, the funding agency terminated this study as of August 1986.

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1a 16e	44 58	a) McClure, Harold M. King, Frederick A. Anderson, Daniel C. Caplan, Daniel C. b) D.V.M.; Ph.D.; D.V.M.; M.D. c) Pathobiology and Immunobiology	X X	X		Macaca mulatta		

 Descriptive Title (80 characters): Genetic Factors in Cystic Fibrosis-like Pancreatic Disease in a Rhesus Monkey

## Abstract:

This study was initiated following the death of a 6-month-old rhesus monkey that was found at autopsy to have pancreatic lesions essentially identical to those seen in CF in humans. Since CF is considered to be genetically transmitted as an autosomal recessive trait, a line breeding program was initiated to evaluate the possible genetic basis for this unique nonhuman primate lesion. This breeding program utilized the father and mother and other relatives of the CF-like case. During the first 3 years of the study, 43 F1 generation offspring were produced, with 21 of these being females. During subsequent years, the breeding program has concentrated on the production of F2 generation offspring (using father of CF-like case and F1 generation females).

To date, eight F2 generation offspring have been born. All offspring are monitored by sweat tests, fecal trypsin determinations and clinical appearance (steat-prine) properties, recurrent respiratory infections and poor growth). None of the offspring have shown any signs or lesions suggestive of a CF-like disease, and sweat test and fecal trypsin values have been within normal limits.

If this CF-like nonhuman primate disease can be shown to have a genetic basis, a controlled breeding program should be able to establish a colony of animals with this trait, and thus provide a nonhuman primate model for cystic fibrosis studies.

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1a 3 6 16b 16F	39 60 64 76	a) Metzgar, Richard S. b) Ph.D. c) Pathobiology and Immunobiology	X		5	Pan troglodytes	·			

Immunological and Molecular Biological Studies of Primate Antigens

#### Abstract:

The overall goals of this project are to continue to define selected antigens of human cells and to establish a nonhuman primate model for oncogene insertion. The uniqueness of the study is that it utilizes the immunologic perspectives of a species remarkably similar to man to recognize epitopes on human antigens that may not be seen by other mammalian species.

The specific aims are to: 1) Produce chimpanzee monoclonal and monospecific polyclonal antibodies to selected human tumor antigens related to growth differentiation and transformation. 2) Transform chimpanzee somatic cells by in vitro transformation/transfection with cloned human oncogenes and/or human tumor DNA.

During the past year as part of specific aim 1, we have continued to immunize chimpanzees with a variety of human tumor antigens and are evaluating their polyclonal antibody response. We will continue these studies in the next year and will also attempt to generate monoclonal antibodies from these animals. Most of the efforts during the past year on specific aim 2 have been concerned with evaluating methods and vectors for the transfection of genes into chimpanzee somatic cells.

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1a 2 7a 14 22	50b 62	a) Offenbacher, Steven b) D.D.S., M.M.Sc., Ph.D. c) Pathobiology and Immunobiology		X	24	Macaca mulatta	•		

Effects of Flurbiprofen on the Progression of Periodontitis in Macaca mulatta

## Abstract:

The effect of the nonsteroidal anti-inflammatory drug flurbiprofen has been studied in the ligature-induced and spontaneous periodontitis model in the rhesus monkey, Macaca mulatta. Twenty-four adult monkeys with incipient periodontitis were divided into three disease-matched groups. Two groups received flurbiprofen at doses of either 0.27 mg/kg/day or 7.1 mg/kg/day delivered systemically via osmotic minipump. A split-mouth approach was used, placing ligatures on one side and monitoring the progression of periodontitis at regular intervals for six months. Clinical measurements included standardized radiographs, Ramfjord attachment level determinations and assessments of redness, edema and bleeding on probing. There was a statistically significant inhibition of attachment loss, P=  $1.7 \times 10^{-5}$ , gingival redness (P 0.05) and bleeding on probing (P 0.05) in ligature-induced and spontaneous periodontitis in the flurbiprofen-treated animals at six months. Eight of 8 ligated control monkeys lost significant attachment (mean loss of 1.03 mm/site). Only 3 of 15 flurbiprofen-treated ligated monkeys lost any significant attachment with an overall mean gain of 0.16 mm/site. The odds of a control ligated monkey undergoing significant attachment loss in 6 months are elevated 29.3 fold, as compared to the flurbiprofen-treated, cohort monkey group. These data provide further evidence for the central role of cyclooxygenase products in the progression of periodontal disease. The ability of flurbiprofen to inhibit periodontal attachment loss, even in the presence of gross plaque accumulation, has significant implications for the potential use of flurbiprofen as an adjunctive periodontal therapeutic modality.

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1a 17	64	a) Oh, Jung H.  McClure, Harold M. b) M.D.; D.V.M. c) Pathobiology and Immunobiology	X	X	12	Macaca mulatta		

Descriptive Title (80 characters):
 Lack of Effect of ACD (acid-citrate-dextrose) Infusion on Blood-Induced Sensitization

# Abstract:

We previously reported that prior transfusion of platelets, irrespective of their origin, inhibited the development of lymphocytotoxic antibodies caused by blood transfusion. Since autologous platelet transfusion was also inhibitory, we decided to rule out a possible effect of ACD (acid-citrate-dextrose) anticoagulant, which was used in all blood samples.

Ten male rhesus monkeys were subjected to the following experimental protocols: (1) infusion of ACD solution (0.3 ml/kg) twice at a one-week interval, and (2) transfusion of fresh whole blood (2 ml/kg) from a random donor twice at a one-week interval. One week after these procedures, a serum sample from each animal was tested for lymphocytotoxcity against the donors.

Nine out of the 10 animals were found to have developed antibodies. The sensitization rate (90%) in this group was equal to that of the control, untreated group, which was also 90% in our earlier study.

Thus, we conclude that the nonspecific immunosuppressive effect of random platelets, including autologous platelets, was not due to ACD solution.

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1a 9 13 21	48 52 70 86	a) Patterson, C. Anne Brann, Alfred W. Klein, Luella b) M.D.; M.D.; M.D. c) Pathobiology and Immunobiology		X X X	20	Macaca mulatta			

Telemetry Documentation of Fetal Heart Rate and EEG Before and During Birth in Rhesus Monkeys

# Abstract:

This project addresses the question of how oxygen deprivation affects the heart rate and electroencephalographic changes in the fetus during the entire birthing process. This work requires expertise in several areas including timed breeding, fetal surgery, and electrical engineering. Timed breeding has continued at the Yerkes Primate Research Center during the past year and is essential for the success of the project. Early in the calender year surgery was performed on one fetus at 138 days gestational age. The infant delivered at 151 days gestation and weighed 200 grams. Heart rate and brain activity were recorded remotely from this fetus. The telemetry device had produced excessive pressure on the back, although the animal lived and is presently doing well. Due to the size of the telemetry device a modification was developed which split the transducer into two separate parts that are joined by two wires. This was implanted into a 7month-old animal. Recordings were easily made of both heart rate and electrolencephalographic activity.

Other sources for telemetry transducers were also explored. A smaller commercially available device was found but its depth is still too large for use without causing undue pressure and it allows for monitoring of heart rate only. A smaller more compact telemetry transducer which will monitor ECG, EEG and EMG is being developed in collaboration with the Georgia Institute of Technology. Equipment including a 4 channel tape recorder and an anesthesia machine for controlling the oxygen environment of the primate, and equipment for monitoring the fetus and mother were acquired. The obstetric anesthesia department has also agreed to provide anesthesia for all future surgery. Utilization of the data assessing the Macaca mulatta pelvis by x-ray pelvimetry was expanded by the performance of MRI on the same 6 animals. Comparison of the two techniques was done and our findings have been submitted for publication.

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1a 2 9 19	39 64 76b	a) Seigler, Hilliard F. b) M.D. c) Pathobiology and Immunobiology	X		2	Pan troglodytes	·

 Descriptive Title (80 characters): The Immunogenicity of Human Tumor Antigens

# Abstract:

The basic goal of this research is to evaluate the immunogenicity of human tumor associated antigens (TAA) and the ways in which the response against these TAA might be selectively manipulated. With the development of monoclonal antibody technology has come the definition of multiple human tumor associated antigens. However, in that most monoclonal antibodies developed to date are of murine origin, the potential clinical impact of the TAA defined by these TAA cannot be evaluated. As an alternative, we are purifying individual TAA from human melanoma cells and are evaluating the chimpanzee response to these TAA. Our first set of manuscript submitted for publication. A second study is now underway using purified GD3 as immunogen. Evaluation of humoral and cell-mediated immune responses to these TAA suggest that each might be of potential clinical benefit as immunotherapeutic agents. A second goal is the development of chimpanzee monoclonal antibodies reactive with the immunizing TAA.

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1a 3	48 52	a) Spector, Myron Swenson, R. Brent b) Ph.D.; D.V.M. c) Pathobiology and Immunobiology	X	X	13	Macaca mulatta	,		

Descriptive Title (80 characters): Porous Polyethylene and Porous Polysulfone Tooth Roots

#### Abstract:

Porous polysulfone coated artificial tooth roots, fabricated in our laboratory, were implanted into edentulous premolar mandibular sites in rhesus monkeys. The objective was to clinically and histologically evaluate the performance of the free-standing implants to test the hypothesis that the bone ingrowth into the porous polysulfone coating will provide long term stabilization of endosseous dental implants. Implants with three diameters and two lengths were fabricated to provide for selected sizing for future investigations of implant performance in anterior and posterior sites.

The specific aims for the study were to: 1) fabricate porous polysulfone coated artificial tooth roots with diameters of 3, 4, and 6 mm and lengths of 7 and 12 mm, 2) characterize the pore structure and mechanical properties of the implants, 3) implant the porous coated artificial tooth roots in rhesus monkeys, 4) clinically evaluate the performance of the implants, 5) continue to construct a survival curve for this implant serving as a free-standing mandibular, posterior tooth in occlusion, and 6) continue to quantitatively evaluate the histological

response to the implants.

The artificial tooth roots were produced by sintering particles of polysulfone to a pure titanium core. The strength of attachment of the coating to the metal core was determined from mechanical pushout testing. The sintering conditions and other details of the fabrication process were determined in the O3 year of the study. Quantitative optical microscopy will be used to determine the percent porosity and average pore size of the porous polysulfone coating. The implantation procedure was the same as previously described. Clinical evaluation including radiography and measurement of mobility, pocket depth, and width of keratinized gingiva were conducted at monthly intervals. Histomorphometric analyses were performed on undecalcified microtome and ground sections of postmortem specimens using a semi-automated image analysis system.

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1a 25b	70 86	a) Sternberg, Paul Michels, Mark b) M.D.; M.D. c) Pathobiology and Immunobiology		X	2	Macaca mulatta			

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Descriptive Title (80 characters):
 Operating Microscope Light Retinal Phototoxicity

## Abstract:

PART II. SECTION A

The concept of instrument-induced retinal light toxicity is well established. Some attribute this damage to ultraviolet (UV) irradiation while others have warned of infrared (IR) effects. We recently demonstrated that the majority of non-visible irradiation emitted from the operating microscope is in the IR range. We also confirmed that the bulk of the IR could be eliminated with a blocking filter without significantly reducing visible light. In this study, using rhesus monkeys, we are investigating whether use of an efficient IR filter would decrease the severity of retinal damage induced by the operating microscope. The light is focused on the cornea and pupils are dilated to simulate surgical conditions. One eye is exposed to the Topcon OMS 300 microscope light at the medium setting fitted with an IR blocking filter (transmitting 375-700 nm) while the fellow eye serves as a control with exposure to the unattenuated light. Various exposure durations were used. The IR filter eliminates 25% of total irradiation. Animals are examined at one and two week intervals by indirect ophthalmoscopy, fundus photography, and fluorescein angiography. They are sacrificed at two weeks and eyes are evaluated histopathologically.

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1a 25b	86	a) Vela, M. Angela b) M.D. c) Pathobiology and Immunobiology		X	3	Macaca mulatta	,			

Goniosynechialysis for Neovascular Glaucoma

#### Abstract:

Three monkeys underwent  $\underline{in}$   $\underline{vivo}$  two-step perfusion to determine baseline facility of outflow OU. Argon laser photocoagulation to the superior and inferior retinal branch veins in one eye of each monkey was performed.

One monkey had an intracapsular cataract extraction with a Weck vitrectomy in the previously lasered eye. This eye developed a retinal detachment. Following appropriate evaluations, the monkey was returned to the colony.

A second and third monkey underwent mechanical lensectomy/vitrectomy in the previously treated lasered eyes. Iris and angle neovascularization developed in both treated eyes. Following neovascularization of the anterior segment, one of the monkeys developed a cyclitic membrane which did not permit continuation of the study (laser to the retina was not possible). This monkey was then returned to the colony after appropriate evaluations determined that the animal was comfortable.

The third monkey with classic anterior segment neovascularization, i.e., neovascular glaucoma, then underwent argon laser panretinal photocoagulation. Once the eye was "quiet", i.e., the neovascularization had regressed, goniosynechialysis was performed. This monkey is currently under observation to assess the results of surgery.

# DIVISION OF REPRODUCTIVE BIOLOGY

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- R. Nadler
- M. Wilson

<u>Associate</u> ,	<u>Affiliate</u>	<u>and</u>	Collaborative	Faculty
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D. Mann	Department of Physiology, Morehouse College School of Medicine
D. Martin	Division of Respiratory Therapy, Georgia State University
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Department of Biology, Clark University

K. Gopalkrishnan

Institute for Research in Reproduction, Bombay, India

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1a 3 23	48 74b 92	<ul> <li>(a) Gould, Kenneth G. Eley, R.M.</li> <li>(b) Ph.D., Ph.D.</li> <li>(c) Reproductive Biology</li> <li>(d) Institute of Primate Research, Nairobi, Kenya</li> </ul>	X	X	17	Papio cynocephalus anubis			

Descriptive Title (80 characters):
 Modification of cervical mucus using intravaginal sponges and the effect
 upon pregnancy

#### Abstract:

The physical characteristics of cervical mucus may be modified by alteration of the concentration of the contained electrolytes. This modification could affect fertility. The experiment will address this question utilizing vaginal sponges as the delivery system for the electrolytes solution. A pilot study was completed during the reporting period to determine the effect of anesthetic and sponge insertion and removal upon pregnancy rate in baboons. Seventeen animals (33 menstrual cycles) were untreated and had a pregnancy rate of 27%. This compared to a 37% rate in 12 animals/16 cycles. Results suggested that there was no evidence that manipulation involved with sponge insertion and removal affected pregnancy. Moreover, as sponges were fitted prior to mating it was apparent that pregnancy could occur even with the nontreated device in place.

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1a 60 23 92	<ul> <li>(a) Gould, Kenneth G. Hinton, Barry T. Young, Leona G.</li> <li>(b) Ph.D., Ph.D., Ph.D.</li> <li>(c) Reproductive Biology</li> <li>(d) University of Virginia School of Medicine</li> </ul>	X	X X	6	Pan troglo- dytes	•			

Alteration of Sperm Composition at Ejaculation and Capacitation

# Abstract:

Motility patterns of caput epididymal chimpanzee sperm, caput epididymal chimpanzee sperm incubated in vitro with chimpanzee cauda epididymal fluid, and cauda epididymal chimpanzee sperm were assessed quantitatively. Sperm recovered from the caput epididymis showed no motility, whereas sperm recovered from cauda epididymis showed progressive forward motility. After incubation in cauda fluid, approximately 25 percent of caput epididymal sperm showed some motile activity. Electrophoretic analysis of  $^{\rm I-labeled}$  sperm plasma membrane preparations revealed that the surface of caput epididymal sperm, incubated in cauda fluid, was modified by the appearance of a major protein-glycoprotein surface component with an apparent molecular weight of 27 Kd. This 27 Kd component was not detected on caput epididymal sperm incubated in buffer or in caput fluid. However, it was present in cauda fluid and on cauda epididymal sperm. Binding to caput epididymal sperm was cell specific in that chimpanzee erythrocytes incubated in cauda fluid did not bind this 27 Kd cauda Motility patterns of ejaculated chimpanzee sperm and of ejaculated chimpanzee sperm incubated in the uterus of adult female chimpanzees also were assessed quantitatively. Ejaculated sperm showed progressive forward motility, whereas in utero incubated ejaculated sperm showed hyperactivated motility typical of "capacitated" sperm. Electrophoretic analysis of  $^{125}\text{I-labeled}$  sperm plasma membrane preparations revealed the loss of a 27 Kd component from the surface of sejaculated sperm after in utero incubation. No significant change in the I-distribution pattern was detectable when ejaculated sperm were incubated in buffer. These results suggest that lumenal fluid component which becomes adsorbed to the surface of chimpanzee sperm during maturation in the epididymis and which is removed from the surface of mature chimpanzee sperm in the female reproductive tract affects sperm motility.

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Alteration in Surface Charge and Motility of Chimp Sperm During Maturation

# Abstract:

Scanning electron microscopy and x-ray analysis (SEM/EDX) has been used previously to examine the surface charge of primate spermatozoa (sp). We used SEM/EDX to analyze total charge and charge distribution in sp from the caput (CA) and cauda (CU) epididymis and ejaculate (E) of chimpanzees. CA and CU sp were obtained using micropuncture. Ejaculates were collected using an artificial vagina. After centrifugation sp were washed in PBS, fixed in 2% glutaraldehyde in PBS, washed and exposed to colloidal Fe for 30 mins at a pH of 1.6, t  $20^{\circ}$ C. After two washes in 12.5% HAc aliquots were air dried on carbon plates and Fe measured. Fe was expressed as % of total elements detected (Na, Cl, S, P, and K). E sp (samples n = 4) showed a range of Fe of Distribution was multimodal with modes of 23, 31, 39 and 46%. relative size of these populations did not correlate with X:y or live dead ratio. CA sp (sample n=2) showed a mean Fe of 21%, and the distribution was unimodal (Range 9 to 40%). CU sp (sample n=2) showed a trimodal distribution with modes at 22, 35 and 42% (range 8 to 72). These preliminary findings support the hypothesis that specific alterations occur in the surface of sperm as they transit the epididymis; that net surface negative charge increases during sp maturation, and the infertility may be associated with altered surface charge in E sp. This work provides evidence of development of distinct populations of sperm during epididymal maturation in the primate. The work is being expanded to include quantitative measurement of sperm motility patterns. This data (motility and charge) will be collated with alteration in fertilizing capacity of sperm.

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Artificial Breeding of Great Apes

# Abstract:

The goal of this project is to further establish artificial breeding of chimpanzees as an effective means for increasing the birth rate at facilities in the United States which house populations of these animals.

The effectiveness of artificial insemination methodology will be improved by evaluation of the type of hormone treatment used to induce and synchronize ovulation time. The optimum route for semen delivery, and the minimum semen quality and optimum concentration will be determined.

Improved methods for cryopreservation of semen from chimpanzees and rhesus monkeys will be evaluated and monitored using  $\underline{in}$   $\underline{vitro}$  tests designed to identify maintained fertilizing capacity and morphological integrity.

A semen bank will be established primarily for chimpanzee semen, with addition of other ape semen when available.

Once developed and ongoing, this artificial breeding program should 1) be inexpensive to maintain, 2) provide additional knowledge concerning the reproductive physiology of the great apes, and 3) be adaptable to zoos desiring to improve their own colonies of these animals. Just as important will be the maintained integrity of these animals through maximum use of the gene pool. It is essential to provide a continued and adequate supply of great apes, particularly chimpanzees, for biomedical research in to human health-related problems for which they are the only applicable models.

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Reduction in neonatal mortality by telemetric monitoring

# Abstract:

The rate of perinatal mortality of chimpanzees could be reduced if it were possible to identify the precise time the infant became at risk of anoxia or other detrimental stimuli. This will be accomplished by implantation of a temperature sensitive radio transmitter in the vagina of pregnant chimpanzees. As soon as delivery is under way we expect the transmitter to be expelled, and the resulting temperature drop will signal the need for immediate observation and, if needed, clinical intervention in the delivery. Initial tests have identified a suitable transmitter and carrier system.

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1. Descriptive Title (80 characters):
Steroid receptor dynamics in the vervet monkey during normal and prolonged menstrual cycles

Abstract: Sixteen individually caged adult female vervet monkeys (Cercopithecus aethiops), whose reproductive parameters had been studied for years were hysterectomized/ovariectomized during either the late follicular (15.4+4.7+S.D.) days or luteal (27.8+4.7 days) phases of the normal cycle (20-50 days), or during prolonged intermenstrual intervals (PII; 99.0+2.5 days) since the previous menses). These latter animals showed characteristics of both follicular and luteal phases with their ovaries containing both corpora lutea and large antral follicles. In addition systemic oestradiol and progesterone concentrations were raised. Analysis of cytoplasmic oestrogen and progestin receptors (CER and CPR) revealed that endometrium during PII had CER levels of 0.58+0.07 pmol/mg protein, similar to those of the follicular phase 0.60+0.12); CPR levels (1.20+0.87) were not different from those of the luteal phase  $(1.05\pm0.45)$ . The ratio of CPR to CER during the luteal phase was about tenfold higher than that of the follicular phase. Levels during PII were intermediate between the two phases. Under receptoractivating conditions, the DNA-binding components of the PII cytoplasmic fraction underwent over 40% loss while those present during both phases of the normal cycle doubled. The hormone-binding sites at all times remained intact indicating that the DNA and hormone-binding sites are distinct on both CER and CPR.

Less than 50% interaction of CER/CPR with DNA-cellulose was obtained, indicating the presence of only limited quantities of cytoplasmic activating factors which may be a prerequisite for receptor binding to the genome. During PII, accumulation of nuclear oestrogen receptor was evident in PII endometrium with luteal PHASES (37 and 52% respectively). These data, suggesting a possible be indicative of endometrial dysfunction during PII. This could lead to a delay in menstruation.

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Descriptive Title (80 characters):
 Combined GnRH Agonist and Testosterone Treatment Induces Azoospermia in Male Monkeys

Abstract:
We examined the effect of continuous sc infusion of a gonadotropin releasing hormone (GnRH) agonist (Ag) and testosterone (T) supplementation on spermatogenesis and the potential fertilizing capacity of sperm in 15 rhesus monkeys in order to determine whether T replacement therapy alters the testicular response to the Ag. Monkeys were divided into three groups of five animals each. One group was treated with a low dose of the Ag (5 ug/day x 24 wk and then 10 ug/day for 20 wk) to prolong the oligospermic phase prior to the onset of Groups two and three were treated with 25 ug/day of the Ag for 44 wk. Group three also received T replacement therapy (sufficient to maintain serum values of T in a normal physiological range, 4-5 ng/ml). There was an initial short-lived rise (lasting approximately a wk) in serum LH and T at the onset of treatment in Groups one and two, but then levels of both hormones fell below pretreatment values where they remained throughout the treatment period. The suppression of LH and T was much greater in the group treated with 25 ug/day of Ag. Similar LH and T changes occurred in Group three except that T supplementation prevented serum T values from falling below the physiological The decline in secretion of LH was associated with a reduction in the pituitary sensitivity to an iv bolus of native 25 ug GnRH. The serum response of LH and T response to GnRH was either abolished or greatly reduced in the two treated with 25 ug/day of Ag, and suppressed to less than 50% of the pretreatment level by 5-10~ug/day of Ag. Four of five monkeys treated with 25 ug/dayof Ag alone became azoospermic within 21 wk. All five animals treated with the high dose of the Ag and T became azoospermic (mean time to onset = 12.6 wk). Four of five monkeys treated with 5-10 ug/day Ag exhibited azoospermic ejaculates during the late treatment and early posttreatment period, but mean sperm count in this group while reduced did not achieve azoospermia. The data suggest that GnRH analogue treatment, combined with androgen therapy to maintain libido and potency, may be workable approach to contraception in the human male.

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1. Descriptive Title (80 characters): Failure of <u>In Vivo</u> and <u>In Vitro</u> Gonadotropin Releasing Hormone Agonist Treatment to Directly Alter Steroidogenesis by the Primate Testis

#### Abstract:

PART II, SECTION A

Three experiments were performed to determine whether gonadotropin releasing hormone (GnRH) agonists can directly alter testicular steroidogenesis in primates. In Experiment 1, adult male monkeys were treated for 10 mo with a GnRH agonist (Ag; 25 ug/day; Wy-40972; Wyeth Labs) alone or in combination with testosterone (T) administration (sufficient to maintain serum T values between 4-5 ng/ml). The testicular response to HCG (50 IU; im) was determined during pretreatment and at the end of the treatment period. In a second experiment, 100 ng of Ag or saline was infused over 1 min into the testicular artery of adult male monkeys (N = 7), and blood samples collected from the testicular and femoral vein over the next 2 h for LH and T assay. In a final experiment, testicular interstitial cells from a peripubertal monkey were incubated for 24 hr. The effect of Ag on basal and HCG-stimulated T production from these interstitial cells was determined. In Experiment 1, basal and peak values of serum T after HCG stimulation were reduced by 10 mo of Ag administration, but the actual sensitivity of the testis to HCG was not altered by Ag treatment alone. In contrast, the combination of Ag and T treatment reduced the sensitivity of the testis to HCG to 28% of the pretreatment level. In Experiment 2, acute infusion of 100 ng of Ag into the testicular artery of adult male monkeys did not alter systemic serum LH or T values or serum T concentrations in the testicular vein over the next 2 h. In Experiment 3, Ag treatment for 24 h failed to alter basal or HCG-stimulated T production from isolated testicular interstitial cells. These data clearly demonstrate that Ag treatment does not directly alter steroidogenesis by the primate testis. However, chronic administration of physiological doses of T greatly attenuated testicular sensitivity to HCG in Ag-treated adult male monkeys. The mechanism of this reduced sensitivity to gonadotropin remains to be determined. (Supported by USAID Grant #DAN-5053-G-SS-5081-00).

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la	14 23	(a) Mann, David. R. (b) Ph.D. (c) Reproductive Biology (d) Morehouse School of Medicine		X	15	Macaca mulatta				

 Descriptive Title (80 characters): Treatment of Endometriosis in monkeys: Effectiveness of continuous infusion of a gonadotropin-releasing hormone agonist compared to treatment with a progestational steroid

#### Abstract:

The use of a GnRH agonist or a progestational steroid (levonorgestrel) for the treatment of endometriosis in monkeys was compared. Four monkeys with spontaneous endometriosis were treated for six months with continuous infusion of a GnRH agonist (25 ug/day). Five animals with surgically-induced endometriosis were treated with the same agonist for three months. An additional group of five monkeys with surgically-induced endometriosis was treated orally with levonorgestrel (1 mg/kg/day), while a final group of four monkeys served as untreated controls. During agonist treatment, the four monkeys with spontaneous endometriosis gained body weight and had a greater than 80% decline in cyst size (representing a decline in secretory activity). Monkeys with surgically-induced endometriosis had almost total resolution of endometrial lesions during agonist treatment, which was maintained throughout a four-month posttreatment period. After initial stimulation at the onset of the GnRH agonist infusion, serum LH, FSH, estradiol, and progesterone levels decreased to near the levels of detection, where they remained until treatment was terminated. In comparison, levonorgestrel reduced endometrial lesion size, but the monkeys did not resume normal cycles as early as those treated with the agonist. Levonorgestrel-treated monkeys had normal serum LH and FSH levels. but low serum estradiol and progesterone levels. The results of this study indicate that either continuous infusion of a GnRH agonist or administration of levonorgestrel is effective for treating endometriosis in monkeys. hormonal data suggest that the GnRH agonist acts at the level of the hypothalamus and pituitary, whereas levonorgestrel acts at the ovarian levels. (Supported by a grant from Wyeth Laboratories).

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Rehabilitation of Reproductive Function in Paraplegic Men

# Abstract:

We continued to clinically evaluate the effectiveness of a rectal probe electrostimulation (RPE) device which we developed for initiating erection and seminal emission in paraplegic patients. Fourteen patients, with injury level ranging from T5 - T12, were studied. Additional experience was gained in the logistics of Foley catheterization to ensure antegrade seminal emission, which are complicated by individual variability due to anatomical differences and, as well, differences in bladder, neck size and tone brought about by surgical intervention to improved urination.

Work was initiated on the design and fabrication of a battery-driven RPE device that could be used in the home setting by patient and spouse. Extensive preconstruction discussion of design details was necessary to ensure that all options for function and safety could be met. Plans include introductory clinical testing of this device in the coming year.

Studies are also continuing on the topic of improved sperm motility, thereby increasing its fertility potential. This is important, since so many patients remain interested in siring children.

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Behavioral Effects of Oral Contraceptives in Chimpanzees

# Abstract:

The aims of the research are 1) to document the relationship between menstrual cycle patterns of female hormones and reproductive behavior of chimpanzees and 2) to determine whether oral contraceptives (OCs) have adverse effects on the behavior patterns. Oppositely sexed pairs of chimpanzees are tested behaviorally during natural cycles (control) and during cycles with OC administration, using two different test paradigms under each condition. Urine is collected from the female for hormone assay to facilitate interpretation of results in terms of the hormonal regulation of behavior. In one paradigm, the female is confined with the male in a single cage, with little opportunity for choice regarding mating. In the second paradigm, the female must work (lever press) to gain access to the male. The two paradigms, previously used successfully with gorillas and orang-utans, permit assessment of different components of male and female behavior, contributing to a comprehensive evaluation of hormone-behavior relationships during natural cycles and cycles with OC adminis-The data from natural cycles will complete our comparative studies of endocrine correlates of reproductive behavior in the great apes. of the endocrine and behavioral similarities between the chimpanzee and human, the results related to OC administration should have implications for humans with sexual problems, where use of OCs is thought to contribute to the etiology of the problems. The results with OCs may also provide us with an acceptable method for experimentally manipulating hormone levels of intact females, necessary for investigating cause and effect relationships (as contrasted with correlations) between hormones and behavior.

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1. Descriptive Title (80 characters):

Biobehavioral Development of Chimpanzees

#### Abstract:

The long-term goal of this research project is to develop a program of captive rearing for chimpanzees that maximizes social, reproductive and maternal competence. The specific objectives are (1) to assess the effect of different rearing conditions on the longitudinal study of chimpanzee biobehavioral ontogeny, (2) to document individual differences in the early temperament, quality or security of attachment bonds and the behavioral and physiological response to mild challenge situations, (3) to investigate the stability and predictability of measures of temperament in chimpanzees, and (4) to determine the long-term consequences of these individual differences, especially in terms of later adequate sexual and maternal behavior. Two groups of chimpanzees will be studied from birth, those raised by their mothers and those raised in the Great Ape Nursery of the Yerkes Regional Primate Research Center of Emory University due to inadequate maternal care. Behavioral observations of the infants and their social partners (i.e., mother or peer) will be conducted through the first year of Additionally, assessments of neonatal reflexes, temperament, social competence, quality of attachment and physiology (salivary cortisol and heart-rate reactivity) will be obtained. Mild environmental challenges that moderately stress the infant's coping mechanisms and the attachment system will be administered in the second years of life. We plan to determine the correlations among these assessments and correlations with behavioral development observed concurrently in free-play social groups to document the stability (over time and across situations, respectively) and predictability of individual differences on these developmental measures. The long-term consequences of different behavioral profiles will be determined as they relate to social, reproductive and maternal competence. Ultimately, such data will be useful in the early identification of chimpanzees that are 'at risk' for behavioral inadequacies and in the development of procedures to promote more adequate behavior.

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1. Descriptive Title (80 characters):

Postpartum Effects of Adolescent Pregnancy

#### Abstract:

Since female primates are capable of reproducing prior to the completion of physical maturation, the effects of pregnancy and lactation on interbirth intervals may be more pronounced in young mothers. We have demonstrated that a significant proportion of primiparous mothers exhibit an extended period of lactational infertility due to a continuation of a more intense pattern of nursing compared to agemates which ovulate within a normal interval. Furthermore, young primiparous females may be more sensitive to the effects of the suckling stimulus on the secretion of gonadotropins. This effect of primiparity is restricted to very young mothers as older primiparous mothers exhibit an adult-like pattern. From these data, it was hypothesized that the effects of suckling on gonadotropin secretion - whether mediated through enhanced estradiol negative feedback or nongonadal restraint-synergizes with the "adolescent" neuroendocrine capacity of young females to prolong lactational infertility in adolescent mothers. In order to investigate this hypothesis, studies were initiated to examine episodic gonadotropin secretion and how it is influenced by suckling and estradiol. Initial studies have indicated that, during the breeding season, estradiol significantly reduces luteinizing hormone pulse amplitude but not frequency.

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Descriptive Title (80 characters):

Hormonal and Seasonal Regulation of Puberty in Females

#### Abstract:

Studies were continued to examine how environmental factors influence the neuroendocrine control of puberty and the timing of first ovulation. In order to examine the role of growth hormone (GH) in the tempo of sexual maturation, hGH (Genentech Inc.) was administered to immature gonadally-intact (n=6) and estradiol-treated, ovariectomized (E2ovx) females (n=5) which were compared to untreated intact (n=7) and E2ovx controls (n=4). Bone ages were higher at an earlier chronological age in GH-treated monkeys. Furthermore, a precocious first ovulation occurred in 50% of the GH-treated intact monkeys compared to 0% of controls. Although maturational increases in luteinizing hormone occurred at the same age in both E2ovx groups, higher levels were achieved in GH-treated animals. These changes occurred independent of differences in body weight gain. These data suggest that elevations in GH may be involved in the final stages of puberty, possibly acting to decrease the negative feedback efficacy of estradiol on LH release.

Environmental factors may override these endogenous changes to restrict first ovulation to the fall months. Spring-born monkeys housed outdoors (SBO:n=7) and winter-born monkeys housed outdoors (WBO:n=9) were compared to spring-born monkeys housed indoors (SBI:n=9). Menarche occurred at a significantly younger age in SBI females (26 mo) and occurred during the outdoor summer months. Menarche occurred at a similar age for WBO and SBO (31 mo) but at different times in the fall (September and November, respectively). Furthermore, 78% of SBI exhibited a precocious first ovulation compared to 0% for SBO 56% for WBO. These ovulations occurred at "32 mo for SBI but at "36 mo for WBO. These data suggest that seasonal factors can override endogenous changes to restrict pubertal events to the fall months in outdoor-housed monkeys.

## DIVISION OF VETERINARY MEDICINE

R. Brent Swenson, D.V.M., Chief

Core Faculty:

J. Orkin

E. Strobert

B. Swenson

Consultants :

B. Gay

Consultant in Medicine Radiology Department Emory University

E. Keener Consultant in Medicine Private Practice in Neurosurgery

Atlanta, GA.

PART II, SECTION A DRR'SCIENTIFIC SUBPROJECT FORM

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 Descriptive Title (80 characters): Establishment of a Chimpanzee Breeding and Research Program

#### Abstract:

A dedicated breeding colony of chimpanzees was established that is expected to produce between 8 and 12 healthy and behaviorally normal offspring per year. These offspring will be used to establish a stable, self-sustaining breeding population of chimpanzees that will help to guarantee the future availability of these animals for biomedical and behavioral research and testing. The breeding pair matings using known breeder animals and artificial insemination. Infants will be managed in such a way as to maximize social experience, including extensive mother-rearing where possible, peer group-rearing when nursery care is required and fostering of nursery-reared infants onto competent mothers.

We also plan to conduct research in areas that will promote improved reproductive success and efficiency and improved behavioral outcome. This research will include investigation of early detection of labor using telemetry to allow vestigation of hormonal manipulation to shorten interbirth intervals without separating infants from their mothers; methods of gamete preservation to improve artificial breeding techniques; investigation of early rearing techniques in order to develop techniques that are conducive to subsequent successful reperformance.

INVESTIGATORS WITH SUPPORT OTHER THAN PUBLIC HEALTH SERVICE  Fill out a separate form for each of the following categories: Check one  CORE RESEARCH & DEVELOPMENT OTHER  1. Last Name, First Middle 3. Sources of Support (Other than this grant)  2. Institution ONLY if Non- Host Institution Host Institution Bernstein, Irwin S. University of Georgia  Byrd, Larry D. IND S.D. Searle Eagles' Max Baer Heart Fund  Gordon, Thomas P. FED NSF BNS-83-10452  Gould, Kenneth G. IND VLI Corp  Herndon, James G. FED NSF BNS-8310195  FDN Suggenheim Foundation OTH Emory BRSG  McClure, Harold M. FDN Cystic Fibrosis Foundation OTH Emory Univ  Seigler, Hillard F. FED VA 821  Smith, Euclid O. OTH Enery Univ. Woodruff Funds  Wallen, Kim FED NSF BNS-81-17627  FED NSF BNS-84-18060 FED NSF BNS-86-07295 OTH Emory BRSG  4. Total Other Support  (a) Ints Page 498,489	PART II, SECTION B GRANT NUMBER P 5 1 R R O O 1 6 5-26									
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PART II, SECTION C GRANT NUMBER P 1 R R O O 1 65 - 26INSTITUTION: Yerkes Regional Primate Research Center REPORT PERIOD: January 1, 1986 to December 31, 1986 Fill out a separate form for each of the following categories: CORE RESEARCH & DEVELOPMENT OTHER Total Number Published: BOOKS **PAPERS** 27 28 ABSTRACTS . . 56 Number in Press: BOOKS 0 PAPERS 19 ABSTRACTS 24 Author(s) Title of Article, Journal, Volume, Number, Pages (e.g., 44-48), Year Published

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- \*Young, L.G., Gould, K.G. and Hinton, B.T.: Changes in binding of a 27 Kd chimpanzee cauda epididymal protein/glycoprotein component to chimpanzee sperm. Gamete Res. (In Press).
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PART II, SECTION C		GRANT N	UMBER	P 5	1	R	R	0	0	1	6	5	_	26	
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# Publications Supported by Receipt of Tissues, Specimens or Other Services from the Yerkes Center\*\*

- \*Brown, C.J., Dunbar, V.G. and Shafer, D.A.: A comparison of the karyotypes of six species of the genus <u>Macaca</u> and a species of the genus <u>Cercocebus</u>. Folia Primatol. 46: 164-172, 1986.
- \*Daiger, S.P., Goode, M.E. and Trowbridge, B.D.: Evolution of nuclear gene families in primates. Copy-number variation in the argininosuccinate synthetase (ASS) pseudogene family and the anonymous DNA sequence, DISI. Genetica (In Press).
- \*Durand, D.B., Kamoun, M., Norris, C.A., Holbrook, N.J., Greengard, J.S., Crabtree, G.R. and Kant, J.A.: Retroviral activation of interleukin 2 gene in a gibbon ape T cell lymphoma line. J. Exp. Med 164: 1723-1734, 1986.
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- \*Else, J.G.: Conservation efforts at the Tana River Primate Reserve, Kenya. Primate Conservation (In Press).
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Indicate by an asterisk (\*) that the resource was given credit.

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- \*Rathbun, W.B.: Activity of glutathione synthesis enzymes in the rhesus monkey lens related to age: A model for the human lens. Curr. Eye Res. 5: 161-166, 1986.
- \*Rathbun, W.B.: Glutathione synthesis in evolution: An Achilles' heel of human and other Old World simian lenses. Ophthalmic Res. 18: 236-242, 1986.
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- \*\*Not previously reported. The variation in dates of publication is related to the length of time taken to acquire notification and/or reprints of publications of this type.

PART III SECT	ION B PROGRAM SPECIFIC DATA FOR PRIMATE RESEARCH CENTERS							
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	January 1, 1986 TO December 31, 1986							
SECTION C	SECTION C SUMMARY STATISTICS							
1. PERSONNEL	NUMBER							

1. PERSONNEL	NUMBER
a. CORE Personnel	165
Doctoral Level Scientists	24
Other Personnel	141*
b. Collaborative or Affiliated Scientists	107
c. Visiting Scientists	3
d. Graduate Students	22

### 2. REGIONALITY

a. Scientists Provided with Specimens	96
b. Number of Specimens Provided	797
c. Scientists Touring the Center	300
d. Other Visitors	500

<sup>\*</sup>lll paid exclusively or partially from base grant.

KKUU165-26

### Appendix 1

### CURRICULUM VITAE

Mark E. Wilson
Yerkes Regional Primate Research Center
Emory University
Field Station
2409 Taylor Road
Lawrenceville, GA 30245

### Personal Information:

Birthdate:

Place of Birth:

Spouse: Children:

Home Address:

Office Phone: Home Phone:

(404) 963-6281; 727-7737

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### Education: .

B.S	1973	Arizona State University, Tempe, Arizona Major: Psychology Minor: Zoology
M.S.	1976	Eastern Washington University, Cheney, Washington Major: Experimental Psychology
	1976-77	Emory University, Atlanta, Georgia
Ph.D.	1979	University of Georgia, Athens, Georgia Major: Biopsychology
Fellow	1979-81	Emory University School of Medicine, Atlanta, Georgia Focus: Endocrinology

#### Professional History:

1985-present Director, Radioimmunoassay Laboratory, Yerkes Regional Primate Research Center, Emory University

1986-present Assistant Research Professor, Divisions of Behavioral Biology and Reproductive

Biology, Yerkes Regional Primate Research

Center, Emory University

Curriculum Vitae Mark E. Wilson

2

### Professional History (continued):

1981-present	Associate in Medicine, Division of Endocrinology, Department of Medicine, Emory University School of Medicine
1981-1986	Research Associate, Division of Behavioral Biology, Yerkes Regional Primate Research Center, Emory University
1983-1984	Interim Head, Radioimmunoassay Laboratory, Yerkes Regional Primate Research Center, Emory University
1979-1981	Postdoctoral Research Fellow; Division of Endocrinology, Department of Medicine, Emory University School of Medicine
1979-1981	Research Fellow; Division of Behavioral Biology, Yerkes Regional Primate Research Center, Emory University
1978-1979	University Assistantship, Department of Psychology, University of Georgia
1977-1979	Research Technician; Yerkes Regional Primate Research Center, Emory University
1976-1977	Research Assistant; Department of Psychology, Emory University
1975-1976	Research Assistant; Regional Primate Research Center-Field Station, University of Washington
1974-1975	Teaching Assistant; Department of Psychology, Eastern Washington University

#### Teaching Experience:

1974-1977 Teaching Assistant and Instructor for undergraduate courses in physiological psychology, scientific methods and statistics, and graduate courses in

biological bases of behavior.

# Consulting Experience:

Member, Reproductive Endocrinology Review Ad Hoc Group, Division of Research Grants, NIH; 1985-1986.

Curriculum Vitae Mark E. Wilson

3

#### Honors:

Graduated "With Distinction" from Arizona State University. Recipient of National Research Service Award from the National Institutes of Health.

# Professional Associations:

Society for the Study of Reproduction The Endocrine Society American Society of Primatologists

### Research Interests:

Neuroendocrine and environmental control of puberty. Neuroendocrine control of seasonal reproduction in rhesus monkeys.

Physiological and behavioral factors controlling lactation induced suppression of ovulation.

Control of prolactin secretion.

Hormonal control of female sexual behavior.

### Support:

#### Current:

NIH-RO1 HD16305-05 "Puberty in female rhesus monkeys: hormonal mechanisms." 30%; P. I. Mark E. Wilson; 4/82-3/89.

NIH-RO1-HD18120-03 "Postpartum effects of adolescent pregnancy." 20%; P. I. Mark E. Wilson; 5/84-4/87.

### Editorial Reviews:

Biology of Reproduction

American Journal of Primatology
Physiology and Behavior
Pharmacology, Biochemistry and Behavior
Zoo Biology
Aggressive Behavior
Journal of Andrology

Special review of Earthwatch, The Center for Field Research Proposal Review for the Emory University Research Committee Curriculum Vitae Mark E. Wilson

### Refereed Publications:

- 1. Scott, M. W. & Wilson, M. E. Predicting high blood levels for animals in a group situation. Behavior Research Methods & Instrumentation, 1976, 8, 465-466.
- Elton, R. H. & Wilson, M. E. Changes in ethanol consumption by pregnant pigtail macaques (<u>Macaca nemestrina</u>). <u>Journal</u> of Studies on Alcohol, 1977, <u>38</u>, 2181-2183.
- 3. Elton, R. H., Wilson, M. E. & Pyle, T. W. Dose dependent alcohol elimination rates in pigtailed macaques (Macaca nemestrina) from a voluntary oral consumption group.

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- 4. Maple, T., Wilson, M. E., Zucker, E. L. & Wilson, S. Notes on the development of a mother reared orang-utan. The first six months. <u>Primates</u>, 1978, 19, 593-602.
- Wilson, M. E., Gordon, T. P. & Bernstein, I. S. Timing of births and reproductive success in rhesus monkey social groups. <u>Journal of Medical Primatology</u>, 1978, 7, 202-212.
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- 7. Wilson, M. E. & Gordon, T. P. Age differences in the duration of mating periods in female rhesus monkeys (Macaca mulatta). Developmental Psycobiology, 1980, 3, 637-642.
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- 9. Wilson, M. E., Gordon, T. P. & Chikazawa, D. Post-copulatory behavior of female rhesus monkeys. American Journal of Primatology, 1982, 2, 21-27.
- 10. Wilson, M. E., Gordon, T. P. & Collins, D. C. Serum 17 estradiol and progesterone associated with mating behavior during early pregnancy in female rhesus monkeys. Hormones and Behavior, 1982, 16, 94-106.
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- 12. Ruiz de Elvira, M. C., Herndon, J. G. & Wilson, M. E. Influence of estrogen-treated females on sexual behavior and male testosterone levels of a social group of rhesus monkeys during the nonbreeding season. Biology of Reproduction, 1982, 26, 825-834.

- 13. Wilson, M. E., Gordon, T. P. & Collins, D. C. Variation in ovarian steroids associated with the annual mating period in female rhesus monkeys (Macaca mulatta). Biology of Reproduction, 1982, 27, 530-539.
- 14. Blank, M. S., Gordon, T. P. & Wilson, M. E. Effects of capture and venipuncture on serum levels of prolactin, growth hormone, and cortisol in outdoor-housed female rhesus monkeys. Acta Endocrinologica, 1983, 102, 190-195.
- 15. Walker, M. L., Gordon, T. P. & Wilson, M. E. Reproductive performance in capture-acclimated female rhesus monkeys (Macaca mulatta). Journal of Medical Primatology, 1982, 11, 291-302.
- 16. Wilson, M. E., Walker, M. L. & Gordon, T. P. Consequences of first pregnancy in rhesus monkeys. American Journal of Physical Anthropology, 1983, 61, 103-110.
- 17. Walker, M. L., Wilson, M. E. & Gordon, T. P. Context-dependent changes in rhesus monkeys. Animal Behaviour, 1983, 31, 1047-1054.
- 18. Walker, M. L., Gordon, T. P. & Wilson, M. E. Menstrual cycle characteristics of seasonally-breeding rhesus monkeys.

  <u>Biology of Reproduction</u>, 1983, <u>29</u>, 841-848.
- 19. Walker, M. L., Schwartz, S. M., Wilson, M. E. & Musey, P. I. Estimation of body fat in female rhesus monkeys. American Journal of Physical Anthropology, 1984, 64, 323-329.
- 20. Wilson, M. E., Walker, M. L. & Gordon, T. P. Effects of age, lactation and repeated cycles on rhesus monkey copulatory intervals. American Journal of Primatology, 1984, 7, 21-26.
- 21. Wilson, M. E., Gordon, T. P., Blank, M. S. & Collins, D. C. Timing of sexual maturity in outdoor-housed female rhesus monkeys (Macaca mulatta). Journal of Reproduction and Fertility, 1984, 70, 625-633.
- 22. Walker, M. L., Wilson, M. E., Gordon, T. P. & Collins, D. C. Endocrine control of the seasonal occurrence of ovulation in outdoor-housed rhesus monkeys. <u>Endocrinology</u>, 1984, <u>114</u>, 1074-1081.
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- 24. Wilson, M. E., Walker, M. L., Schwartz, S. M. & Gordon, T. P. Gonadal status influences developmental patterns of serum

- prolactin in female rhesus monkeys housed outdoors. Endocrinology, 1985,  $\underline{116}$ , 640-645.
- 25. Bruot, B. C., Gearing, M., Musey, P. I., Wilson, M. E. & Collins, D. C. Steroidogenesis by the immature rhesus monkey ovary in vitro. Journal of Endocrinological Investigation, 1986, 9, 171-175.
- 26. Wilson, M. E., Gordon, T. P. & Collins, D. C. Ontogeny of luteinizing hormone secretion and first ovulation in seasonal breeding rhesus monkeys. <u>Endocrinology</u>, 1986, <u>118</u>, 293-301.
- 27. Pope, N. S., Gordon, T. P. & Wilson, M. E. Age, social rank and lactational status influence ovulatory patterns in seasonal breeding rhesus monkeys. <u>Biology of Reproduction</u>, 1986, <u>35</u>, 353-359.
- 28. Osterud, E. L., Lackey, S. L. & Wilson, M. E. Estradiol increases somatomedin-C concentrations in adolescent rhesus monkeys. American Journal of Primatology, 1986, 11, 53-62.
- 29. Wilson, M. E. Gonadal steroids influence somatomedin-C concentrations in prepubertal female rhesus monkeys.

  <u>Endocrinology</u>, 1986, <u>119</u>, 663-673.
- 30. Schwartz, S. M., Wilson, M. E., Walker, M. L. & Collins, D. C. Social and growth correlates of puberty onset in female rhesus monkeys. <u>Nutrition and Behavior</u>, 1985, <u>2</u>, 225-232.
- 31. Estep, D. W., Gordon, T. P., Wilson, M. E. & Walker, M. L. Social stimulation and the resumption of copulation in rhesus and stumptail macaques. International Journal of Primatology, 1986, 7, 505-517.
  - 32. Wilson, M. E., Pope, N. S. & Gordon, T. P. Seasonal modulation of luteinizing hormone secretion by estradiol in female rhesus monkeys. Biology of Reproduction, in press.
- 33. Pope, N. S., Gordon, T. P. & Wilson, M. E. Induction of female sexual behavior by estradiol is modified by season in rhesus monkeys. Biology of Reproduction, in press.
  - 34. Wilson, M. E., Walker, M. L., Pope, N. S. & Gordon, T. P. Prolonged lactational infertility in adolescent rhesus monkeys. Under editorial review, Biology of Reproduction.

# Abstracts Presented at Professional Meetings

- 1. Wilson, M. E., Greaves, D. A., Lewis, L., Anderson, B. & Elton, R. H. Changes in patterns of ethanol ingestion by a group of pigtailed macaques (M. nemestrina) with the onset of sexual maturity and as a function of social stress. Presented at the joint meeting of the Washington State and Oregon Psychological Association, Orcas Island, Washington, May 1976.
- Wilson, M. E., Maple, T., Nadler, R. D., Zucker, E. L. & Hoff, M. Characteristics of paternal behavior in captive gorillas and orangu-tans. Presented at the Inaugural meeting of the American Society of Primatologists, Seattle, Washington, April 1977.
- Wilson, M. E. & Zucker, E. L. Early social development in the orang-utan. Presented at the 23rd Annual Convention of the Southeastern Psychological Association, Hollywood, Florida, May 1977.
- 4. Wilson, M. E. Age and rank influences on patterns of sexual behavior in female rhesus monkeys. Presented at the 2nd Annual Meeting of the American Society of Primatologists, Atlanta, Georgia, September 1978.
  - 5. Wilson, M. E. Female postcopulatory behavior in social living rhesus monkeys. Presented at the 3rd Annual Meeting of the American Society of Primatologists, Winston-Salem, North Carolina, June 1980.
  - 6. Wilson, M. E., Gordon, T. P. & Bernstein, I. S. Serum testosterone and social context influences on behavior of adult male rhesus monkeys. Biology of Reproduction, 22 (Sep 1) 1980 p. 137A.
  - 7. Wilson, M. E., Gordon, T. P. & Collins, D. C. Serum progesterone and copulatory activity during early pregnancy in female rhesus monkeys. Presented at Federation Proceedings, Atlanta, Ga., April 1981.
  - 8. Wilson, M. E., Gordon, T. P., Chikazawa, D. & Collins, D. C. Changes in behavior during the peri-ovulatory period of female rhesus monkeys. Presented at Annual Meeting of American Society of Primatologists, San Antonio, Texas, June 1981.
  - 9. Blank, M. S., Gordon, T. P. & Wilson, M. E. Serum levels of prolactin, growth hormone and cortisol at various times after capture in outdoor living female rhesus monkeys (Macaca mulatta). Presented at Annual Meeting of Endocrine Society, Cincinnati, Ohio, June 1981.

- 10. Wilson, M. E. Variations in ovarian steroids and female copulatory behavior in rhesus monkeys. Biology of Reproduction, 1981, 24, 50A.
- 11. Wilson, M. E. & Gordon, T. P. Seasonal occurrence of first ovulation in rhesus monkeys.
  1982, 26 (Suppl. 1), 126A.
- 12. Gordon, T. P. & Wilson, M. E. Hormonal regulation of copulatory activity in female rhesus monkeys.

  International Journal of Primatology, 1982, 3, 288.
- 13. Walker, M. L., Wilson, M. E. & Gordon, T. P. Context-dependent changes in female rhesus monkey behavior during the menstrual cycle. International Journal of Primatology, 1982, 3, 344.
- 14. Wilson, M. E., Gordon, T. P., Walker, M. L. & Collins, D. C. Age and seasonal influences on reproductive behavior and physiology in female rhesus monkeys. International Journal of Primatology, 1982, 3, 349.
- 15. Schwartz, S. M. & Wilson, M. E. Social and growth factors that influences puberty onset in female rhesus monkeys. Presented at Annual Meeting of Endocrine Society, San Antonio, TX, June, 1983.
- 16. Wilson, M.E., Walker, M. L. & Gordon, T. P. Natural infertility and reproductive dysfunction: common hormonal mechanisms. American Journal of Primatology, 1983, 4, 325.
- 17. Gordon, T. P., Blank, M. S., Walker, M. L. & Wilson, M. E. Influence of lactation and prolactin on seasonal reproduction. American Journal of Primatology, 1983, 4, 344.
- 18. Bruot, B. C., Gearing, M., Musey, P. I., Wilson, M. & Collins, D. C. Steroidogenesis by the prepubertal rhesus monkey ovary in vitro. Presented at the Seventh International Congress of Endocrinology, Quebec, Canada, July 1984.
- 19. Schwartz, S. M., Wilson, M. E. & Collins, D. C. Diet influences on growth and sexual maturation in premenarchial rhesus monkeys. <u>Biology of Reproduction</u>, 1984, <u>30</u>, (Suppl. 1), 267.

- 20. Gordon, T. P., Walker, M. L. & Wilson, M. E. Seasonally restricted reproduction in rhesus monkeys. American Journal of Primatology, 1984, 6, 405.
- 21. Gordon, T. P., Walker, M. L. & Wilson, M. E. Prolonged lactational infertility in primiparous rhesus monkeys.

  American Journal of Primatology, 1985, 8, 340.
- 22. Osterud, E. L. & Wilson, M. E. Age and reproductive status influence somatomedin-C secretion in rhesus monkeys.

  American Journal of Primatology, 1985, 8, 355.
- 23. Walker, M. L., Wilson, M. E., Schwartz, S. M. & Gordon, T. P. Influence of prolactin on gonadotropin secretion in postpartum females. Biology of Reproduction, 1985, 32 (Supp 1), 168.
- 24. Wilson, M. E., Gordon, T. P. & Collins, D. C. Ontogeny of LH secretion in seasonal breeding rhesus monkeys. <u>Biology of Reproduction</u>, 1985, <u>32</u> (Supp 1), 178.
- 25. Wilson, M. E., Osterud, E. L., Gordon, T. P., Schwartz, S. M. & Walker, M. L. Developmental increases in estradiol enhance growth in female monkeys. Endocrine Society, Baltimore, 1985, no. 589.
- 26. Wilson, M. E., Pope, N. S., & Gordon, T. P. Seasonal modulation of luteinizing hormone (LH) secretion by estradiol (E2) in rhesus monkeys. <u>Biology of Reproduction</u>, 1986, 34(Supp 1), 185.
- 27. Wilson, M. E. & Gordon, T. P. Ontogeny of the positive feedback response of luteinizing hormone in seasonal breeding rhesus monkeys. Endocrine Society, Anaheim CA, 1986, no. 913.

### Appendix 2

# CURRICULUM VITAE

Kim Wallen

Current Address:

Department of Psychology Emory University Atlanta, Georgia 30322

(404) 727-4125

Social Security No.:

Date and Place of Birth:

Education:

1965-1970 Antioch College B.A., Biology,

Yellow Springs, Ohio

1973-1978 University of Wisconsin 1978 Ph.D., Neurosciences Madison, Wisconsin

# Professional Appointments:

1970-1971

1986-present	Associate Research Professor, Yerkes Regional Primate Research Center, Emory University, Atlanta, Georgia
1985-present	Associate Professor, Department of Psychology, Emory University, Atlanta, Georgia
1979-1986	Affiliate Scientist, Yerkes Regional Primate Research Center, Emory University, Atlanta, Georgia
1979-1985	Assistant Professor, Department of Psychology, Emory University, Atlanta, Georgia
1979	Project Associate, Neurosciences Division, Wisconsin Regional Primate Research Center, University of Wisconsin, Madison, Wisconsin
1977-1978	Predoctoral Fellow, Wisconsin Regional Primate Research Center, University of Wisconsin, Madison, Wisconsin
1973-1976	Graduate Research Assistant, Wisconsin Regional Primate Research Center, University of Wisconsin, Madison, Wisconsin
1974-1975	Teaching Assistant, Department of Zoology, University of Wisconsin, Madison, Wisconsin
1971-1973	Project Specialist, Wisconsin Regional Primate Research Center, University of Wisconsin, Madison, Wisconsin
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Research Associate, Reproductive Physiology and Behavior, Oregon Regional Primate Research Center, Beaverton, Oregon

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#### Awards:

1977-1978 National Research Service Award Predoctoral Fellowship

1973-1974 University of Wisconsin Dean's Fellowship

# Professional Service:

Reviewer, Psychobiology Program, National Science Foundation, 1979-present

Member, Executive Committee, Atlanta Area Chapter, Society for Neuroscience,

President, Atlanta Area Chapter, Society for Neuroscience, 1984-1985

Member, Publications Committee, American Society of Primatologists, 1980-1984 (Chairman, 1980-1982; Member, Awards Committee, 1985-1986)

Member, Executive Committee, American Society of Primatologists, 1980-1982

Member, Program Committee, IXth Congress of the International Primatological Society, 1982

# Service - Emory University:

Member, Graduate Faculty, 1979-present

Member, Computer Advisory Committee to the Deans of the College of Arts

and Sciences and the Graduate School, 1982-present

Member, Graduate Selection Committee, Neuroscience Training Program, 1986-present

# Department of Psychology:

Departmental Secretary, 1979-1981 Chairman, Research Group Committee, 1982 Member, Graduate Curriculum Committee, 1981-1983 Chairman, Teaching Evaluation Committee, 1982-1983 Member, Honors Committee, 1980-1986 Member, Electronics Shop Committee, 1981-1986 Member, Space Utilization Committee, 1983-1986 Chairman, Departmental Computer Committee, 1983-present

# Yerkes Regional Primate Research Committee:

Member, Breeding Resources Committee, 1979-1981

Member, Computer Task Force, 1981

Member, Behavioral Biology of Primates Training Committee, 1981-1983

Manager, Field Station 11/23 Computer Facility, 1980-present

Member, Computer Committee, 1980-present (Chairman, 1981-present)

Member, Field Station Animal Resources Committee, 1982-present

K. Wallen

# Editorial Service:

Reviewer: Hormones and Behavior, 1979-present;

Biology of Reproduction, 1985-present

Ad hoc reviewer: Science; Physiology and Behavior; Psychology Bulletin;

Nutrition and Behavior; Ethology and Sociobiology; Biology of Reproduction; Animal Behavior

# Professional Affiliations:

American Association for the Advancement of Science American Society of Primatologists: Animal Behavior Society International Primatological Society Society for Neuroscience Society for the Study of Reproduction Sigma Xi

# History of Research Support:

- January 1, 1980 December 31, 1980: "Spatial Influences on the Sexual Behavior of Heterosexual Pairs of Rhesus Monkeys". Emory University Research Council,
- January 1, 1981 December 31, 1981: "Sexually Dimorphic Behavior in Group Living Rhesus Monkeys". Emory University Research Council, #4330 (\$3,707).
- September 1, 1981 December 31, 1981: "Primate Behavior: Spatial and Hormonal Influences". Emory University Research Council, #4448 (\$6,416).
- August 1, 1981 July 30, 1982: "Rhesus Sex Behavior: Spatial and Hormonal Influences". ADAMHA Small Grants Program, #MH-35835 (\$10,000).
- June 1, 1982 March 30, 1986: "Rhesus Female Proceptivity: Ovarian Steroid Influences". National Science Foundation, #BNS 81-17627 (\$144,984).
- September 1, 1984 August 31, 1986: "Influence of Prenatal Gonadotropin-Releasing Hormone (GnRH) Agonist Treatment on Behavior and Endocrine Function of Rhesus Monkeys". Emory University Research Committee, #8911 (\$5,000).
- June 1, 1985 February 28, 1987: "Androgenic Influences on Female Sexuality". National Science Foundation, #BNS 84-18060 (\$60,000).
- September 1, 1983 August 31, 1987: "Developmental Influences of Neonatal Testosterone in Male Rhesus Monkeys" (D. R. Mann, P.I.). Division of Research Resources, #SRI/BISRIP (\$244,843).
- September 1, 1986 August 31, 1987: "Androgenic and Environmental Influences on Male Sexuality". National Science foundation, #BNS 86-07295 (\$120,000).

#### Publications:

- Clemens, L. G., Wallen, K., and Gorski, R. A. Mating behavior: facilitation in the female rat after cortical application of potassium chloride. <u>Science</u> 157: 1208-1209, 1967.
- Goy, R. W., Wallen, K., and Goldfoot, D. A. Social factors affecting the development of mounting behavior in male rhesus monkeys. In: <u>Reproductive Behavior</u>, W. Montagna and W. A. Sadler, eds. Plenum Publishing Corp., New York, 1974.
- Wallen, K., Goy, R. W., and Phoenix, C. H. Inhibitory actions of progesterone on hormonal induction of estrus in female guinea pigs. Hormones and Behavior 6: 127-138, 1975.
- Goy, R. W., Slimp, J., and Wallen, K. Endocrine aspects of sexually dimorphic behavior. Acta Endocrinologica (Kbh.) Suppl. 199: 432, 1975 (Abstr.).
- Buss, D. H., Cooper, R. W., and Wallen, K. Composition of lemur milk. Folia Primatologica 26: 301-305, 1976.
- Wallen, K. and Goy, R. W. Effects of estradiol benzoate, estrone and propionates of testosterone or dihydrotestosterone on sexual and related behaviors of ovariectomized rhesus monkeys. Hormones and Behavior 9: 228-248, 1977.
- Wallen, K., Bielert, C. F., and Slimp, J. Foot-clasp mounting in the prepubertal rhesus monkey: social and hormonal influences. In: Biosocial Development among Primates, F. E. Poirier and S. Chevalier-Skolnikoff, eds. Garland Publishing Co., New York, 1977.
- Goldfoot, D. A. and Wallen, K. Development of gender role behaviors in heterosexual and isosexual groups of infant rhesus monkeys. In: Recent Advances in Primatology, Vol. 1, Behaviour, D. J. Chivers and J. Herbert, eds. Academic Press, New York, pp. 155-159, 1978.
- Wallen, K. and Thornton, J. E. Progesterone and duration of heat in estrogentreated ovariectomized guinea pigs. <u>Physiology and Behavior 22</u>: 95-97, 1979.
- Goy, R. W. and Wallen, K. Experiential variables influencing play, foot-clasp mounting and adult sexual competence in male rhesus monkeys. <u>Psycho neuro-endocrinology</u> 4: 1-12, 1979.
- Wallen, K. Review of <u>Behavior Sex Differences in Nonhuman Primates</u>. <u>Journal of Sex Research 16</u>: 183-184, 1980.
- Wallen, K., Higgins, S. A., and Winston, L. A. Spatial influences on copulation by rhesus monkeys. <u>American Journal of Primatology 1</u>: 351, 1981 (Abstr.).
- Wallen, K., Goldfoot, D. A., and Goy, R. W. Peer and maternal influences on the expression of foot-clasp mounting by juvenile male rhesus monkeys. <u>Developmental Psychobiology 14</u>(4): 299-309, 1981.
- Wallen, K. Influence of female hormonal state on rhesus sexual behavior varies with space for social interaction. Science 217: 375-376, 1982.

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# Publications (continued):

- Wallen, K. and Winston, L. A. Social complexity and hormonal influences on sexual behavior in rhesus monkeys (Macaca mulatta). International Journal of Primatology, 3: 344, 1982 (Abstr.).
- Wallen, K. and Winston, L. A. Social complexity and hormonal influences on sexual behavior in rhesus monkeys (Macaca mulatta). Physiology and Behavior 32:
- Goldfoot, D. A., Wallen, K., Neff, D. A., McBrair, M. C., and Goy, R. W. Social influences on the display of sexually dimorphic behavior in rhesus monkeys: isosexual rearing. Archives of Sexual Behavior 13: 395-412, 1984.
- Wallen, K., Davis-DaSilva, M., Mann, D. R., Gaventa, S., and Lovejoy, J. C. Suppression of ovulation and sexual behavior in group-living rhesus by GnRH agonist treatment. <u>Biology of Reproduction 30</u>(Suppl. 1): 76, 1984 (Abstr.).
- Mann, D. R., Davis-DaSilva, M., Wallen, K., Coan, P., Evans, D. E., and Collins, D. C. Blockade of neonatal activation of the pituitary-testicular axis with continuous administration of a gonadotropin-releasing hormone agonist in male rhesus monkeys. <u>Journal of Clinical Endocrinology and Metabolism</u> 59: 207-211, 1984.
- Wallen, K., Winston, L. A., Gaventa, S., Davis-DaSilva, M., and Collins, D. C. Periovulatory changes in female sexual behavior and patterns of ovarian steroid secretion in group-living rhesus monkeys. Hormones and Behavior 18: 431-450, 1984.
- Lovejoy, J. C. and Wallen, K. Sex differences in group-housed rhesus macaques at one year of age. American Journal of Primatology 10: 415, 1986 (Abstr.).
- Davis-DaSilva, M. and Wallen, K. Effects of acute testosterone suppression on male rhesus sexual behavior in a social group. American Journal of Primatology 10: 397, 1986 (Abstr.).
- Wallen, K., Mann, D. R., Davis-DaSilva, M., Gaventa, S., Lovejoy, J. C., and Collins, D. C. Chronic gonadotropin-releasing hormone agonist treatment suppresses ovulation and sexual behavior in group-living female rhesus monkeys. Physiology and Behavior 36: 369-375, 1986.
- Hennessey, A. C., Wallen, K., and Edwards, D. A. Preoptic lesions increase the display of lordosis by male rats. <u>Brain Research 370</u>: 21-28, 1986.

# Papers Presented:

- Wallen, K., Goldfoot, D. A., and Goy, R. W. The role of specific social environments upon the display of sexually dimorphic behavior in juvenile rhesus monkeys. Eastern Conference on Reproductive Behavior, Saratoga, New York, June, 1976.
- Wallen, K. and Goy, R. W. Rhesus female sexual behavior: the effect of estradiol, estrone, testosterone, and dihydrotestosterone on female proceptivity, receptivity, yawning behavior, and male ejaculation. Inaugural Meeting, American Society of Primatologists, Seattle, Washington, June, 1978.

## Papers Presented (continued):

- Wallen, K. Genetic differences in response to estradiol benzoate (EB) and testos terone propionate (TP) treatment of female strain 2 and 13 guinea pigs. Annual Meeting, Animal Behavior Society, Seattle, Washington, June, 1979.
- Wallen, K., Thornton, J. E., and Goy, R. W. Strain differences in the hormonal induction of female receptivity in male and female guinea pigs. Eastern Conference on Reproductive Behavior, New Orleans, Louisiana, June, 1979.
- Wallen, K., Higgins, S. A., and Winston, L. A. Spatial influences on copulation by rhesus monkeys (Macaca mulatta). Annual Meeting, American Society of Primatologists, San Antonio, Texas, June, 1981.
- Wallen, K., Winston, L. A., and Higgins, S. A. Spatial influences on copulation by rhesus monkeys in relation to the female's menstrual cycle. Conference on Reproductive Behavior, Nashville, Tennessee, June, 1981.
- Wallen, K. and Winston, L. A. Social complexity and hormonal influences on sexua behavior in rhesus monkeys (Macaca mulatta). IXth Congress of the International Primatological Society, Atlanta, Georgia, August, 1982.
- Wallen, K. and Higgins, S. A. Sexually differentiated behavior of infant rhesus monkeys living in an age-graded social group. Serono International Symposium on Sexual Differentiation, Carmel, California, March, 1983.
- Wallen, K., Winston, L. A., Gaventa, S. G., and Collins, D. C. Sexual initiation by group-living female rhesus in relation to changes in ovarian steroids. Conference on Reproductive Behavior, Boston, Massachusetts, June, 1983.
- Wallen, K., Davis-DaSilva, M., Mann, D. R., Gaventa, S., and Lovejoy, J. C. Suppression of ovulation and sexual behavior in group-living rhesus by GnRH agonist treatment. Annual Meeting, Society for the Study of Reproduction, Laramie, Wyoming, July, 1984.
- Wallen, K. and Gaventa, S. G. Hormonal replacement therapies in ovariectomized group-living rhesus. Conference on Reproduction and Behavior, Asilomar, California, June, 1985.

# Invited Presentations and University Colloquia:

- Early social experience and the development of sexual competency in laboratoryreared male rhesus monkeys. Upjohn Laboratories, Kalamazoo, Michigan, May, 1979.
- Environmental influences on rhesus sexual behavior. Behavioral Biology Seminar, Emory University, Atlanta, Georgia, May, 1982.
- Social and environmental influences on hormonal regulation of rhesus sexual behav Seminar, Department of Anatomy, Emory University, Atlanta, Georgia, Septembe 1983.
- Endocrine influences on male and female sexual behavior in group-living rhesus monkeys. Eli Lilly Laboratories, Indianapolis, Indiana, October, 1984.