TABLE OF CONTENTS

TABLE OF CONTENTS (CONT'D)

FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

Emory University

Atlanta, Georgia, U.S.A.

ADMINISTRATION

Yerkes Position	
Director	F.A. King, Ph.D., Research Professor, Division of Neurobiology, Yerkes Center; Professor of Anatomy and Cell Biology; Adjunct Professor of Psychology; Associate Dean of Medicine, Emory University.
Associate Director for Scientific Programs	H.M. McClure, D.V.M., Research Professor and Chief of Pathobiology and Immunobiology, Yerkes Center; Assistant Professor of Pathology, Emory University.
Associate Director for Administration	J.M. Magnotta, B.A.
Head of Animal Resources and Associate Research Professor	J.G. Else, M.S., D.V.M., M.P.V.M.
Administrative Associate	R.W. Buddington, Ph.D.
Chief, Public Affairs and Administrative Associate for Special Projects	C.Y. Yarbrough, A.B.J.

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Special Consultant in Wildlife Conservation and Paleobiology	R.E. Leakey, Director, Kenya Wildlife Service; Adjunct Professor of Anthropology, Emory University.
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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF BEHAVIORAL BIOLOGY
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Section of General Psychobiology and Psychopharmacology
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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF BEHAVIORAL BIOLOGY (CONTINUED)

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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF BEHAVIORAL BIOLOGY (CONTINUED)

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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

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Affiliate Scientist

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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF BEHAVIORAL BIOLOGY (CONTINUED)

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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF NEUROBIOLOGY

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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF NEUROBIOLOGY (CONTINUED)

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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF NEUROBIOLOGY (CONTINUED)

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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF PATHOBIOLOGY AND IMMUNOBIOLOGY
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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF PATHOBIOLOGY AND IMMUNOBIOLOGY (CONTINUED)

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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF PATHOBIOLOGY AND IMMUNOBIOLOGY (CONTINUED)

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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF PATHOBIOLOGY AND IMMUNOBIOLOGY (CONTINUED)

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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF PATHOBIOLOGY AND IMMUNOBIOLOGY (CONTINUED)

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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF PATHOBIOLOGY AND IMMUNOBIOLOGY (CONTINUED)

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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF REPRODUCTIVE BIOLOGY

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FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF REPRODUCTIVE BIOLOGY (CONTINUED)

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K.A. Platzman, Ph.D., Collaborative Scientist in Reproductive Biology, Yerkes Center; Assistant Professor of Psychiatry, Emory University.

P.N. Srivastava, Ph.D., Collaborative Scientist in Reproductive Biology, Yerkes Center; Professor of Biochemistry, University of Georgia.

S.J. Suomi, Ph.D., Collaborative Scientist in Reproductive Biology, Yerkes Center; Chief, Laboratory of Comparative Ethology, National Institute of Child Health and Human Development, Bethesda, Maryland.

M.J. Tucker, Ph.D., Collaborative Scientist in Reproductive Biology, Yerkes Center; Scientific Director, Reproductive Biology Associates.

Visiting Scientists

O.J. Castejon, Ph.D., Visiting Scientist in Reproductive Biology, Yerkes Center; Director of Latin American School of Electron Microscopy, Venezuela.

D.C. Joy, Ph.D., Visiting Scientist in Reproductive Biology, Yerkes Center; Director of EM Facility and Professor of Zoology, University of Tennessee at Knoxville.

FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF REPRODUCTIVE BIOLOGY (CONTINUED)

G. Pasquinelli, Ph.D., Visiting Scientist in Reproductive Biology, Yerkes Center; Adjunct Professor of Hematology, University of Bologna, Italy.

R. Reichelt, Ph.D., Visiting Scientist in Reproductive Biology, Yerkes Center; Research Associate, M.E. Muller Institute for High Resolution Electron Microscopy, University of Basel, Switzerland.

Consultants

D.S. Eley, M.S., Consultant in Reproductive Biology, Yerkes Center and Institute of Primate Research, Kenya.

R.M. Eley, Ph.D., Consultant in Reproductive Biology, Yerkes Center and Institute of Primate Research, Kenya.

C.E. Graham, Ph.D., Consultant in Reproductive Biology, Yerkes Center; Research Professor and Deputy Director, Primate Research Institute, New Mexico State University.

J.R. Preedy, M.D., Consultant in Reproductive Biology, Yerkes Center; Professor of Medicine, Emory University; Associate Chief of Staff, Research and Development, Atlanta Veterans Administration.

FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

DIVISION OF VETERINARY MEDICINE

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

Core Scientists

R.B. Swenson, D.V.M., Senior Veterinarian and Chief of Veterinary Medicine, Yerkes Center.

G.C. Choi, D.V.M., Assistant Veterinarian and Research Associate of Pathobiology and Immunobiology, Yerkes Center.

A.B. Kelly, D.V.M., Associate Research Professor of Veterinary Medicine and Associate Research Professor of Pathobiology and Immunobiology, Yerkes Center.

J.L. Orkin, D.V.M., Associate Veterinarian, Yerkes Center.

E.A. Strobert, D.V.M., Associate Veterinarian, Yerkes Center.

Consultant

B.B. Gay, Jr., M.D., Consultant in Medicine, Yerkes Center; Professor of Radiology, Emory University.

Part I: NARRATIVE DESCRIPTION

A. SUMMARY OF ACCOMPLISHMENTS

1) Strengths and Weaknesses of Current Program

Major strengths of the Yerkes Center during 1989 include continued growth of our research programs, increased interaction with investigators at the host institution, further expansion of our adjunct faculty program, and continued expansion and improvement in the physical plant and animal housing facilities.

Expansion of our research programs, particularly with reference to increased interactions with investigators at the host institution and 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 increased development and expansion of this program contributes substantially toward fulfillment of the Center's commitment and responsibility to serve as a regional and international resource for the conduct of behavioral and biomedical research using nonhuman primates as the animal model system. During 1989, the number of adjunct faculty members at the Yerkes Center totalled 136; this included 114 affiliate and collaborative scientists, five visiting scientists, five research associates and 12 consultants. In addition, there is continued and increasing utilization of Center resources by undergraduate, graduate, and postdoctoral students from the host institution as well as other regional universities. This area of Center activity provides a unique and valuable resource for students and 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 research, cardiovascular research, development and utilization of nonhuman primate models for AIDS research, and research on aging, parasitic diseases, behavior and reproductive biology. A further contribution of the Yerkes Center to regional, national and international biomedical investigators is the provision of a variety of biological specimens collected from our nonhuman primate colony. This important activity of the Yerkes Center has increased substantially over the past few years, with over 6,000 specimens provided to 94 investigators during 1989.

Improvements in the physical plant and animal housing facilities were continued in 1989, and have resulted in improved and expanded animal housing facilities and in increased research space. These continuing efforts have strengthened our position as a research institution, and made it possible for the Yerkes Center to remain fully accredited by the American Association for Accreditation of

Laboratory Animal Care (AAALAC). During 1989, four additional Field Station compounds were renovated and terraced, construction of two additional compounds and 16 indoor-outdoor runs at the Field Station was completed to allow expansion of our rhesus and pig-tailed macaque breeding colonies, a new rodent-proof food storage building was provided at the Field Station, additional observation towers were added to compounds at the Field Station to facilitate behavioral research, an employee lounge was added at the Main Station, new office facilities were provided at both the Main Station and Field Station, the Center's operating room was renovated to meet new federal requirements, a section of the great ape wing was enclosed with screen to facilitate conduct of a research program on filariasis and a two-story, 2600 square feet addition to the Main Center was provided to accommodate a major cardiovascular research program that was initiated at the Center in mid-1989. In addition, work has been initiated on construction of a two-story, 5200 square feet facility that will provide for an expansion of our AIDS animal model studies, an 1800 square foot animal quarantine facility, renovation of existing facilities to provide additional runs for group housing of monkeys, and construction of a facility that will provide additional animal housing and animal test rooms. These additional facilities should be completed by mid-1990.

A continued weakness of the current program is our inability, due to fiscal constraints, to adequately expand the number of core faculty and technical positions and to upgrade and modernize major items of equipment, as needed, to meet the increased demands of expanding research programs and increasing numbers of animals in the colony. Despite the expansion and improvement of the physical plant and animal housing facilities, as summarized above, the Center is unable to provide sufficient personnel, research laboratory space and equipment and animal housing space to accommodate increased research demands in a timely manner. Continued erosion of core grant funding, rather than needed increases commensurate with expanded research programs, has made it difficult for the Center to provide an adequate support system for the advances that have been achieved.

2) Changes in Professional Personnel

During 1989, Drs. James Else and Andrew Kelly were added to the Center's core faculty. Dr. Else joined the Center as Head of Animal Resources and is responsible for administration and coordination of animal resources, clinical medicine and laboratory animal management, and will also be instrumental in the coordination of the Center's international programs in primate research and conservation. Dr. Kelly provides care and oversight to the experimental animals used in the recently added cardiovascular research program at the Center and also participates in specific cardiovascular research projects conducted at the Center. Biographical sketches for Drs. Else and

Kelly are included in the appendix.

3) Major Problems Encountered or Anticipated

The major problem faced by the Yerkes Center is the continued erosion of base grant funding support. We estimate conservatively that over the past eight years base grant support from NIH to the Center has been eroded by 35% to 40% in real dollars, by actual reduction and no increases, combined with inflation. The effect of this is to erode the core scientific programs of the Center, and has made it difficult for the Center to provide the support services (animal care, clinical medicine, pathology, etc.) needed to accommodate expanding core and adjunct faculty research programs. This decrease in core support will eventually result in loss of quality and number of core scientists research programs and thereby decrease the acquisition of baseline data, limit pilot studies and new innovative projects, and adversely affect the establishment of new technology and training of specialized personnel, all of which are the resources needed to obtain funding for targeted research programs and to encourage, expand and support adjunct faculty research programs. Significantly increased base grant funding support is essential if we are to maintain an acceptable level of scientific excellence, continue the highest possible standards for animal care and use, and adequately provide for the support of adjunct faculty research and thereby fulfill our responsibility as a regional resource.

A continuing problem faced by the Yerkes Center, due in large part to the decreasing core grant support, is our lack of sufficient laboratory and animal housing space to accommodate expanding research programs of both core and adjunct faculty in a timely manner. Due to these increasing research programs and our inability to expand adequately our physical plant, it may soon become necessary to delay approved projects until space becomes available upon completion of ongoing projects. Another anticipated problem is the impending shortage of inhouse produced nonhuman primates that will be needed to accommodate increased numbers of research programs. This situation will likely worsen if the importation of nonhuman primates is eventually banned as a result of the recent finding of Ebola-like virus infections in imported macaques. Primate facilities that do not have their own breeding colonies will turn to the Regional Primate Centers as a source of animals for research and vaccine testing; this will place even greater demands on the domestic breeding colonies supported by the Regional Primate Centers program. It is imperative, therefore, that we obtain sufficient funding to expand and maintain Center breeding programs that will provide adequate numbers of animals for our research programs.

Other major problems faced by the Yerkes Center, as well as behavior and biomedical research in general, is the constant harassment by animal activists and the increasing number of

federal rules and regulations that govern the use of animals in research. These have resulted in the increased need for security, increased cage sizes, ever expanding record keeping and revised procedures for animal housing. All of this has increased substantially the costs associated with research using nonhuman primates.

4) Major Equipment Items Purchased

Base Grant*

Quantity	Description	Cost
1	Mail Box System	$ 2,407
1	Gauss Maus Meter	504
1	Signal Level Meter	930
* 1	Gradient Mixer	567
* 3	Ultralow Cryofridge Freezer	13,534
* 1	Tissue Tek Vacuum Infiltrator Processor	19,240
3	Fax Machine	5,518
* 1	Zeiss Microscope with Accessories	2,676
* 1	Ultramicrotome Diamond Knife	3,250
* 1	Power Supply 200/20	658
* 1	Centrifuge HN-S11	1,348
* 1	Rotor	757
* 2	Dual Head Microscopes with Accessories	8,146
* 1	Florescent Screen for JEM-100C	856
* 1	Orion PH Meter	1,570
* 1	Microcentrifuge	1,695
* 1	Shortwave UV Lamp	575
1	Ford Aerostar Van	13,260
1	Water Bath	525
* 1	Cell Counter	714
1	Wet Pipe Sprinkler System	8,916
1	Fire Alarm System	1,690
2	Five Drawer Lateral File Cabinet	1,100
1	Shredder	3,155
* 1	Genie Lift (10' Lifting Height)	823
* 1	Magnetic Stirrer	659
1	Core Drill	1,375
* 1	Cell Harvester 290	3,960
* 1	Sysmex F800 (Parameters)	19,145
* 1	Olympus Microscope	4,262
*30	Rack Units with 120 Primate Cages	110,160
1	Interior Primate Caging	5,235
** 2	Cushman Vehicles	17,933
** 1	Cage & Rack Washer	50,355
** 1	Caloric Gas Range	605
** 1	Floor Scale with Platform	7,813
** 1	Two-Way Communication System	2,240

Base Grant (Cont'd)

Quantity	Description	Cost
** 1	Forklift	15,950
** 1	Steam Boiler	18,623
** 1	Belt/Disc Sander	1,015
** 1	Refrigerator	1,437
** 1	Freezer	1,960
* 1	Gravity Sterilizer	32,112

* AIDS Funds
** Improvement and Modernization Funds

Computer Equipment Purchased

Quantity	Description	Cost
1	27" Sharp Color Video Monitor	754
1	Photometric 250 Upgrade for PC	1,350
1	8MB 17" Mono Desktop Workstation	6,074
1	Video 3/4" Recorder	2,550
1	Multiport Transceiver	757
1	HP Scanjet Plus	1,306
1	HP Laserjet Printer	1,432
1	Kinetic Fast Path	2,055
1	1.1GB Disk Subsystem & 16MB M/Board	20,380
* 2	Compaq 286 Desk Pro Computer	3,450
1	Emory-286 EGA System	2,424
* 2	Zenith 1490 Monitor	1,280
1	Apple Macintosh SE Computer with Memory Upgrade	2,589
1	NEC 80 Column Printer	558
1	IBM Model 30 Computer with accessories	1,623
* 1	Paintjet Color Printer	1,395
* 1	Print Buffer	1,495
* 1	Unipac II	3,400
1	Laserwriter II	2,982

* AIDS Funds
** Improvement and Modernization Funds

Other Grants

Quantity	Description	Cost
1	Clinical centrifuge with Accessories	$ 1,324
1	Dia-Tech Diamond Knife	1,686
1	Chromatography Refrigerator	3,680
5	Programmable Infusion Pump	6,250
1	Pette Multi Channel Pipet	595
1	Mini-Protein II 20 Cell	540
1	Rotator	590
1	Multicap Breath Monitor	5,178
1	Contact Lens Edge Polisher	1,500
1	Seagate 80 MEG Drive	555
1	Vertexometer	2,560
1	Nikon Video Unit	1,800
1	CO2 Monitor	3,020
1	Table Model Horizontal Clean Bench	2,420
1	DNA Thermal Cycler	7,413
4	Monochrome Z-159 Computer	5,246
2	Portable Sony 8mm Playback Deck with 5" Monitor	2,458
1	Slab Gel Dryer	898
1	Video Tape Controller	1,512
1	Computersave Mark II	6,174

5) Improvements and Additions to Facilities

	Cardiovascular Addition	$581,916
	Refurbishing of laboratory and offices in Reproductive Biology Department at Main Station	28,163
*	AIDS Research Facility Addition	903,042
	Screen Enclosure for caging in D Section at Main Station	18,744
	Fabrication of two (2) observation platforms at Field Station	6,300
**	Renovation of Operating Prep Area at Main Station	5,475
	Installation of Boiler and Cage Washer at Main Station	18,526
	Installation of wooden ramps and decking for Employee Lounge and office trailers at Main Station	17,430
**	Installation of Varmintproof Metal Building at Field Station	3,964

Improvements and Additions to Facilities (Cont'd)

Renovation of Metabolism Rooms at Main Station	9,220
Completed rehabilitation of compounds BC1A, A-2, A-3 and G-1 to prevent soil erosion and provide proper drainage at Field Station	22,401
Renovation of Vision Laboratory at Main Station	2,258
Renovation of rooms 302, 307, 308, 357 and 359 at Main Station	16,725
Stonglaze for Quarantine Isolation Building at Main Station	6,505
** Fabrication and Installation of Interior Caging in A-2 and A-3 Compounds at Field Station	6,714
Installation of crosstie retainer wall for office area at Field Station	1,500
Modification of Employee Locker Room at Field Station	2,270
Raise H.V.A.C. Unit and Add Catwalk on Quarantine and Isolation Building at Main Station	3,400
Installation of additional Security Equipment to connect to Main Security System at Main Station	10,876
Installation of Security Equipment at Resident Trailer, Vehicular and Pedestrian Gates at Field Station	4,025

* AIDS Funds
** Improvement and Modernization Funds

6) Conferences, Workshops and Seminars

"Interactions between the Immune System and the Brain," Atlanta Chapter of Society for Neuroscience's Spring Symposium, April 22, Emory University. Yerkes was a co-sponsor.

"Cultural Transmission in Chimpanzees?" Yerkes presentation by Dr. Michael Tomasello of Emory Psychology Department, May 24, Yerkes Center.

"Fertility in the Great Apes," international conference hosted and co-sponsored by the Yerkes Center, June 15 to 17, Colony Square Hotel, Atlanta, Georgia. Co-sponsors included NIH/DRR, Ford Motor Company, Zoo Atlanta/Friends of Zoo Atlanta and Friends of

National Zoo/National Zoo of the Smithsonian Institution.

"Why are Gibbons Monogamous?" Yerkes presentation by Drs. Ronald Nadler and Jeremy Dahl of Yerkes, July 12, Yerkes Center.

"Why Research with Primates: 60 Years of Scientific Advances," Emory Faculty Dinner presentation by Yerkes Director Dr. Frederick A. King, Oct. 3, Houston Mill House, Atlanta, Georgia.

"Recent Advances in Biomedical Studies at Yerkes," Plastic Surgery Research Council presentation by Dr. Frederick A. King, Oct. 24, Emory University

Emory Psychobiology Program Research Seminar Speakers:

"Social Context and Endocrine Modulation of Rhesus Sexual Behavior," presented by Dr. Kim Wallen, Associate Research Professor at Yerkes, February 2, 1989, Emory University.

"Paternal Kin Recognition in a Captive Group of Rhesus Monkeys," presented by Elizabeth St. Andre, a graduate student doing research at Yerkes, February 16, 1989, Emory University.

"Effects of Abnormal Visual Experience on Visual Development in Monkeys," presented by Michael C. Quick, a graduate student doing research at Yerkes, March 23, 1989, Emory University.

"Socially Modulated Acquisition of a Color Discrimination Task in a Group of Rhesus Monkeys," presented by Christine Drea, a graduate student doing research at Yerkes, April 6, 1989, Emory University.

7) Yerkes Visiting Speakers Series

"Female Mate Choice and Patterns of Male Migration in Ring-Tailed Lemurs," Presentation by Dr. Michael Pereira, Duke University, at Emory University, Nov. 30. Co-sponsored by Yerkes and Emory Department of Anthropology.

8) Administrative and Operational Changes

During 1989, Dr. James Else joined the Center faculty as Head of Animal Resources. Dr. Else will be responsible for administration and coordination of veterinary services, animal records and animal husbandry and management. He will also be active in the coordination and expansion of the Center's international programs in primate research and conservation.

The Center's Division of Behavioral Biology has been restructured to include three distinct sections. These are: (1) Section of General Behavioral Biology and Psychopharmacology, Larry D. Byrd, Section Head; (2) Section on Behavioral Neuroendocrinology and

Social Behavior, Thomas P. Gordon, Section Head; and (3) Section on Language and Cognition, Duane M. Rumbaugh, Section Head. Dr. Larry Byrd remains as Chief of the Division of Behavioral Biology.

9) Narrative Progress Report for Non-Research Units

A) Animal Resources: The expansion of Yerkes research programs and the resultant increased number of primates over the past several years led to the need to restructure the animal care and veterinary support services during 1989. To this end, Dr. James G. Else was recruited to take charge of the newly created Animal Resources, an administrative unit which encompasses all aspects of animal support services. This has been done in such a way as to not compromise the integrity of the various departments and divisions which now fall under this unit.

Yerkes Animal Resources is comprised of the Division of Veterinary Medicine, Animal Records, and the three Animal Care units of the Great Ape Wing, Small Primate Wing and the Field Station.

Significant changes that have taken place during this period include:

*** Mr. Jimmy Roberts was promoted to Chief Superintendent of the Yerkes Center.

*** Recruitment of Ms. Karen Pralinsky as Superintendent, Animal Care, Main Station.

*** Expansion of the Primate Care employment categories to provide a suitable career structure and enhanced training and promotion opportunities. Animal Care Technicians now have the option of selecting management, medical and research career tracks.

*** Recruitment of a fourth clinical veterinarian, Dr. Gwen Choi, by the Division of Veterinary Medicine to provide the Field Station with full-time veterinary care. A third veterinary technician was also recruited for the Main Station.

*** The establishment of a succinct animal records unit and the recruitment of Ms. Sue Rust to oversee it. This coincides with instituting a comprehensive computerized animal records system. A second data entry clerk was also recruited.

*** The provision of research support services by the Animal Care Unit. Ms. Toni Duffey was recruited to oversee this new service function and the training programs outlined

below.

*** Development of expanded animal care and safety training programs for animal care and research technicians and scientists working with the animals. This is being done in accordance with the new USDA regulations and is being overseen by K. Pralinsky and T. Duffey.

*** Establishment of a Primate Subcommittee of the Emory Institutional Animal Care and Use Committee. This committee reviews all studies involving primates at Emory University.

*** Recruitment of a Divisional Secretary, Ms. Elizabeth J. Lovell, for Animal Resources.

1. Clinical Medicine

The Division of Veterinary Medicine is a service unit that provides health care for approximately 2300 great apes and monkeys at the Atlanta, Lawrenceville and Panthersville facilities. The Division is also responsible for providing research support to core and affiliate investigators. The unit consists of 4 veterinarians, a registered nurse and 4 veterinary technicians.

The Division supervises the Center's two operating rooms where all non-terminal surgical operations are performed. In 1989 a total of 273 major surgical operations were performed under the supervision of the veterinary unit. Of these, 200 were experimental procedures done by the investigator, 33 were experimental procedures done by the veterinary staff for investigators and 40 were diagnostic or therapeutic procedures done by the veterinary staff. Anesthesia or surgical assistance was provided in approximately 90 % of the investigator performed surgery and all post-operative care including round-the-clock analgesic administration, nursing care and suture removal was done by the veterinary staff.

The radiology service of the Division was utilized to radiograph 792 animals for a total of 1068 films. Of these, 696 animals were radiographed for clinical reasons (illness, injury or health surveillance) and 96 were done for experimental reasons.

During 1989, 1125 new cases of illness or injury were treated; 1035 of these were in monkeys and 90 were in apes. The preventive medicine program for the colony is administered by the Division of Veterinary Medicine. This includes physical examination, hematology, blood chemistries, tuberculin testing and chest radiography

conducted annually on great apes. Tuberculin tests on all individually housed monkeys are done every 4 months and annually on compound housed animals. All primates received from outside the Center are quarantined prior to entry into the colony. All apes are immunized against polio, influenza, Streptococcus pneumoniae and Hemophilus influenzae. All personnel are tuberculin tested semi-annually if they have animal contact and annually if they do not have regular animal contact. Positive reactors are radiographed annually and the films are submitted to a radiologist at Emory for evaluation. Pre-employment reference serum is collected and repeated every two years and stored in the Pathology Division.

The Division provided support in the form of collection of biological samples, surgery, anesthesia, radiography and consultation to 38 core and affiliate scientists. In addition, a number of biological samples were made available to outside investigators. These are listed elsewhere.

2. Primate Care and Housing---Main Station

a) Great Ape Wing

Seven exterior cages on the Great Ape Wing had a prototype screen enclosure erected. This enclosure is designed to keep out insects and reduce the summer heat, and has clear lexan panels which can be easily attached to "winterize" the cages.

Four small testing/holding rooms on the Great Ape Wing were converted into one large room capable of accommodating five metabolism cages. This allows singly housed animals to have visual and auditory contact as well as facilitating caretaking activities.

A twenty five year old pit mounted scale which had rusted beyond repair was replaced with a stainless steel digital platform scale.

Water damaged sheetrock ceilings in the Infectious Disease Building were replaced with a fiber resinous ceiling material which is maintenance free.

The restructuring of animal care included expanding the primate care technician categories. Primate Care Technician III and Primate Care Technician II (research) categories were created. The Primate Care Technician III is a working supervisor who has daily responsibility for the Primate Care Technician I and II's in his or her area and for daily work

assignments. Two Primate Care Technician III positions were created on the Great Ape Wing including the Great Ape Nursery.

b) Small Primate Wing

Three trailer units, T-6, T-10 and T-11A, B, C which had housed animals were taken out of service and removed to make room for an addition to the Ophthalmic Research Laboratory Facility and a relocateable exterior primate enclosure. The addition will have six animal rooms for housing up to 150 monkeys involved in acquired immunodeficiency syndrome research. The relocatable enclosure will have four animal housing rooms, plus five rooms to be used by research faculty for animal testing.

The Quarantine and Isolation Facility's sheetrock ceilings were replaced with a maintenance free fiber resinous ceiling material.

A second utility vehicle (Cushman) was purchased to facilitate moving food, bedding, cages and miscellaneous material between animal housing areas.

Two Small Primate Wing primate care technicians were promoted to Primate Care Technician III (see Great Ape Wing). Additionally, four primate care technicians were selected to participate in two research projects as part-time research technicians (Primate Care Technician II - research), thus offering career enrichment to the technicians and a valuable service to research faculty who do not have to recruit research staff.

3. Primate Care and Housing---Field Station

During 1989, 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:

1. Assembly of two 100' x 100' compounds with attached relocatable primate enclosures was completed. These compounds will provide space for two large breeding groups of macaque monkeys.

2. The rehabilitation of the inside of compounds A-2 and A-3 was completed to prevent further erosion of the soil and damage to the structural integrity of the compound walls. This was accomplished by grading the soil, installing retaining walls, drainage ditches,

and underground drain pipe and applying a layer of crushed rock to the surface.

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

4. An additional rodent-proof chow shed was built to provide space for more chow storage. This was done to accommodate the increased population and resultant greater consumption of chow.

5. Erosion control concrete channels were constructed at BC1A, A-2 and A-3 Compounds. These structures will reduce erosion and provide drainage and a clean area for feeding.

6. A new passenger van with removable seats was purchased this year. This vehicle will be used to transport people, animals, supplies and mail between the Field Station and Main Station.

7. Two new walkie-talkies with two channel capabilities were purchased and two walkie-talkies and the base station were converted to provide 2 channel capabilities. The second channel enables us to communicate with different parts of our operation separately.

8. A new refrigerator, freezer and stove were purchased for the kitchen. These kitchen appliances will enable us to prepare specialized primate diets more efficiently and store them properly.

9. The indoor quarters of A-2 and A-3 Compounds were renovated. The additional light fixtures, new paint, perching and caging, Stonhard flooring and more efficient ventilation system has brightened the animal areas, improved the air quality and made it easier to maintain.

10. Sixteen new indoor-outdoor runs were completed during this year. The area will be used to house harem breeding groups.

11. A concrete erosion control structure/walkway was built around the G-1 Compound. This structure will promote drainage, eliminate standing water and provide a walkway around the facility from which the animals can be observed.

12. The ceiling of the BC2 indoor quarters was completely renovated and the walls repainted. The new ceiling

helps to maintain the structural integrity of the building and the new paint has provided a brighter indoor area for the animals.

13. Portions of the chain link fencing around the A-2 and A-3 Compounds were replaced. The new fencing will prevent escapes and possible injuries caused by broken pieces of wire.

14. A new training program for the Animal Care personnel was instituted. The program covers such varied subjects as First Aid, Field Research, Safety, Animal Handling Techniques, current Research Programs at the Field Station and other related topics. The benefits of the program are a more knowledgeable and safety conscious staff that knows how important their performance is to the ongoing research.

15. Two (2) night security positions were created. The night personnel are responsible for the well being of the animals, proper functioning of the Physical Plant, security of the buildings and grounds and the distribution of medication to the animals under veterinary care during the hours not covered by the day personnel.

B) Physical Plant

1) Main Station

The following items were accomplished during 1989:

a) A portion of trailer 11C (Cardiovascular Studies) was renovated to temporarily house a scanning X-ray laboratory for Dr. Harker's cardiovascular studies.

b) A 2-story, 2,600 square feet facility was constructed for cardiovascular studies. The first floor contains a scanning X-ray laboratory, camera laboratory, computer room and an office. The second floor contains a radioimmunoassay laboratory and two offices.

c) Trailer 6 (503 square feet of animal housing for AIDS related research) and Trailer 10 (585 square feet of animal housing space) were removed to make room for a new AIDS Addition research facility.

d) Construction began on the AIDS Addition research facility which will contain 5,200 square feet of animal housing and laboratory space. This facility will connect to the Ophthalmic Research building and

will contain animal housing on the first floor and laboratories on the second floor.

e) A new cage washer was installed to maintain approximately 250 cages housed in REPEs A and B. Included in the project was the purchase and installation of a cage washer, purchase and installation of a boiler to generate steam, and construction of a shed.

f) Six outside cages on the Great Ape Wing were enclosed using roof panels with sky lights and ventilators. The sides are reinforced with plexiglass panels and screen wire. Enclosure was necessary to keep flying insects away from animals used in a particular study. Enclosure also prevents animals from being confined to small indoor cages during inclement weather.

g) The Reproductive Biology Laboratory, a 421 square feet laboratory, was completely renovated in order to remove decaying wood casework and to more effectively utilize the space. Renovation included new sheet vinyl flooring, clean room ceiling tiles, painting, new case work and redistribution of electricity and plumbing.

h) The HVAC unit serving the Quarantine and Isolation Facility was relocated in order to increase efficiency of the system by reducing the number of ninety degree turns and shortening the duct. Secondly, relocation allowed more working room to the facility next door.

i) Two HVAC units serving Scanning Electron Microscopy (T-12) were relocated to create additional space necessary for construction of a new facility.

j) The Metabolism Room Complex located in the Great Ape Wing was renovated to allow more flexible use of the area. Renovation primarily consisted of converting the complex from four small rooms into one large room. Also included was resurfacing of the floor with Stonhard (an epoxy flooring resistant to cleaning compounds and moisture) and extensive rerouting of electrical work.

k) The Vision Laboratory in the Ophthalmic Research Building was renovated to satisfy the needs of new research grants. Renovation included removal of some casework, rearrangement of electrical, plumbing and gas lines, and new vinyl flooring.

l) The Surgery Room prep area was renovated to create

separate facilities for humans and animals in order to satisfy new regulations for surgery preparation. Renovation included the addition of a partition wall, new sink, additional lighting and extension of HVAC duct work.

m) Overhead telephone lines serving the security temperature alarms and regular voice lines were relocated underground to increase protection.

n) The water damaged sheetrock ceiling in the Quarantine & Isolation Facility was replaced with FRP (fiber resonance products) board which is more resistant to water and high humidity. Interior and exterior walls were repainted with epoxy paint for added protection against moisture.

o) Faculty and staff locking mailboxes were installed to replace open-rack shelves in order to provide privacy and security.

p) The Center's security system was expanded and updated to add new rooms and facilities to the card access system.

q) Additional parking spaces were created by grading and graveling to accommodate additional personnel as well as visitors and clients.

r) Vending machines were relocated from the Main Building and the vacated space was converted to much needed file storage.

s) A new Cushman was purchased to transport supplies, equipment and maintenance items to remote buildings.

t) Several dead trees that posed potential danger to the Gibbon housing units and other animal housing facilities were removed.

u) The floors in the Quarantine & Isolation Facility and T-14 were resurfaced with Stonhard products totaling approximately 2,400 square feet.

v) Three freezers containing AIDS related specimens were added to the emergency generator.

w) Three offices in the Main Building were repainted and new lay-in ceilings were installed.

2) Field Station

During 1989 the following items were accomplished:

a) The Field Station roads and perimeter were graded and crushed rock spread on them. This will reduce the wear and tear on our vehicles.

b) A forklift was purchased this year. The forklift will enable us to load, unload and move supplies, and other heavy objects more efficiently and considerably reduce the risk of injury to our personnel.

c) A new triple-wide office trailer was installed. This facility has provided much needed office space for our research, and secretarial staffs. In addition to office space, the trailer provides us with a conference room and an animal records area.

d) A plasma metal cutter, grinder/sander and electric welder were purchased for the shop. These pieces of equipment will enable our shop personnel to take care of fabrication and repair needs more efficiently.

C. Service Pathology

Necropsy Service: During 1989, 301 nonhuman primates were submitted for postmortem examination, and 137 biopsies were submitted for histopathologic evaluation. When compared to the preceding year (1988), this represents an increase of 5.6% (16 cases) in the number of necropsies; the number of biopsies decreased 11.6% during the same period.

The postmortem examinations done in 1989 can be categorized as follows:

	Total Number	Percent Total
Deaths Associated with Experimental Procedures	90	29.9
Deaths During Quarantine Period	2	0.7
Deaths Associated with Clinical Problems	97	32.2
Abortuses/Stillbirths	49	16.3
Neonatal Deaths	41	13.6
Deaths Due to Accidents/Fights/Exposure	20	6.6
Necropsies on Other than Center Animals	2	0.7

Selected postmortem observations recorded during 1989 are summarized as follows:

	Total Number	Percent Total
Animals with Parasite Infections	34	12.6
Animals with Pneumonia	9	3.0
Animals with Gastritis/Enteritis/Colitis	35	11.6
Animals with Tumors	5	1.7
Animals with Yersiniosis	14	4.7
Animals with Mycobacteriosis	1	0.3
Animals with Shigellosis	9	3.0
Animals with Campylobacteriosis	53	17.6
Animals with Amyloidosis	5	1.7
Animals with Listeriosis	4	1.3

When compared with the preceding year (1988), the above information reflects the following:

1) The number of deaths associated with experimental procedures increased from 76 to 90 (18% increase), reflecting a significant increase in biomedical research projects related to human disease problems.

2) There was a decrease in 1989 in the number of deaths associated with clinical problems (decrease of 11%---12 animals), when compared to the number of deaths associated with clinical problems in 1988. The number of abortuses and stillbirths was the same in 1989 as in 1988, whereas the number of neonatal deaths increased by 24% (8 animals) when compared to the number noted during the preceding year. The number of deaths associated with accidents, fights or exposure increased by 11% (2 animals) when compared to the preceding year.

3) Only five cases of amyloidosis were diagnosed in 1989. This represents a significant decrease from the 26 cases of amyloidosis diagnosed in 1988. Amyloidosis continues to be a problem in Field Station animals, with 116 cases diagnosed from 1975 through 1989. Studies are currently underway to further characterize the pathogenesis of the disease and to use these naturally occurring cases as models for the study of amyloidosis.

4) An additional 14 cases of yersiniosis were diagnosed at necropsy during 1989. This naturally occurring enteric bacterial infection continues to be a problem in our Field Station colony. Yersinia species have been isolated from 174 necropsy cases since the disease was first diagnosed in 1968. Most of the cases have been due to either Yersinia enterocolitica or Y. pseudotuberculosis

infection, although a small number of Y. intermedia, Y. fredericksenii and Y. kristensenii organisms have been isolated. Some of these isolates represent nonpathogenic, environmental strains of Yersinia, as lesions were not detectable in some animals from which Yersinia were isolated.

5) Five animals (1.7% of necropsies) were found to have neoplasms in 1989; two of these five animals had two different neoplasms. Tumors encountered in 1989 included a subcutaneous lipoma in a 16-year-old rhesus, a carcinoma of the thyroid and a kidney carcinoma in a 22-year-old rhesus; a colon carcinoma and a kidney adenoma in a 25-year-old rhesus; a carcinoma of the small intestine (jejunum) in an 18-year-old rhesus and a thyroid adenoma in an 18-year-old rhesus.

6) Four additional cases of listeriosis were diagnosed in 1989. These included one newborn rhesus, two newborn mangabeys and one day old mangabey. This brings the total number of cases of listeriosis seen in our colony to 39, since the disease was first diagnosed in 1982.

Significant lesions observed in the 137 surgical pathology specimens examined in 1989 included amyloidosis, chronic colitis, subcutaneous lipoma, chronic dermatitis, carcinoma of the small intestine (jejunum), carcinoma of the ileocecal region and herpetic lesions of the skin (varicella-zoster).

Histopathology Service: During 1989 the histopathology laboratory processed 312 necropsy cases and/or biopsies. This entailed the production, and subsequent filing of 7,972 paraffin blocks. A total of 8,488 microslides were prepared from these blocks. Following microscopic review, all slides are maintained on file in the light microscopy laboratory.

Clinical Pathology Service: During 1989, the clinical pathology laboratory received 10,185 specimens for evaluation. These determinations can be categorized as follows:

Laboratory Determination	Number of Specimens
Hematology Examinations	2,180
Bone Marrow Examinations	3
Bacterial Cultures	3,202
Mycoplasma Cultures	2
Viral Cultures	1
Fungal Cultures	15
Fecal Parasitology Examinations	685
Serum Chemistries	1050
Pregnancy Tests	90
Urine Analysis	139

Imprint Smear Preparations	680
Spinal Fluid Examinations	105
Immunologic Examinations	2028
Specific Gravity	3
Special Chemistries (Kidney Stone Analysis, Fluid protein)	2

When compared with 1988, this number of laboratory specimens represents an increase of 1,485 submissions (17.1% increase). Significant increases were noted in the number of hematology examinations, bacterial cultures, spinal fluid examinations and immunologic evaluations.

Selected pathogenic microorganisms isolated during the past year include:

Staphylococcus aureus	Streptococcus pneumoniae
Campylobacter pylori	Cryptococcus neoformans
Candida albicans	Listeria monocytogenes
Salmonella enteriditis	Shigella flexneri
Yersinia pseudotuberculosis	Yersinia enterocolitica
Yersinia kristensenii	Yersinia frederickseni
Yersinia intermedia	Campylobacter coli
Enteropath. E. coli	Campylobacter fetus
Campylobacter jejuni	Klebsiella pneumoniae

A total of 637 antibiograms were done on bacterial isolates during the year.

The most frequently encountered parasites continue to be Balantidium coli, Trichomonas species, Blastocystis species and Trichuris species. During 1989, strongyloidiasis occurred in 7 animals and one case of giardiasis and one case of cryptosporidiosis were diagnosed.

Pathology Electron Microscopy Laboratory: During 1989, the pathology electron microscopy laboratory received 135 specimens for processing for ultrastructural evaluation. Specimens received included 64 cell cultures, 29 lymph nodes, 18 Peyer's patch specimens, 6 spleen specimens, 6 placental specimens, 3 liver specimens, 3 specimens of choroid plexus, 2 small intestine specimens, and 1 each of colon, kidney, skin lesion and lung.

Specimens Collected for Other Investigators: During 1989, 6043 specimens were collected and shipped to 94 investigators. A partial listing of specimens provided includes serum, blood, a variety of tissue specimens, carcasses, eyes, bone, brain, bone marrow, cerebrospinal fluid, bacterial isolates (Streptococcus pneumoniae and Yersinia species), hair, spines and fecal samples. This includes 36,595 ml of whole blood, 1440 ml of serum and 57 ml of plasma from 14 nonhuman primate

species. When compared to 1988, the number of specimens shipped represents an increase of 34%.

D) Radioimmunoassay

The Yerkes Radioimmunoassay (RIA) Laboratory is a fully equipped laboratory providing services of radioimmunoassay, bioassay, spectrophotometric analyses, and fluorometric analyses of biological samples. The Yerkes RIA facility provides this service to Yerkes core faculty and affiliated scientists, scientists from Emory University, and other investigators outside of the Emory community. Determinations are provided on a sample charge basis comprised of the cost of technical time, chemical reagents, equipment used, and waste disposal. During calendar year 1989, individuals which utilized the services of the RIA Laboratory are as follows:

Yerkes Core Scientists

Dr. Harold McClure: specific activity of tissue samples was determined as a part of a project on treatment of urinary tract disorders.

Dr. Irwin Bernstein: gonadal and pituitary hormone determinations were performed for his project on socialization in male monkeys.

Dr. Ken Gould: gonadal and pituitary hormones were determined as a part of his studies of fertility in great apes and exotic mammals.

Dr. Kim Wallen: adrenal, gonadal, and pituitary hormone determinations were performed for his projects on the endocrine control of female sexuality in monkeys.

Dr. Mark E. Wilson: adrenal, gonadal, pituitary, pineal and metabolic hormones were determined as a part of his projects on the neuroendocrine regulation of puberty, growth and lactational infertility.

Dr. Ron Nadler: pituitary hormone determinations were made for his projects on sexuality in chimpanzees and gibbons.

Mr. Tom Gordon: adrenal, gonadal, pituitary, and pineal hormone determinations were performed as a part of his projects on seasonal reproduction and psychoneuroimmunology.

Dr. Jim Herndon: pituitary and pineal hormone determinations were performed as a part of his studies on male sexuality in monkeys.

Division of Clinical Veterinary Medicine: analyses performed to provide information on gonadal and pituitary function.

Yerkes Affiliated Scientists

Dr. David Mann (Morehouse School of Medicine): gonadal and pituitary hormone determinations were performed for his projects on steroidogenesis, development, and osteoporosis in rats and monkeys.

Dr. David Martin (Georgia State University): gonadal and pituitary hormones were determined as a part of his project on sexuality in quadriplegic men.

Dr. Robert Donahoe (Georgia Mental Health Institute): pituitary hormones were analyzed as a part of his project on drug abuse and immune function.

Dr. Susan Schwartz (Caribbean Primate Research Center): gonadal, pituitary, and metabolic hormone determinations were made as a part of her research on puberty in monkeys.

Emory University Scientists

Dr. David Edwards - Department of Psychology
Dr. Edwin Dale - Department of Obstetrics and Gynecology
Dr. Eugene Emory - Department of Psychology
Dr. Jennifer Lovejoy - Department of Medicine
Dr. John Parks - Department of Pediatrics
Dr. Larry Phillips - Department of Medicine
Dr. Mario DeGirolamo - Department of Medicine
Dr. Patrick Delafontaine - Department of Medicine

Non-Emory University Scientists

Dr. Carol Shively - Bowman Gray University School of Medicine
Dr. Jay Kaplan - Bowman Gray University School of Medicine
Dr. John Grostic - Life Chiropractic College

During the calendar year 1989, the RIA Laboratory performed 25,088 determinations as follows:

Hormone	Number
B-endorphin	166
androstenedione*	62
cortisol*	589
creatinine	622
DHEA-S*	92
estradiol (free)*	80

estradiol*	4829
estriol glucuronide*	359
estriol*	31
estrogens (total)*	7
estrone glucuronide*	359
estrone sulfate*	49
estrone*	111
FSH (human, ape)	5
FSH (monkey)	1834
GH	629
IGF-1	1311
insulin*	2679
lactose (milk)*	41
LH (bioassay)	2632
LH (human, ape)	5
LH (monkey)	1203
melatonin	441
osteocalcin*	18
pregnenediol*	358
progesterone*	4227
prolactin	1641
protein (milk)*	53
SHBG*	80
T4 (total)*	36
testosterone (free)*	80
testosterone (total)*	459

The following is a list of assays currently available in the RIA Laboratory:

Steroid Hormones:

androstenedione	testosterone (male)
dihydrotestosterone	testosterone (free)
testosterone (female)	progesterone
cortisol	estradiol (free)
estradiol	estriol
estrone	estriol glucuronide
estrone glucuronide	pregnenediol
estrone sulfate	dehydroepiandrosteone sulfate
pregnenediol (EIA)	
sex steroid binding globulin	

Other:

osteocalcin	B-endorphin
creatinine(spectrophotometric)	glucose (spectrophotometric)
glucagon	
melatonin	custom iodinations

Protein hormones:

adrenocorticotropin hormone
luteinizing hormone (human, ape)
luteinizing hormone (rat)

follicle stimulating hormone (human, ape)
follicle stimulating hormone (monkey)
growth hormone (human, monkey)
insulin-like growth factor-1 (human, monkey)
insulin (free)
C-peptide of insulin
T3
T4 (total)
oxytocin
T4 (free)
somatostatin

human chorionic gonadotropin
luteinizing hormone (monkey)
luteinizing hormone (bioassay)
luteinizing hormone (urine)
follicle stimulating hormone(bioassay)
prolactin (human, monkey)
insulin (primate)
insulin (rat)
thyroid stimulating hormone
T3 (reverse)

E) General Office Services

This office is responsible for the following functions:

a) processing and distribution of mail
b) answering telephone calls
c) greeting and assisting visitors
d) maintaining and distributing office supplies
e) assisting in the operation of the photocopying machines

F) Information Services

The Information Services Office, which was created in November, 1979, is headed by an Administrative Associate for Special Projects who also holds the title of Chief, Public Affairs.

The Office is responsible for the Center's internal and external communications as well as special projects. The latter include many of the workshops and conferences that are hosted and organized by the Center. Through these activities, the Center endeavors to improve understanding and support of its goals, programs and accomplishments.

During 1989, the Administrative Associate for Special Projects developed a plan of activities to recognize, during 1990, the Center's 60th anniversary, the 30th anniversary of the establishment of the NIH Regional Primate Research Centers Program, and the 25th anniversary of the Center's move to Emory in Atlanta from Orange Park, Florida, where the institute was founded by Dr. Robert M. Yerkes. However, due to limited funding, the Center is not able to sponsor anniversary recognition activities during 1990.

Significant activities in the following program areas of the Information Office are reported.

Audiovisual and print materials: During August 1989, the Administrative Associate for Special Projects was provided with a second-hand word processing system with software for "desktop publishing." The office is therefore equipped to produce fact sheets, the Inside Yerkes newsletter and other printed materials much more rapidly and with a much more professional appearance than previously possible. Two issues of Inside Yerkes, the Progress Report: NIH Chimpanzee Breeding and Research Program, and a fact sheet on the Yerkes Center's research on addictive drugs were produced during the Fall by the Administrative Associate.

The main advantage of "desktop publishing" is cost. Because the word processor performs the typesetting, and the software is used for layout and design, much of the cost of publishing brochures and other materials is eliminated by "desktop publishing." Realizing the advantages of "desktop publishing," the Administrative Associate in consultation with the Yerkes Director began planning an approach to publications that will take advantage of "desktop publishing." As part of the plan, a Public Affairs Assistant was hired in early 1990. She occupies the position formerly held by the secretary to the office.

During 1989, a paper about the Yerkes Center's history and current programs was drafted for submission to Emory Journal of Medicine.

Due to limited funding, the Administrative Associate was unable to prepare any audiovisual programs about the Center.

News media relations: The following are examples of the Administrative Associate's initiation of news media coverage and/or assistance to journalists:

NBC-TV story about births of Yerkes gorillas at Zoo Atlanta and the role of Yerkes studies on gorilla behavior/reproduction.

Japan cable TV documentary on bonobo chimpanzees. The television program, to be broadcast in 1990, included interviews and filming at the Yerkes Field Station and the Language Research Center.

Day in the Life: The Power to Heal, Ancient Arts and Modern Medicine. The Administrative Associate for Special Projects arranged for a photograph of a Yerkes research study to be taken for possible use in this book, to be published in 1990.

Science et Vie. French science magazine, story on AIDS. Interviews and photography arranged by Administrative Associate.

British Broadcasting Corporation series, "The Art of Language." Arrangements were made for Dr. Jonathan Miller to visit the Yerkes Center and interview two scientists for this series, to be broadcast in 1990.

Workshops and Conferences: The Administrative Associate assisted the Yerkes Center's Chief of Reproductive Biology in the organization and conduct of the "Fertility in Great Apes," conference. Preparation for this international meeting involved a significant commitment of time and resources by the Administrative Associate for Special Projects. Her activities included: developing and maintaining a time schedule of deadlines for tasks to be completed in organizing the conference; arrangements for transportation, coffee breaks and meals; coordination of information packets, signage, name badges, and other conference materials; and public relations.

Tours and presentations: Over 800 people visited the Yerkes Center during 1989. The majority were part of tours that the Administrative Associate for Special Projects hosted or arranged. A significant number of tours were provided to Emory student groups, particularly members of Freshman Seminar classes.

The Administrative Associate for Special Projects spoke at the annual conferences of the Society for Neuroscience and the American Medical Writers Association during 1989.

Students working on class projects about the study of laboratory animals and other topics were assisted by the Administrative Associate for Special Projects. Two examples of assistance to students are provided: a Fernbank Elementary School student whose term paper subject was gorillas. The Administrative Associate provided the student with printed materials, an interview and a tour of Zoo Atlanta where Yerkes gorillas are on loan for exhibit and conservation-oriented research. A second example: a Sutton Middle School student whose class project was titled, "Why is it important to study primate behavior to understand human behavior?" The Administrative Associate provided the student with printed information and videos, arranged for the student to interview a Yerkes scientist, and spoke to the student's class.

The Administrative Associate for Special Projects also represented the Yerkes Center in the Clifton Corridor Communications Committee and on the Friends of Zoo Atlanta's Board of Directors.

G) Administrative Associate to the Director

The Office of the Administrative Associate is responsible for coordination of computerization at the Yerkes Center, oversight of contracts and agreements with the private sector, liaison with selected government and professional agencies, and administrative coordination of fund raising activities. In addition the Administrative Associate serves as chairman of the Yerkes "No-Smoking" Task force and as chairman of the Animal Records Committee.

Computerization - The following were areas of special emphasis during 1989:

An assistant for the Coordinator of Computer Services was added to support the installation and maintenance of the expanding base of established computer hardware and software. An in-house programmer was hired to maintain the Animal Records Database program and to reprogram the entire Budget and Accounts system.

An Animal Records Database manager was hired to replace the original system administrator and data entry support was increased by hiring two data entry operators for the Animal Records System. Data input was further facilitated by distributing entry. Caging data began to be input by personnel located on the animal wing, veterinarians began to enter clinical data directly into the database via a specially designed access sheet, records were generated from the Field Station for animals housed there, and so forth.

A Broadband/Ethernet Bridge was installed to connect the Center's main computer with the campus computer network, thus giving all users access to the major national and international computing and electronic communication networks.

The number of users for the Center's main computing capabilities doubled, totalling approximately 100. Utilization of the Sun 3/260 grew close to 100% of maximum CPU load and 70% of total disk capacity.

Consulting services were provided to the Language Research Center regarding the networking of the computers and establishing closer computer communications with the Main Center.

Contracts and Agreements with Outside Agencies: The Yerkes Center is currently involved in 39 agreements and contracts, an increase of 10 over last year, for research sponsored by or carried out for private industry, universities, and other outside agencies. Another 11 contracts or agreements are in various stages of negotiation. In addition, the Yerkes Center has agreements with 41 organizations, two more than last year, regarding animals on loan. Finally, the Yerkes Center is involved in three agreements relating to patents. The following is a partial list of organizations with one or more current agreements with the Center.

American Paralysis Association
American Parkinsons Disease Association
American Society for Aesthetic Plastic Surgery, Inc.
Bard, Inc.
Behringwerke AG
Biotech Research Laboratories
Boston University
Burroughs Wellcome Co.
Busch Entertainment Corp.
Chiron Corp.
Dana Farber Cancer Institute
Deknatel Div. of Pfizer Hospital Products Group
Eagles Max Baer Heart Fund
The Edna McConnell Clark Foundation
Emory - Georgia Tech Biotechnology Research Center
Genentech, Inc.
General Electric Company
Genetics Institute
Georgetown University
Georgia State University
Harvard University
Institute of Primate Research and California Primate Research Center
Johns Hopkins University

Metters Industries and Southern Research Institute
Morehouse University School of Medicine
Pasteur Vaccins
Rockefeller Foundation
Sandoz Research Institute
Searle Research and Development
Summit Technology, Inc.
Syntro Corporation
University of Alabama
VLI Corporation
Zoo Atlanta
Zeus Scientific, Inc.

Liaison with Selected Government and Professional Organizations: In 1989 the Administrative Associate's office provided support to two developing organizations promoting biotechnology and research: the DeKalb Chamber of Commerce Biotechnology Research Council, and the American Psychological Society.

The DeKalb Chamber of Commerce Biotechnology Research Council - The Yerkes Center has been involved with the development of the biomedical technology industry in Georgia through its participation in both the Steering Committee and the Task Force Committee of the DeKalb Chamber of Commerce Biotechnology Research Council. In addition various members of the Yerkes Center have served on several committees of the Council and promoted its activities by providing educational tours for Dekalb County businessmen, political figures, and for businessmen from other countries through liaison activities with the French and German Consulates in Atlanta. The DeKalb Chamber of Commerce Biomedical Research Council mission is to bring together the many biotechnology resources of the area known as the Clifton Corridor. The Clifton Corridor is not a geographical designation but instead refers to the facilities of Emory University, including the Yerkes Center, Georgia Tech, the U. S. Centers for Disease Control, the national headquarters of the American Cancer Society, and the many surrounding academic and private facilities involved in biotechnology research and development. The aim of the DeKalb Biotechnology Research Council is to stimulate advances in biotechnology research and technological development, not only in the DeKalb County areas but also in the state of Georgia. The strategy will be to invite biotechnology industries to locate in the DeKalb area based on cooperative projects with the academic and existing government and private biotechnology facilities in the county. DeKalb's initiative will then be used as a model for development of similar initiatives throughout the state. The Yerkes Center, as a regional research facility, has been supportive of this

program since early in its inception.

The American Psychological Society - The formation in 1988 of the American Psychological Society had as its' stated purpose the promotion of academic research and training in the field of psychology. The APS quickly obtained several thousand members. The office of the Associate Administrator acted as the liaison to the new Society and worked to inform all core and relevant collaborative faculty members of its government liaison activities, scientific meetings, and program development activities. A very high percentage of the faculty members contacted at the Yerkes Center have become members of the APS.

Coordination of Fund Raising - In 1989 the Administrative Associate's office provided assistance to the Director in promoting fund raising for expansion of the Center. The Yerkes Center is working directly with the Emory's Office of Development and for the first time will be part of the fund raising campaign being organized for the University. In addition, fund raising consultants are being evaluated for possible initiatives in addition to the Emory campaign if necessary. In addition, the Next Corporation donated a Next Computer to the Yerkes Center for research support and development. This computer is valued in excess of $10,000 and the Yerkes center is grateful to the Emory University Vice Provost for Information Services for support in obtaining this Center asset.

H) Bioelectronics and Instrumentation Shops

The major activities of the Bioelectronics and Instrumentation Shops during 1989 are summarized below:

Scientific Projects: Numerous projects involving data collection devices were carried out by the Electronics Shop during 1989. Among these were the design, programming and construction of a computerized portable system for testing grip strength for a visiting scientist, Dr. Joel Fagot in the Division of Behavioral Biology. Numerous repairs and modifications were carried out for Dr. Boothe's data acquisition systems. These include: repair of infrared detectors, repair of Schmidt trigger, modifications to a retinoscope, design and construction of light sources and experimental stimuli. The Center's SEM facility requested and received several repairs from the Electronics Shop. An experimental control device for operant studies was designed and constructed for Dr. Nadler. Custom-designed black bulb radiant heat sensing thermostats for the Center's gibbon units were replaced or repaired as a part of Dr. Dahl's studies of gibbons. Repairs of electronic equipment were conducted for

Dr. Wilson, and for the Pathology Division. Many miscellaneous repairs were also carried out.

Work conducted for other service units: Security devices were repaired or replaced. Numerous computer items were repaired, including the Center's Ethernet System, annex terminal server boxes, as well as phone and printer cables. Miscellaneous repairs include replacement of printer heads, typewriter motors, power connectors and outlets, as well as miscellaneous word processing equipment repairs.

Consultant services provided to the Center by Professor Harold Warner: During the past year, Professor Harold Warner, retired Chief of Biomedical Engineering, continued to provide consultation and service to the Yerkes Center. Professor Warner's consultation has included assistance given to faculty members on various projects, as well as consultation on numerous projects undertaken by the Instrumentation and Electronics Shops personnel.

I) 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 1989, the General Shop responded to 224 emergency repair calls. During the same period, the General Shop completed 183 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.

J) Library

The Yerkes Research Center Library is an essential resource in the research process. The library serves the information needs of the research staff and administration and provides full library service by acquiring, organizing, and disseminating information for current use, and by preserving relevant materials for future access.

The library contains 2,000 journal volumes and 2,000 books. There are 725 books and 4,500 reprints in special collections. These consist of archival and personal books from the libraries of former directors, and from a reprint collection begun by Robert M. Yerkes. Faculty publications added to the volumes, "Contributions from Yerkes Regional Primate Research Center," now total 2,950. This bound, indexed, reprint collection dates back to 1925.

Circulation figures, 6,000, remained approximately the same as

for the previous year. This figure includes inhouse use, as routing journals, checking out books, photocopying requested materials, loaning or dispensing reprints (publications of Yerkes' faculty and collected reprints); borrowing and photocopying at Campus libraries; and borrowing through interlibrary loan from libraries off campus.

Journal subscriptions increased from 53 to 65 and book purchases increased from 39 to 43 from the previous year.

The online databases, DIALOG and VUTEXT, and DOBIS the online catalog of Emory's library holdings, were indispensable for reference use, and for literature and bibliographic searches. The FAX machine was used for urgent interlibrary loan requests.

K) Business Office

During the 1989 calendar year the Center reorganized several of its management functions under an administrative structure called the Business Office. The following four management functions have been consolidated within the newly designated Business Office:

1. Purchasing - includes procurement, accounts receivable, accounts payable, inventory control, shipping/receiving and express mail.

2. Budget and Accounts - includes grant preparation and grant administration.

3. Travel - includes travel arrangements and travel voucher processing.

4. Payroll - includes leave accrual record keeping, time cards processing and paycheck distribution.

L) Photography

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

During 1989, 527 request for photographic services were received and processed. The types of photographic illustrations provided included black and white photographs, color slides and prints 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 were done in cooperation with investigators;

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

Black and white line negatives, prints and 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;

Computer-generated charts, graphs and slides were prepared using Sigma-Plot, Freelance Plus, and Picture It software;

Acted as liaison with color lab for color prints for poster sessions and wall displays;

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

Photographs, letters and certificates were framed for display.

M) Scanning Electron Microscopy and X-ray Microanalysis Unit

The scanning electron microscopy/microanalysis facility provides scanning electron microscopy (ISI DS130) and energy dispersive x-ray analysis (Tracor TN5500) for use in research and training. Recent upgrades to the equipment have maintained their status as superior. The availability of chromium coating and delicate handling procedures for biological specimens have attracted increased collaboration with American and European institutions. Research areas in the facility include high resolution imaging and development of improved methods of chromium coating for high resolution imaging.

During 1989, staff of the facility organized a successful short course on high resolution imaging, and provided support for research projects including the development of novel methods for sperm preparation and evaluation of morphological changes associated with freeze preservation; enamel crystal structure in man; adrenal ultrastructural changes with age; monitoring of intra arterial stents in the pig and rabbit; and the efficacy of laser surgery of the cornea.

The following investigators conducted research using Scanning Electron Microscopy at the Center during 1989:

Name:	Affiliation:
K. Robinson	Cardiovascular Center, Emory University
T. Tsuno	Chemistry Department, Emory University
K. Thompson	Ophthalmology Dept., Emory University
M. Farley	School of Medicine, Emory University
D. Stephens	School of Medicine, Emory University
G. Waring	Ophthalmology Dept., Emory University
K. Gould	Yerkes Research Center, Emory University
R. Hunter	Pathology Department, Emory University
L. Young	Physiology Department, Emory University
R. Apkarian	Yerkes Research Center, Emory University
F. Menger	Chemistry Department, Emory University
Mead Paper Co.	Commerical

Visiting Scientists at the SEM Facility in 1989 included:

Dr. Jean Schoknect, Univ. of Indiana, Indianapolis, Indiana
Dr. Susan Tai, Universidad de Oriente, Cumana, Venezuela
Dr. Orlando Castejon, University of Zulia, Maricaibo, Venezuela
Dr. Bill Chissoe, University of Oklahoma, Norman, Oklahoma
Dr. Ed Basgall, University of Illinois, Urbana, Illinois

B. HIGHLIGHTS

1. Research Completed

a) Correction of Monocular Aphakia with Intraocular Lens

For human infants born with monocular cataracts, visual outcome is usually poor even after early removal of the cataract. The postoperative correction of the resulting aphakia is the limiting factor in visual rehabilitation of these eyes. Correcting the aphakic eyes with contact lenses, epikeratoplasty or spectacles, magnifies the image in the aphakic eye, thereby creating a disparity in the image size between the 2 eyes, resulting in amblyopia. Intraocular lens (IOL) implantation is a promising new approach to this problem with the potential to optimize vision in the aphakic eye. Although IOL are routinely used in adult human patients, their efficacy and safety in an eye that is still growing is not known. Therefore, a pilot study was initiated using newborn rhesus monkeys as an animal model to evaluate the efficacy and safety of IOL. Two neonatal monkeys underwent monocular lensectomies with the implantation of a posterior chamber intraocular lens.

A detailed histopathologic study of the pseudophakic eye of the second monkey revealed that a posterior chamber IOL can be implanted safely. Better visual acuity was also achieved in the pseudophakic eye than in an aphakic eye corrected with an extended-wear contact lens. Examination of the striate cortex with neuroanatomical methods revealed that a pseudophakic eye can compete successfully with an unmanipulated fellow eye for cortical territory. There was only a slight shift in ocular dominance columns in favor of the unmanipulated eye. Since congenital cataracts are one of the most common causes of impaired vision during childhood, this animal model system will be important for the design and testing of treatment methods to preserve good visual functions in human infants with congenital visual system disorders.

b) Language Acquisition in Chimpanzees

These studies were designed to further our understanding of the processes underlying language development through comparative research so that what is learned might be applied toward intervention for alinguistic humans. During the past year, the principal focus was to test sentence comprehension in our most sophisticated symbol-using subject, Kanzi, a 9-year-old bonobo (Pan paniscus). Data were also collected on one of the human subjects, aged 18-23 months. Complex and novel English sentences were presented to both subjects under carefully controlled, blind conditions. A total of 728 sentences were presented to Kanzi; 698 sentences were also presented the human child. Results revealed comprehension of similar forms of syntax, with similar errors, in the ape and the child. This testing advances previous measures of syntax comprehension because such comprehension is not occurring in context.

Language acquisition continues to be compared in bonobo (Pan paniscus) and common chimpanzee (Pan troglodytes) subjects which have been co-reared since shortly after birth. Both apes have continued to acquire additional symbols without specific training. Formal (blind) tests (approximately 1,000 trials per subject) of comprehension of the English language were completed during the past year. These tests revealed that, overall, the bonobo selected the appropriate symbol from an array, in response to the spoken work, with 90% accuracy. The common chimpanzee responded with approximately 50% accuracy. The bonobo demonstrated comprehension with 100% accuracy of at last 140 different words and the chimpanzee comprehended at least 39 different words with 100% accuracy.

2. Research in Progress

a) Novel Approaches for the Diagnosis of Retrovirus Infection

Peripheral blood mononuclear cells (PBMC) from SIV seropositive and seronegative (by ELISA, radioimmunoprecipitation assay, and Western blot analysis) sooty mangabeys and rhesus macaques were cultured in vitro with pokeweed mitogen (PWM), and supernatant fluids were assayed for antibody against SIVsmm using routine ELISA and Western blot assays. As expected, the supernatant fluids from PWM stimulated cultures of ten uninfected rhesus macaques were all negative for anti SIV antibodies, whereas supernatant fluids from PWM stimulated cultures from eight rhesus macaques experimentally infected with SIVsmm and 12 naturally infected, clinically asymptomatic SIVsmm seropositive mangabeys were all positive for antibodies against SIVsmm. Surprisingly, supernatant fluids of PWM stimulated cultures from ten SIVsmm seronegative mangabeys had significant antibody titers against SIVsmm. These findings were highly reproducible upon repeated testing of each seropositive and seronegative monkey. In addition, depletion of $CD8^+$ T cells from PBMC from SIV seronegative mangabeys prior to culture in vitro with PWM resulted in marked increases in titers of antibodies against SIVsmm.

These findings in seronegative mangabeys prompted an evaluation of supernatant fluids from PWM stimulated cultures of PBMC from a random population of high risk humans. Findings in this preliminary survey revealed that 39 of 161 (24%) seronegative individuals who were considered to be at high risk for HIV infection had circulating B cells which, upon in vitro activation with PWM, produced antibodies reactive with HIV. Furthermore, PCR analysis of samples of 20 of these 25 seronegative individuals tested revealed the presence of HIV specific sequences in the DNA. In addition, depletion of $CD8^+$ T cells from PBMC prior to in vitro culture with PWM resulted in increased sensitivity for detecting HIV reactive antibodies. These observation have obvious epidemiological implications with respect to the extent of HIV infection in the population. This assay also provides a simple technique to enhance our capability for detecting HIV-infected individuals.

b) Characterization of Onchocerca Antigens and Animal Model Development

The major objective of this study was to compare the response of primates infected with Onchocerca volvulus to the responses detected in humans residing in endemic areas. Although chimpanzees were the primary nonhuman primate species studied,

due to their know susceptibility to the parasite, other nonhuman primates were also studied. One chimpanzee which became microfilaria positive 21 months post-inoculation, developed recognition of two low molecular weight antigens (22 and 14KD) at 9.5 and 13 months, respectively. Two mangabey monkeys also developed recognition of this antigens, but in addition also recognized one or two other low molecular weight antigens. One of these, a 20 KD antigen, was recognized by both animals at 3.5 and 5 months post-inoculation. One mangabey subsequently developed a patent infection first detectable at 17 months post-inoculation. Comparison to the profiles of infected humans revealed several very interesting and potentially useful findings. First, through the longitudinal evaluation of experimental infections, we now have an understanding of when during the course of infection these different antigen bands are first recognized, and some idea of what they may be in response to. Several of the recognized antigens are candidates for development in diagnostic tests as markers of early infection. Second, and possibly more important, the recognition in mangabey monkeys of an antigen band (20KD) also recognized in "immune" individuals may be of significance in the understanding of resistance and development of potential vaccines.

This represents the first demonstration of infection with O. volvulus in a nonhuman primate species other than chimpanzees, and additional studies are underway to more fully evaluate mangabey monkeys as a primate model for study of this infection. It is especially interesting that preliminary studies indicate that immunological responses in mangabey monkeys more closely mimic those detected in human populations exposed to and infected with O. volvulus. The recognition of a similar antigen in mangabeys and putatively "immune" people may play a key role in developing a candidate vaccine as well as understanding the nature of resistance versus infection.

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 Pathobiology and Immunobiology	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.
J. Else	D.V.M.	Head, Division of Animal Resources, Associate Research Professor	Animal Resources	Yerkes
K. Gould	D.V.M. Ph.D.	Research Professor and Chief, Division of Reproductive Biology	Reproductive Biology	Yerkes
		Adjunct Professor	Biology	Emory Univ.

Executive Committee (Cont'd)

Name	Degree	Academic Titles	Department or Division	Institution
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.	Associate Research Professor and Field Station Coordinator	Behavioral Biology	Yerkes
		Adjunct Professor	Psychology	Emory Univ.
D. Rumbaugh	Ph.D.	Affiliate Scientist and Director, Language Research Center	Behavioral Biology	Yerkes
		Professor	Psychology	Georgia State Univ.

2) Yerkes Animal Resources Committee

The 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 specifically charged with the following responsibilities: (a) evaluate and make recommendations to the Center Director regarding all proposed Center research projects; review of proposals takes 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 subcommittee for the Emory University 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. In early 1990, this committee will be replaced by an IACUC Primate Subcommittee and a Yerkes Resources and Science Review Committee (YRSRC). The former will review research proposals with respect to satisfying USDA and NIH requirements concerning the humane care and use of laboratory animals. The YRSRC review will take into consideration scientific merit, Center resources, etc. The composition of the Animal Resources Committtee 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
		Assistant Professor	Pathology	Emory Univ.
T. Gordon (Co-Chair)	M.S.	Associate Research Professor and Field Station Coordinator	Behavioral Biology	Yerkes
		Adjunct Professor	Psychology	Emory Univ.
D. Anderson	D.V.M.	Associate Research Professor	Pathobiology and Immunobiology	Yerkes
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.
J. Else	D.V.M.	Head, Division of Animal Resources, Associate Research Professor	Animal Resources	Yerkes

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)	B.A.	Associate Director for Administration	Administration	Yerkes
R. Nadler	Ph.D.	Research Professor	Reproductive Biology	Yerkes
		Adjunct Associate Professor	Psychology	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.

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 has remained active. The committee meets 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	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
		Assistant Professor	Pathology	Emory Univ.
B. Swenson	D.V.M.	Associate Research Professor and Chief, Division of Veterinary Medicine	Veterinary Medicine	Yerkes
J. Roberts		Chief Superintendent	Main Station, Division of Animal Resources	Yerkes
D. Chikazawa		Superintendent	Field Station Animal Care Unit	Yerkes
J. Magnotta	B.A.	Associate Director for Administration	Administration	Yerkes
T. Gordon	M.S.	Associate Research Professor and Field Station Coordinator	Behavioral Biology	Yerkes
		Adjunct Professor	Psychology	Emory Univ.
J. Else	D.V.M.	Head, Division of Animal Resources, Associate Research Professor	Animal Resources	Yerkes

4) 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.
R.Buddington	Ph.D.	Administrative Associate	Administration	Yerkes
J. Herndon	Ph.D.	Associate Research Professor	Neurobiology	Yerkes
		Adjunct Assistant Professor	Biology	Emory Univ.
		Adjunct Assistant Professor	Psychology	Emory Univ.
C. Lin	B.S.	Computer Services Coordinator	Computer Services	Yerkes
J. Magnotta	B.A.	Associate Director for Administration	Administration	Yerkes
E. Smith	Ph.D.	Associate Research Professor	Behavioral Biology	Yerkes
		Associate Professor	Anthropology	Emory Univ.
		Adjunct Associate Professor	Biology	Emory Univ.
K. Wallen	Ph.D.	Associate Research Professor	Behavioral Biology	Yerkes
		Associate Professor	Psychology	Emory Univ.

5) 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	Degree	Academic Titles	Department or Division	Institution
E. Smith (Chair)	Ph.D.	Associate Research Professor	Behavioral Biology	Yerkes
		Associate Professor	Anthropology	Emory Univ.
		Adjunct Associate 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.
N. Johns		Librarian	Administration	Yerkes
J. Magnotta	B.A.	Associate Director for Administration	Administration	Yerkes
B. Swenson	D.V.M.	Associate Research Professor and Chief, Division of Veterinary Medicine	Veterinary Medicine	Yerkes
M. Wilson	Ph.D.	Assistant Research Professor	Behavioral Biology and Reproductive Biology	Yerkes
		Associate in Medicine	Endocrinology	Emory Univ.

6) 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 or 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	Degree	Academic Titles	Department or Division	Institution
D. Anderson (Chair)	D.V.M.	Associate Research Professor	Pathobiology and Immunobiology	Yerkes
D. Houseworth		Asst. Superintendent	Animal Care	Yerkes
K. Pralinsky	B.A.	Assistant Superintendent, Main Station	Physical Plant	Yerkes
F. Jewell		Receptionist	Administration	Yerkes
J. Magnotta (ex officio)	B.A.	Associate Director for Administration	Administration	Yerkes

7) Task Force on 1989 Budget

Due to projected changes for FY 1989-90 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:

1989 Budget Task Force

Name	Degree	Academic Titles	Department or Division	Institution
J. Magnotta (Chair)	B.A.	Associate Director for Administration	Administration	Yerkes

1989 Budget Task Force (Cont'd)

Name	Degree	Academic Titles	Department or Division	Institution
J. Else	D.V.M.	Head, Division of Animal Resources, Associate Research Professor	Animal Resources	Yerkes
T. Gordon	M.S.	Associate Research Professor and Field Station Coordinator	Behavioral Biology	Yerkes
		Adjunct Professor	Psychology	Emory Univ.
H. McClure	D.V.M.	Associate Director for Scientific Programs; Research Professor and Chief, Division of Pathobiology and Immunobiology	Pathobiology and Immunobiology	Yerkes
		Assistant Professor	Pathology	Emory Univ.
B. Swenson	D.V.M.	Associate Research Professor and Chief, Division of Veterinary Medicine	Veterinary Medicine	Yerkes

8) 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 mangagement, medical history and research utilization. It is anticipated that Dr. Else will join this committee in 1989, and Dr. Buddington as well. The composition of this committee is as follows:

Animal Records Committee

Name	Degree	Academic Titles	Department or Division	Institution
R.Buddington (Chair)	Ph.D.	Administrative Associate	Administration	Yerkes

Animal Records Committee (Cont'd)

Name	Degree	Academic Titles	Department or Division	Institution
R. Boothe	Ph.D.	Associate Research Professor	Neurobiology	Yerkes
		Associate Professor	Psychology	Emory Univ.
		Assistant Professor	Ophthalmology	Emory Univ.
S. Klumpp,	D.V.M.	Associate Scientist and Veterinary Pathologist	Pathobiology and Immunobiology	Yerkes
S. Rust	----	Supervisor Animal Records	Animal Resources	Yerkes
B. Swenson	D.V.M.	Associate Research Professor and Chief, Division of Veterinary Medicine	Veterinary Medicine	Yerkes
D. Vinson	----	Secretary I	Field Station	Yerkes

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

Biohazard Safety Committee (Cont'd)

Name	Degree	Academic Titles	Department or Division	Institution
K. Pralinsky	B.A.	Assistant Superintendent, Main Station	Physical Plant	Yerkes
J. Magnotta	B.A.	Associate Director for Administration	Administration	Yerkes

10) 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 agreement 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	Degree	Academic Titles	Department or Division	Institution
H. McClure	D.V.M.	Associate Director for Scientific Programs; Research Professor and Chief, Division of Pathobiology and Immunobiology	Pathobiology and Immunobiology	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.
M. Riemann	---	Department Administrator	Ophthalmology	Emory Univ.

11) 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 appropriately be assigned. The composition of this committee is as follows:

Summer Internship Committee

Name	Degree	Academic Titles	Department or Division	Institution
L. Byrd (Chair)	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.
D. Anderson	D.V.M.	Associate Research Professor	Pathobiology and Immunobiology	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 societies 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 presented 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 universities, 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.

RR00165-29

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

Associate, Affiliate and Collaborative Faculty:

R. Barr	Department of Pediatrics, McGill University
G. Berntson	Departments of Psychology and Pediatrics, Ohio State University
S. Boysen	Department of Psychology, Ohio State University
C. Ehardt	Department of Anthropology and Linguistics, University of Georgia
J. Ellis	Yerkes Regional Primate Research Center, Emory University
H. Gouzoules	Department of Psychology, Emory University
S. Gouzoules	Yerkes Regional Primate Research Center, Emory University
D. Gust	Yerkes Regional Primate Research Center, Emory University
L. Howell	Yerkes Regional Primate Research Center, Emory University
M. Konner	Department of Anthropology, Emory University
T. Maple	School of Psychology, Georgia Institute of Technology, and Zoo Atlanta
M. Marr	School of Psychology, Georgia Institute of Technology
E. Menzel	Department of Psychology, State University of New York at Stony Brook
R. Morris	Department of Psychology, Georgia State University
M. Romski	Department of Communication, Georgia State University
D. Rumbaugh	Department of Psychology, Georgia State University
A. Smith	School of Psychology, Georgia State University
H. Terrace	Department of Psychology, Columbia University
M. Tomasello	Department of Psychology, Emory University
R. Tuttle	Department of Anthropology, Evolutionary Biology and The College, University of Chicago
E. Visalberghi	Primate Laboratory Unit, Institute of Psychology (CNR), Rome, Italy
D. Wenzel	Yerkes Regional Primate Research Center, Emory University
P. Whitten	Department of Anthropology, Emory University
I. Wundram	Department of Anthropology, Oxford College of Emory University

Visiting Scientist:

J. Fagot	Unité de Neurosciences Cognitives, Université aix Marseille I, CNRS, Marseille, France

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Modification of Abnormal Male Aggression

AXIS I: 1a, 15

AXIS II: 36, 60, 72, 82

PRC UNIT: Behavioral Biology

INVES1: Bernstein, Irwin S.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: C

SPECIES1: Macaca mulatta
NUM1: 30

NON-HOST INST: University of Georgia

ABSTRACT: Following completion of adolescence in the absence of adult males, sixteen male rhesus monkeys (Macaca mulatta) were transferred from their natal groups into social groups that contained normal adult males. The unusual aggressive behavior that developed in these males is now being studied and compared with the same behavior in control males that were not transferred from their natal groups. Following an initial period of xenophobic aggression, patterns which are expected to alter the unusual agonistic behavior observed in the young males are being documented. As the behavior of the young males continues to be modified, the frequency of agonistic responses is expected to decline. In fact, the severity of each episode has already declined. These ongoing studies will continue in order to determine whether the patterns of agonistic behavior exhibited by the young males will approximate normal patterns of male agonistic behavior following this resocialization.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Psychophysiological & Electrophysiological Indices of Cognitive Processes in Apes

AXIS I: 1a, 13, 21

AXIS II: 36, 68

PRC UNIT: Behavioral Biology

INVES1: Berntson, Gary G.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: 0

INVES2: Boysen, Sarah T.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: 0

SPECIES1: Pan troglodytes
NUM1: 5

NON-HOST INST: Ohio State University

ABSTRACT: The Primate Cognition Project has continued to pursue two major research efforts during the project period. The goal of the first area of investigation is to develop an understanding of the cognitive processes which support the complex social and behavioral abilities of the great apes. Current work in this area includes studies of the development of numerical concepts and the nature of cognitive representations of number. The second research effort is focused on examining perceptual development in infant great apes through the application of psychophysiological measures of functional response (cardiovascular responses and cerebral event-related potentials). Studies conducted during the project period included (1) the ontogeny of species-characteristic patterns of physiological responses to vocal stimuli, (2) the specific acoustic features which are critical in the elicitation of these responses, and (3) the potential contribution of specialized perceptual mechanisms to the disposition of these responses. The long-term objective of these projects is to increase our understanding of the nature of cognitive representations and transformations in the apes, their similarities and differences from those of humans, and the underlying neural processes which support these functions.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Recall and Recognition in Aged Rhesus Monkeys

AXIS I: 1a, 2, 9, 21, 25b

AXIS II: 30, 36, 46, 50b, 72

PRC UNIT: Behavioral Biology

INVES1: Byrd, Larry D.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: C

INVES2: Ellis, Jane E.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: O

SPECIES1: Macaca mulatta
NUM1: 10

ABSTRACT: The American public is becoming increasingly aware of the problems associated with an aging population and its health requirements. Moreover, the rapid increase in the elderly population in the United States has made a valid animal model of memory essential for developing and testing strategies to alleviate severe memory impairment. Since studies of memory typically have involved linguistically-competent human subjects, memory processes have been confounded with linguistic ability. Studies on human and animal memory have demonstrated remarkable similarities in human and nonhuman memory processes, and they indicate that findings derived from animal experiments, which are not confounded by linguistic ability, can enhance our understanding of human memory. The present, ongoing project has developed the rhesus monkey as a model for studying human memory by examining the performances of old, mid-age and young animals on a delayed-recall task which is similar to tasks commonly used to study human memory. The methodology used in this study is based on a touch-sensitive cathode ray tube (CRT) upon which a microcomputer displays visual stimuli that a subject must acknowledge then recall and reproduce after an intervening period of time (delay) has elapsed. High levels of accuracy on the recall task following very brief delays are characteristic of all three age groups. Accuracy levels declined with increasing delays for all age groups, although the decline was more pronounced for the oldest animals. Similar results are obtained typically with humans performing analogous tasks. Several pharmacologic compounds were tested to determine their potential effect on test performance and to enhance our understanding of the neuropharmacology of memory and aging. The long-range objective of the research is to characterize the neuropharmacology of memory so that decrements in memory can be prevented or treated therapeutically.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Behavioral and Physiological Concomitants of Drug Abuse

AXIS I: 1a, 2, 13, 21

AXIS II: 36, 50b, 54b, 72, 87

PRC UNIT: Behavioral Biology

INVES1: Byrd, Larry D.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: C

INVES2: Howell, Leonard L.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: O

SPECIES1: Saimiri sciureus
NUM1: 24

ABSTRACT: This research is intended to characterize the effects selected drugs can have on the central nervous system of nonhuman primates by studying the effects of these drugs on learned behavior. In addition, studies will determine the effects the drugs can have on heart rate, arterial blood pressure and core temperature at doses that have effects on behavior mediated via the central nervous system, and determine whether the behavioral, cardiovascular or thermoregulatory effects are enhanced, diminished or blocked by other drugs or by behavioral procedures. Methods used include 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, schedule-controlled behavior as an index of central nervous system activity. Experiments have demonstrated the involvement of the dopamine system in the behavioral and reinforcing effects of cocaine through the use of specific dopamine agonists and antagonists including the antagonists Sch 23390 (D_1), spiperone (D_2), raclopride (D_2) and haloperidol (D_1 and D_2), and the agonists SKF 38393 (D_1) and apomorphine (D_1 and D_2). 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 animals and to identify ways in which undesirable effects of the drugs can be attenuated. The long-range objective is to characterize the behavioral, cardiovascular and thermoregulatory effects of various drugs that may have abuse liability or, consequently, may have therapeutic value in treating drug abuse.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Behavioral Modulation of Cardiovascular Activity

AXIS I: 1a, 2, 13, 21

AXIS II: 36, 50b, 54b, 72

PRC UNIT: Behavioral Biology

INVES1: Byrd, Larry D.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: C

INVES2: Howell, Leonard L.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: O

SPECIES1: Saimiri sciureus
NUM1: 24

ABSTRACT: The long-range objective of this research is to characterize relations between changes in cardiovascular activity and ongoing behavioral processes. The central nervous system is known to be the source of control of learned behavior, especially as differentiated from reflexive behavior. The central nervous system is also recognized now as being involved in the regulation of cardiovascular activity, particularly the regulation of blood pressure and heart rate. How the modulation of cardiovascular activity becomes integrated with or influenced by ongoing, centrally-mediated behavior is not well understood. Laboratory studies have 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 studied decreased cardiovascular activity in the squirrel monkey in an attempt to identify factors determining its development and the conditions under which decreases can be maximized. A more thorough understanding of modulatory influences and the mechanisms by which they regulate cardiovascular activity can be influential in protecting individuals from premature morbidity or mortality.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Asymmetrical Hand Use in Rhesus Monkeys in Tactually & Visually Regulated Tasks

AXIS I: 1a

AXIS II: 36

PRC UNIT: Behavioral Biology

INVES1: Fagot, Joël
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: 0

INVES2: Drea, Christine, M.
DEGREE2: M.A.
DEPT2: Behavioral Biology
STAFF2: 0

INVES3: Wallen, Kim
DEGREE3: Ph.D.
DEPT3: Behavioral Biology
STAFF3: C

SPECIES1: Macaca mulatta
NUM1: 74

ABSTRACT: Asymmetrical hand usage by socially-housed rhesus monkeys was investigated using a series of tactually- and visually-guided tasks. The first experiment recorded the manual preferences of 29 rhesus monkeys in solving a haptic-discrimination task requiring a hanging posture. There was a significant left-hand population bias, with 21 monkeys having a significant left-hand bias, four having a significant right-hand bias, and four having no significant hand bias. A second experiment, consisting of four tasks, investigated the critical components of the first experiment by varying posture (hanging, sitting or tripedal) and sensorial requirements (tactile or visual). A significant left-hand bias was found for both sensory modalities, but the bias was stronger in the tactually controlled tasks. Posture influenced hand bias, with an almost symmetrical distribution of hand usage in the tripedal posture, and a population-level left-hand bias in the sitting and hanging postures. The results suggest a possible specialization of the right hemisphere for tactile, visual or spatial processing in the rhesus monkey.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Social and Endocrine Effects on Immune Function

AXIS I: 1a, 15

AXIS II: 36, 62, 64

PRC UNIT: Behavioral Biology

INVES1: Gordon, Thomas P.
DEGREE1: M.S.
DEPT1: Behavioral Biology
STAFF1: C

INVES2: Gust, Deborah A.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: O

INVES3: Wilson, Mark E.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: C

INVES4: McClure, Harold M.
DEGREE4: D.V.M.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

SPECIES1: Cercocebys atys
NUM1: 36

SPECIES2: Macaca mulatta
NUM2: 14

ABSTRACT: Group-living nonhuman primates typically exhibit a social organization which includes a dominance hierarchy which is often maintained by relatively high rates of social conflict and agonistic behavior. Consequently, stress-inducing events may be experienced by any individual and may be chronic for some. Conversely, social support, which is often found in stable, social environments, may modulate the effects of potentially stressful stimuli. A growing literature has provided compelling evidence that factors associated with social life and changes in the social environment may lead directly to alterations in immune function and, thus, to increased susceptibility to pathogens. Moreover, steroid hormones are known to affect immune function and act as immunoregulators. Recent evidence indicates that the hypothalamic-pituitary-gonadal-thymic axis plays an important role in the hormonal regulation of immune function, and spontaneous variations in the activity of the hypothalamic-pituitary-gonadal axis are characteristics of many species. For example, the rhesus macaque exhibits an annual mating cycle in association with which mature animals show dramatic changes in gonadal, pituitary and hypothalamic activity and, thus, possible alterations in immune function. Therefore, the immune system may be viewed as a major integrative network

involved in biological adaptation, with a large number experimental and clinical studies showing that psychosocial changes and/or stress can produce both an endocrine response, including changes in adrenal, pituitary and gonadal secretion, and direct effects on humoral and cell-mediated immune responses. Such stimuli induce adaptive hormonal responses and immune alterations via integration with other physiological systems which may, in some instances, increase the organism's susceptibility to infection and disease. This project focuses on rhesus and mangabey monkeys in order to examine the social and endocrine modulation of immune function.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Factors Influencing Primate Reproduction

AXIS I: 1a, 15, 23

AXIS II: 36

PRC UNIT: Behavioral Biology

INVES1: Gordon, Thomas P.
DEGREE1: M.S.
DEPT1: Behavioral Biology
STAFF1: C

INVES2: Gust, Deborah A.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: O

INVES3: Wilson, Mark E.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: C

SPECIES1: Macaca mulatta
NUM1: 24

SPECIES2: Cercocebus atys
NUM2: 16

ABSTRACT: This research examines the proximate variables that control or influence reproductive phenomena in Old World monkeys. The long-range goal is to provide a basis for interpreting the functional significance of primate reproductive mechanisms from an evolutionary-biology perspective. Social, environmental and endocrine variables are examined independently and in confluence to determine the effects of these factors on sexual behavior, gonadal function and reproductive success. Ovulatory function is assessed by monitoring ovarian and pituitary gonadotropic hormones as well as other hormones, including prolactin and pineal melatonin, implicated in the control of primate reproduction. Ten adult, female mangabey monkeys, living in a large social group, were studied for 14 months to characterize the relationship among sexual behavior, species-typical perineal swelling patterns, demographic variables and reproductive status. Weekly blood samples were assayed for adrenal, ovarian and pituitary hormones. Nine females became pregnant, and eight surviving births were recorded. Pregnancy was marked by characteristic ovarian hormone patterns at conception, with progesterone ranging from 4-6 ng/ml during the first weeks of pregnancy. Progesterone levels declined significantly during the seventh week, when a secondary perineal swelling peak and sexual receptivity also were observed. Progesterone levels continued to increase throughout pregnancy and declined abruptly following parturition. Cortisol levels were somewhat higher than those obtained from rhesus monkeys, but showed a decline throughout the study and were not related consistently to reproductive condition or demographic variables. In a second study, ten

female rhesus monkeys were examined from July (non-mating season) through the annual onset of ovarian cyclicity and sexual behavior (fall months) to determine a possible seasonal role for prolactin and/or endogenous opioid peptides (EOPs). Analysis revealed no changes in EOPs associated with mating onset; however, prolactin values declined between July and October, suggesting a possible mediating role as has been demonstrated in other species.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Comparative Studies of Primate Vocal Communication

AXIS I: 1a

AXIS II: 36, 40

PRC UNIT: Behavioral Biology

INVES1: Gouzoules, Harold T.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: 0

INVES2: Gouzoules, Sarah, M.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: 0

SPECIES1: Macaca nemestrina
NUM1: 45

ABSTRACT: Pigtail macaque (Macaca nemestrina) screams were studied using spectrographic and multivariate analyses. These calls, produced during agonistic encounters, are important in the recruitment of support from allies against opponents. Direct discriminant analysis was used to classify screams recorded from 45 monkeys living in a stable, captive group at the Yerkes Regional Primate Research Center. Pigtail macaques used acoustically-distinct classes of screams depending upon features of the agonistic context: four types of screams were associated with the relative rank of the opponent and the severity of the aggression. Comparison of rhesus macaque (M. mulatta) screams with those of pigtail macaques revealed that the acoustic features of calls used by the two species in identical agonistic contexts were very different. Matrilineal relatedness did not emerge as a factor that was associated with specific call types for pigtail macaques as it did for rhesus macaque screams. Significantly more classification errors were made for calls recorded from monkeys under three years of age than for those of older monkeys in each of the four agonistic contexts. The calls which were classified correctly into the four agonistic contexts were assigned a significantly higher probability for older monkeys, suggesting that the call renditions of older monkeys were closer to the "prototype" for a particular context than were those of younger monkeys. Proper contextual usage and scream production appeared to undergo developmental modification. Among juveniles, females were found to be more proficient than males in proper contextual usage and in production of recruitment screams. These differences in phonological and semantic usage suggest a nonhuman primate model for understanding human sex-related differences in the development of communicative competence. Analyses also indicate the existence of matrilineal vocal signatures that may serve to identify kin-related groups and to promote efficient communication.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Kin Recognition in Primates

AXIS 1: 1a

AXIS 2: 36

PRC UNIT: Behavioral Biology

INVES1: Gouzoules, Harold T.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: 0

INVES2: Gouzoules, Sarah, M.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: 0

SPECIES 1: Macaca mulatta
NUM1: 75

ABSTRACT: Many Old World monkeys, especially females, behave preferentially toward their maternally-related kin, but there is less evidence supporting the existence of paternal kin recognition in these species. This study attempted to ascertain whether young rhesus monkeys recognize their paternally-related siblings and how gender might influence such kin recognition. Subjects were 23 immature members of a captive group of rhesus macaques (Macaca mulatta) maintained in a large outdoor compound at the Yerkes Regional Primate Research Center. Paternity was determined using blood-typing reagents and a serum protein polymorphism developed for paternity designation in rhesus monkeys. Focal data on the frequency and duration of behaviors were recorded blind for all interactions between subjects. The results indicated that dyads consisting of paternally-related, female siblings engaged in grooming behaviors and were in proximity significantly longer and more frequently than non-sibling dyads. In addition, there were consistent trends toward behaviors such as contact, approach and play. Paternally-related female sibling dyads engaged in these behaviors more frequently than did non-sibling dyads, while male-female dyads showed the opposite pattern. The results for the small number of male-male dyads failed to reveal a clear preference for paternally-related siblings or non-siblings. The study suggests that female rhesus monkeys show some ability to recognize paternally-related siblings. However, preliminary analyses suggest that this recognition does not extend to patterns of agonistic aiding.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Reproduction in the Sooty Mangabey

AXIS 1: 1a, 15

AXIS 2: 31, 36

PRC UNIT: Behavioral Biology

INVES1: Gust, Deborah A.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: O

INVES2: Gordon, Thomas P.
DEGREE2: M.S.
DEPT2: Behavioral Biology
STAFF2: C

SPECIES 1: Cercocebus torquatus atys
NUM1: 80

ABSTRACT: This study was conducted in a captive group of sooty mangabeys to describe several reproductive parameters, examine copulatory patterns based on male age class, and compare female sexual behavior during tumescence associated with ovulation and during tumescence associated with the 50-day, post-conception swelling. Data from over 7.5 years, including perineal swelling and reproductive data from 67 females, were analyzed to examine the relationship between demographic variables and reproductive events. Sexual maturation, marked by onset of swelling, was recorded at approximately 36.4 months and first parturition at 56.52 months, indicating an adolescent sterility of over one year. Both parity and duration of infant survival influenced interbirth interval. Infant survival did not vary significantly according to maternal age class. Birth distribution peaked during the spring and summer; swelling cycles and conceptions rarely occurred during the summer. Analysis of sexual activity based on male age class revealed that young males (2 and 3-4 years) exhibited the greatest frequency of total mounts. However, data on female perineal swelling showed that young males primarily mounted females exhibiting moderate swelling and adult males primarily mounted females during maximum or near maximum tumescence. Subadult males (5-6 years) mounted females less frequently than 3-4 year old males, with most mounts directed toward moderately tumescent females. Comparison of sexual behaviors during pre- and post-conception stages of maximum tumescence showed that males of all age classes mounted females with equal frequency, but there was a significant difference in mounting frequency by adult males (>7 years) during the two phases. Adult males mounted females significantly less frequently during the 50-day, post-conception swelling than during ovulatory swelling. These studies were undertaken to gain a better understanding of reproduction in sooty mangabeys, a species that carries, but is not clinically affected by, a simian immunodeficiency virus, to promote breeding programs and examine a possible mode of virus transmission.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Social Relationships and Stress

AXIS I: 1a, 15

AXIS II: 31, 36

PRC UNIT: Behavioral Biology

INVES1: Gust, Deborah A.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: O

INVES2: Gordon, Thomas P.
DEGREE2: M.S.
DEPT2: Behavioral Biology
STAFF2: C

INVES3: Wilson, Mark E.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: C

SPECIES1: Macaca mulatta
NUM1: 8

ABSTRACT: A lack of social support has been correlated with increased risk of morbidity and mortality in humans and with increased pituitary-adrenocortical activity and decreased immune capacity in animals. Three preliminary studies were conducted to (1) examine the effect of social relations on pituitary-adrenocortical hormones in an established social group of rhesus monkeys (2) assess the ability of dexamethasone to suppress cortisol secretion in monkeys, and (3) determine the relationship among rank, feeding order and body weight in a provisioned group. Low rates of aggression and little variability in basal pituitary-adrenocortical hormones were noted among individuals in the established, provisioned group, but there were indications of inter-individual variability in response to potential stressors. For example, dexamethasone's ability to suppress cortisol secretion was not equal across individuals, and there was a rank-related order in which individuals obtained food. Body weight did not co-vary with feeding order, but there may have been a cost, in terms of pituitary-adrenocortical activation, to animals which fed last. The results of these studies in an established group were consistent with the hypothesis that, in terms of basal measures, social relationships play a modulating role only during perceived stressful situations, but they suggested the existence of subtle differences in stress reactivity. These studies led to a successful proposal for a longitudinal comparison of two social groups, one group with an established social support network and a newly-formed group which lacks such a network. These studies will provide longitudinal reference data on pituitary-adrenocortical activity associated with social context and reproductive state complemented with experimental procedures to elucidate the relationship of social factors and the behavioral and hormonal correlates of stress.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Behavioral and Respiratory Effects of Methylxanthines

AXIS I: 1a, 21, 24

AXIS II: 50b, 87

PRC UNIT: Behavioral Biology

INVES1: Howell, Leonard L.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: 0

SPECIES1: Macaca mulatta
NUM1: 8

ABSTRACT: Caffeine and related methylxanthines are clinically useful respiratory stimulants used to treat respiratory depression, bronchial asthma and breathing difficulties in newborn infants. Previous studies have indicated that methylxanthines stimulate respiration directly by altering sensitivity to CO_2, but the specific mechanisms that mediate this effect have not been clearly identified. Research is ongoing to examine relative contributions of phosphodiesterase (PDE) inhibition and adenosine receptor blockade. Ventilation in unanesthetized monkeys is monitored continuously using a pressure-displacement head plethysmograph. Drug effects are determined on ventilation during exposure to normal atmospheric conditions and on ventilation stimulated by elevated concentrations of CO_2 in inspired air. The effects of caffeine have been compared to those of two adenosine agonists which differ in their relative affinities for adenosine receptor subtypes (NECA and CPA), a non-xanthine compound that is a potent adenosine antagonist (CGS 15943), and a non-xanthine compound that is a selective inhibitor of cAMP phosphodiesterase (rolipram). Caffeine and the PDE inhibitor altered sensitivity to CO_2 in a similar manner. The magnitude of the increase in ventilation was comparable at all concentrations of CO_2. The potent adenosine antagonist did not increase ventilation under any condition. Both adenosine agonists increased respiratory frequency during exposure to air, but neither altered sensitivity to CO_2 in a manner similar to caffeine. The results indicate that antagonism of adenosine does not appear to be critical for the respiratory-stimulant effects of caffeine. Rather, inhibition of PDE activity may have mediated caffeine's respiratory-stimulant effects. A separate group of monkeys has been trained under an operant schedule of reinforcement, and studies are presently underway to assess the behavioral pharmacology of caffeine and related compounds. The results will provide information regarding the neurochemical basis of respiratory function and will increase the likelihood of improving pharmacological intervention in pathological states of respiratory dysfunction.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Georgia State University Mental Retardation Project

AXIS I: 5a, 5b

AXIS II: 36, 40, 41, 60, 71

PRC UNIT: Behavioral Biology

INVES1: Romski, Mary Ann
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: O

INVES2: Sevcik, Rose A.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: O

INVES3: Savage-Rumbaugh, E. Sue
DEGREE3: Ph.D.
DEPT3: Behavioral Biology
STAFF3: C

SPECIES1: Homo sapiens
NUM1: 13

NON-HOST INST: Georgia State University (all)

ABSTRACT: During calendar year 1989, this project continued to analyze data derived from the longitudinal study of augmented symbol acquisition in 13 school-aged children (mean CA = 12:8) with mental retardation. First, a study to provide an initial illustration of emerging non-taught symbol combinations was completed. All of the sampled symbol combinations produced by seven of the symbol-experienced subjects were examined to characterize their acquisition patterns in terms of semantic relations, positional ordering of symbols and generalization across symbols. Their patterns of use resembled those found in the spoken combinations of typical children. The subjects' combinations were not dependent on rote imitation since few such patterns were found within the partners' augmented input to the children. Second, in order to study the relationship between the subjects' symbol communications and their partners' subsequent utterances in terms of effectiveness, an additional level of coding was developed and is currently being appended to the original Communication Coding Scheme on 487 transcripts of the subjects' communicative interactions during the study. Preliminary findings suggest that symbols may be a more effective mode of communication with respect to partner response than are extant unconventional forms of communication. Third, a study which compared the communicative acquisition of symbols plus the printed English language with the acquisition of printed English alone by symbol-experienced subjects was completed. The meanings of printed English were learned equally as well as were symbols plus printed English, suggesting that experience with symbols may provide a foundation for the acquisition of more advanced symbolic development, such as printed English.

P5IRR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Cognitive Studies in Pan troglodytes

AXIS I: 1a

AXIS II: 36, 40, 92 (comparative psychology)

PRC UNIT: Behavioral Biology

INVES1: Rumbaugh, Duane M.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: O

INVES2: Savage-Rumbaugh, E. Sue
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: C

SPECIES1: Pan troglodytes
NUM1: 3

NON-HOST INST: Georgia State University (both)

ABSTRACT: The Cognitive Project is designed to investigte competencies for learning the values of numbers, counting, combining quantities and reading "maps" in great apes and rhesus monkeys. Great apes can count out the appropriate number of boxes (by putting either dots or numerals on them) as instructed by the value of the Arabic numeral (1 through 5) portrayed on a video screen. Rhesus monkeys have learned the relative values of pellets in reliable association with the numeral selected. Thus, they prefer 9 over 8 over 7, and so on. Chimpanzees will choose the one of two pairs of piles of chocolates which nets for them the greater total. On a low-fidelity, black-and-white monitor, they can watch food being placed in various sites in their exercise yards and then search accordingly to find the food. A variety of projects with the rhesus monkeys has affirmed their competencies for a wide variety of tasks which have been presented on the Language Research Center's Computerized Test System (LRC-CTS). The LRC-CTS constitutes a major system for comparative psychological research.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Bio-behavioral Studies of Language and Cognition

AXIS I: 1a, 5a, 5b

AXIS II: 36, 40, 41, 92 (comparative psychology)

PRC UNIT: Behavioral Biology

INVES1: Rumbaugh, Duane M.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: 0

INVES2: Savage-Rumbaugh, E.S.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: C

INVES3: Romski, Mary Ann
DEGREE3: Ph.D.
DEPT3: Behavioral Biology
STAFF3: 0

INVES4: Morris, Robin
DEGREE4: Ph.D.
DEPT4: Behavioral Biology
STAFF4: 0

SPECIES1: Pan troglodytes
NUM1: 5

SPECIES2: Pan paniscus
NUM2: 4

HUMANS1: Homo sapiens
NUM1: 13

NON-HOST INST: Georgia State University (all)

ABSTRACT: This research program comprises four projects of comparative inquiry into the processes and parameters which are requisites to symbol learning, language and complex cognition. Project 1 is the Language Acquisition in Pan paniscus. That species is remarkable for its readiness to learn the meanings of symbols spontaneously, to comprehend human speech, and to carry out novel requests conveyed by spoken sentences. Project 2, Cognitive Studies in Pan troglodytes, focuses, at present, upon the abilities of that species to count, which it can do from 1-5, through the use of a new test apparatus (LRC-CTS) described elsewhere. Project 3, the GSU Mental Retardation Project, focuses on the language-acquisition processes of mentally-retarded children in public schools. Project 4, the Neuropsychological Foundations Project, investigates the relative roles of the right and left cerebral hemispheres in learning and using symbols and words by chimpanzees and children with mental retardation.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Language Acquisition in Pan paniscus

AXIS I: 1a, 5c, 5d

AXIS II: 36, 40, 41

PRC UNIT: Behavioral Biology

INVES1: Savage-Rumbaugh, E. Sue
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: C

INVES2: Rumbaugh, Duane M.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: 0

INVES3: Sevcik, Rose, A.
DEGREE3: Ph.D.
DEPT3: Behavioral Biology
STAFF3: 0

INVES4: Romski, Mary Ann
DEGREE4: Ph.D.
DEPT4: Behavioral Biology
STAFF4: 0

SPECIES1: Pan paniscus
NUM1: 2

SPECIES2: Pan troglodytes
NUM2: 1

SPECIES3: Homo sapiens
NUM3: 3

NON-HOST INST: Georgia State University (all)

ABSTRACT: The objective of this project is to further our understanding of the processes underlying language development through comparative research so that what is learned might be applied toward intervention for alinguistic humans. During this report period, the principal focus was to test sentence comprehension in this project's most sophisticated symbol-using subject, Kanzi, a 9-year-old bonobo (Pan paniscus). Data were also collected on one of the human subjects, aged 18-23 months. Complex and novel English sentences were presented to both subjects under carefully-controlled, blind conditions. A total of 728 sentences were presented to Kanzi; 698 sentences were also presented to the human child. Preliminary results reveal comprehension of similar forms of syntax, with similar errors, in the ape and the child. This testing advances previous measures of syntax comprehension because such comprehension is not occurring in context. Language acquisition continues

to be compared in bonobo (P. paniscus) and chimpanzee (P. troglodytes) subjects which have been co-reared since shortly after birth. Both apes have continued to acquire additional symbols without specific training. Formal (blind) tests (approximately 1,000 trials per subject) of comprehension of the English language were completed during this report period. These tests reveal that, overall, the bonobo selected the appropriate symbol from an array, in response to the spoken word, with 90% accuracy. The chimpanzee responded with approximately 60% accuracy. The bonobo demonstrated comprehension with 100% accuracy of at least 140 different words, and the chimpanzee comprehended at least 39 different words with 100% accuracy. Both of the human subjects continued to use the keyboard productively in addition to normal speech. Analysis of both symbol- and speech-acquisition data collected during the past two years is underway. A third infant was added to the project shortly after birth, and is also receiving exposure to the symbol system.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Male Migration in Savanna Baboons in the Tana Primate Reserve

AXIS I: 1a

AXIS II: 34, 36, 78, 92 (behavioral ecology, sociobiology)

PRC UNIT: Behavioral Biology

INVES1: Smith, Euclid O.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: C

SPECIES1: Papio cynocephalus cynocephalus
NUM1: 85

ABSTRACT: This project is a longitudinal study of the behavioral ecology and sociobiology of a group of free-ranging, savanna-dwelling yellow baboons (Papio cynocephalus cynocephalus) in the Tana River Primate National Reserve, southeastern Kenya. Baseline data have been collected on a group of 82 individually-known baboons. These data included daily census records, the reproductive condition of all adult females, ad libitum observations on group movement and home-range utilization, ad libitum data on the major food items consumed, ad libitum observations on inter-group encounters, and ad libitum data on social interactions. The long-term objectives are to compare the behavior and ecology of the yellow baboons at the present study site with members of the same subspecies and with those of different subspecies living at other East African study sites. These comparative data will elucidate taxa-wide behavior commonalities. In addition, short-term data were also collected on the interactions between males and infants. Preliminary analyses suggest support for the contention (Smith and Whitten, Int. J. Primatol. 9:409-416, 1988) that males selectively use infants to cultivate relationships with adult females. These males maintain such relationships when females are not cycling regularly, and those that do enjoy preferential access to females when they are sexually receptive. Pilot focal data characterizing the same interactions between these adult males and infant have been collected.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Social Learning of Tool Use in Young Chimpanzees

AXIS I: 1a

AXIS II: 41

PRC UNIT: Behavioral Biology

INVES1: Tomasello, W. Michael
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: 0

INVES2: Bard, Kim A.
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF2: 0

SPECIES1: Pan troglodytes
NUM1: 4

ABSTRACT: The learning of complex tool use by chimpanzees (Pan troglodytes) ranging in age from two to four years is being investigated. This study was designed to examine (1) the development of the ability to use a simple tool, (2) the cognitive substrate necessary for tool use, and (3) comparison of the learning process when the task is learned by trial-and-error and when the task is learned through social observation. During the past year, a 3-1/2-year-old subject learned to use a tool through trial-and-error learning in 25 trials. Subsequent errors led to the conclusion that he lacked a mental representation of the characteristics necessary to solve the task. A second chimpanzee, aged two years, required more than 150 trials prior to learning to use a tool via trial-and-error learning. That subject also demonstrated a lack of mental representation with regard to solving the tool-use task. Data collection and analysis are still in progress and additional subjects are currently being tested.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Influence of Social Factors on Acquisition of a Learning Set in Rhesus Macaques

AXIS I: 1a

AXIS II: 36

PRC UNIT: Behavioral Biology

INVES1: Wallen, Kim
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: C

INVES2: Drea, Christine, M.
DEGREE2: M.A.
DEPT2: Behavioral Biology
STAFF2: O

SPECIES1: Macaca mulatta
NUM1: 74

ABSTRACT: The relationship between social factors, including age, sex and social dominance, on acquisition of a discrimination-reversal task was investigated. A large social group of rhesus monkeys was presented with a color-discrimination task (25 trials) and three successive reversals (19-24 trials each). Subjects were required to discriminate between one set of green and one set of orange rock- and sand-filled boxes; color indicated presence or absence of hidden rewards. By the end of the initial discrimination series (trials 20-25), the subjects' increased proximity to, and manual search of, stocked boxes during early minutes of a trial and throughout the duration of a trial indicated some acquisition of color discrimination. After the first reversal (trials 1-4), subjects made significantly more errors during early minutes of trials, shown by increased proximity to, and manual searches of, nonstocked boxes. There were significantly more correct responses during early minutes of trials 12-18. Responses were allocated equally between stocked and nonstocked zones during the second and third reversals. There were significantly more correct responses by early minutes of later trials of these reversals, and subjects became more efficient at retrieving rewards across trials. There was progressive improvement within a reversal series, and discrimination and improvement across successive reversals, suggesting learning-set formation. During all series of trials, members of the alpha matriline were in proximity to and manually searched stocked boxes more often, and retrieved significantly more rewards, than did lower-ranking animals. Subadults were more successful than infants, juveniles and adults on all measures. There was no significant relation between sex and any measure of success used. These results provide data about learning-set formation in a complex social context, enhance knowledge of social influences on cognitive function, and demonstrate that social factors, such as rank and age, can define individual opportunities to acquire color discrimination.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Hormonal and Environmental Influences on Behavior

AXIS I: 1a, 15, 23

AXIS II: 36

PRC UNIT: Behavioral Biology

INVES1: Wallen, Kim
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: C

INVES2: Mann, David
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF1: O

SPECIES1: Macaca mulatta
NUM1: 7

ABSTRACT: This is a continuing project to study the role of testosterone in male sexual behavior and the role of social conditions on the effects of testosterone suppression. Seven adult, male rhesus monkeys, living as part of a 75-member social group, were studied before, during and after treatment with a GnRH antagonist (Nal-Lys antagonist, Antide). Each male was observed for four weeks (two hours/day, three days/week) for occurrences of sexual and agonistic behaviors. At the end of the pretreatment period, each male received a bolus i.v. injection of GnRH (50.0 μg/kg), and blood was sampled 15, 30, 60 and 120 minutes following GnRH. Immediately following the GnRH challenge, each male received a subcutaneous injection (15.0 mg/kg) of Antide. Behavior and testosterone levels were monitored for eight weeks after Antide injection. Males received additional GnRH challenges at two, four and eight weeks post-Antide. For all males, testosterone decreased within 48 hours following Antide administration and remained suppressed for three weeks. Some males started to recover testicular function at three weeks; others remained suppressed for up to five weeks. Sexual behavior declined significantly during the first week postinjection and continued to decline, reaching a nadir at three weeks postinjection. Sexual behavior was not significantly different from pretreatment levels by eight weeks postinjection. Male response to the GnRH challenge was completely suppressed at two weeks, muted at four weeks and at normal levels by eight weeks postinjection. These results demonstrate an immediate and profound effect of a GnRH antagonist on testicular function and behavior. The decline in male sexual behavior was more rapid than that reported following castration when males were tested in pairs in small cages, suggesting that the opportunity for male-male competition provided in the present study enhances the importance of male testosterone as a determinant of male sexual behavior.

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P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: CNS Grafting for Parkinsonism

AXIS I: 1a, 6, 9, 21

AXIS II: 30, 36, 41, 46, 50a, 62, 64, 88

PRC UNIT: Neurobiology

INVES1: Bakay, Roy A.E.
DEGREE1: M.D.
DEPT1: Surgery (Neurosurgery)
STAFF: O

INVES2: Watts, Ray L.
DEGREE2: M.D.
DEPT2: Neurology
STAFF: O

INVES3: Byrd, Larry D.
DEGREE3: Ph.D.
DEPT3: Behavioral Biology
STAFF: C

INVES4: Iuvone, P. Michael
DEGREE4: Ph.D.
DEPT4: Pharmacology
STAFF: O

SPECIES1: Macaca nemestrina
NUM1: 9

ABSTRACT: The objective is to determine whether adrenal medullary tissue can be successfully transplanted into primates in order to improve neurological deficits. The model uses the administration of MPTP to selectively destroy the dopaminergic cells in the nigro-striatal pathway, which results in a Parkinson-like movement disorder. Preliminary studies have demonstrated the potential for correcting the Parkinson-like movement abnormalities using either adrenal medullary tissue or fetal mesencephalic tissue. These studies show that modification of the grafting technique is required when dealing with primates and that direct application of rodent techniques is inadequate.

Behavioral testing consists of clinical examination, quantitative analysis of drug-induced rotation, evaluation of performance on learned tasks, and computer analysis of spontaneous cage activity. Biochemical assessment is performed by serial measurements of dopamine metabolites in CSF. After baseline data are obtained, serial injections of MPTP are administered through the left internal carotid artery to produce a stable hemiparkinson-like state. Behavioral performance with adrenal medullary grafted monkeys is then compared to nonoperative and surgical controls that receive the same operation, but without placement of the graft. The goal is first to determine whether the grafting of adrenal medullary tissue to the head of the caudate by transcortical intraventricular approach can produce statistically significant improvement in Parkinson-like behavior. Once this is evaluated, multiple

aspects of the grafting technique will be explored (i.e., purity of the tissue separation, quantity of the graft, location of the graft, etc. Furthermore, attempts are made to further improve cell survival by co-grafting the adrenal tissue with sural nerve. If the neurological deficits can be successfully improved in monkeys with Parkinson-like syndrome, the implications are extremely important, not only for the potential treatment of Parkinson's, but also for any disease having a neurochemical deficiency responsible for a neurological deficit.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Plasticity of the Neocortex and the Development of Epilepsy

AXIS I: 1a, 6, 9, 21

AXIS II: 36, 50b, 62, 86, 90

PRC UNIT: Neurobiology

INVES1: Bakay, Roy A.E.
DEGREE1: M.D.
DEPT1: Surgery (Neurosurgery)
STAFF: O

INVES2: Epstein, Charles
DEGREE2: M.D.
DEPT2: Neurology
STAFF: O

INVES3: Ribak, Charles E.
DEGREE3: Ph.D.
DEPT3: Anatomy
STAFF: O

SPECIES1: Macaca mulatta
NUM1: 6

NON-HOST INSTITUTION: University of California, Irvine (CER)

ABSTRACT: We employ alumina in nonhuman primates to determine the anatomical basis for the development of focal epilepsy. This technique produces spontaneous seizures which is very similar to injury-induced human epilepsy. By evaluating specific alterations of multiple neurotransmitters in the neocortex as the maturation of the epileptic focus progresses, we elucidate the sequence of events required in focal cortical epileptogenesis.

Our data clearly demonstrate a GABAergic cell loss early in the developing epileptic focus which becomes statistically significant when seizure activity becomes manifest. Accompanying the initial loss of GABAergic terminals is an initial increase in the number of GABA neurotransmitter receptor binding sites observed. As cell loss progresses, the epileptiform activity fully develops and the number of GABA receptors markedly decreases in the epileptic focus. Surrounding the focus is an area of increased GABA numbers of receptors. The loss of GABA receptors is absolute and not a change in receptor affinity. Other neurotransmitter receptors are also lost in the epileptic focus but not to the same degree. An ultrastructural survey demonstrates a greater loss of symmetrical (presumably inhibitory) synapses with the development of seizure activity.

Loss of (GABAergic) inhibition and relative increase in excitation appears to be critical in the development of an epileptic focus in neocortex as a result of injury. Similar changes are not observed on the contralateral homotopic cortex or in surgical or non-surgical controls. These results suggest that future therapy for epilepsy might be directed at either preventing the GABAergic cell loss or by replacement of the GABAergic cells

(i.e., a graft). Alternatively, the inhibitory surround might be augmented by medication or isolated surgically from the focus in order to control seizure. The lack of epileptogenesis changes following surgery also supports the use of surgery to treat epilepsy.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Behavioral Studies of Strabismus and Amblyopia

AXIS I: 1a, 21, 25b

AXIS II: 36, 44, 60

PRC UNIT: Neurobiology

INVES1: Boothe, Ronald G.
DEGREE1: Ph.D.
DEPT1: Neurobiology/Neuropsychophysics
STAFF1: C

SPECIES1: Macaca nemestrina
NUM1: 10

SPECIES2: Macaca mulatta
NUM2: 10

ABSTRACT: We are conducting psychophysical tests of 10 Macaca nemestrina monkeys that have a naturally occurring strabismus. The goal of these studies is to determine the long-term sensory consequences that result from an untreated strabismus. We are collecting quantitative data regarding both the sensory and motor deficits in these animals, and these results are being used to develop models of their underlying neural mechanisms. These studies provide a standard against which treatments of strabismus can be compared. Results obtained from monkeys have clinical relevance for human patients with strabismic amblyopia.

We are also conducting behavioral tests of 10 Macaca mulatta monkeys that have an experimentally induced aphakia. These monkeys have been assigned to various treatment groups, and we are comparing the behavioral outcomes for each treatment. Our studies have been designed to compare the costs and benefits of various combinations of optical corrections and patching regimens that might be used as treatments for children born with unilateral cataracts.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Reproductive Function in Primates: Influences of Behavioral Environment

AXIS I: 1a, 2, 15

AXIS II: 36, 92, Neuroendocrinology

PRC UNIT: Neurobiology

INVES1: Herndon, James G.
DEGREE1: Ph.D.
DEPT1: Neurobiology/Neuropsychobiology
STAFF1: C

INVES2: Collins, Delwood C.
DEGREE2: Ph.D.
DEPT2: Medicine
STAFF2: O

SPECIES1: Macaca mulatta
NUM1: 35

NON-HOST INSTITUTION: VA Medical Center (DCC)

ABSTRACT: Studies related to this project dealt with the nature and cause of seasonal differences in reproductive physiology and behavior. One group of studies examined the pulsatile patterns of release of testosterone and luteinizing hormone in rhesus monkeys during the breeding and non-breeding seasons. This work confirmed the pulsatility of androgen and LH secretion in macaques, and suggested that although pulse frequency in the pituitary-gonadal axis may be reduced during the non-breeding season, the magnitude of individual pulses may remain unchanged. In another study, we tested the hypothesis that the pattern of hormonal stimulation, rather than absolute estrogen levels, of the female may be important in determining the response of the male to hormone treated females. Specifically, we found that a pattern of estradiol treatment which resembled the pattern seen during the normal menstrual cycle resulted in lowered frequency of behaviors indicating male sexual motivation (mount attempts, for example) at times when the female was apparently unreceptive (as indicated by incomplete mounts). We interpreted the data as an indication that the natural physiological pattern of hormone exposure has importance for the coordination of male and female motivation. In a study now underway, we are investigating the influence of prolonged daily melatonin stimulation on seasonal aspects of male reproductive physiology and behavior.

These experiments and others conducted as part of this same project contribute to an understanding of seasonal mechanisms of hormonal function. Season influences many human and animal physiological and behavioral functions, including emotional state, propensity toward violence and, in subarctic latitudes, gonadal function. By providing knowledge concerning seasonal regulation in monkeys this research will contribute to an understanding of seasonal mechanisms in all primates. Since breeding seasonality is merely a special case of physiological regulation, such studies

have implications for concepts of endocrine and behavioral regulation in general.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Effect of Topical Apomorphine on Development of Myopia in Infant Rhesus Monkeys

AXIS I: 1a, 21, 25b

AXIS II: 60, 62

PRC UNIT: Neurobiology

INVES1: Iuvone, P. Michael
DEGREE1: Ph.D.
DEPT1: Pharmacology, Ophthalmology
STAFF: O

INVES2: Tigges, Margarete
DEGREE2: Ph.D.
DEPT2: Neurobiology/Neural Ultrastructure
STAFF: C

INVES3: Lambert, Scott
DEGREE3: M.D.
DEPT3: Ophthalmology
STAFF: O

INVES4: Stone, Richard A.
DEGREE4: M.D.
DEPT4: Ophthalmology
STAFF: O

INVES5: Laties, Alan M.
DEGREE5: M.D.
DEPT5: Ophthalmology
STAFF: O

SPECIES1: Macaca mulatta
NUM1: 8

NON-HOST INSTITUTION: University of Pennsylvania (RAS, AML)

ABSTRACT: Visual deprivation-induced myopia appears to involve alterations in retinal function. In a chick model of myopia, deprivation-induced decreases of dopamine synthesis in retina may relate to exaggerated postnatal axial growth of the eye. A similar relationship between retinal dopamine and ocular growth may exist in primates. Visual deprivation of infant rhesus monkeys, using opaque extended-wear contact lenses, decreases retinal dopamine synthesis and metabolism and increases axial growth of the eye. As an initial test of the hypothesis that decreased dopamine receptor occupancy may be related to abnormal ocular growth in primates, we examined the effects of administering apomorphine, a dopamine receptor agonist, on deprivation-induced ocular growth and myopia. Eight rhesus monkeys were deprived of vision from birth unilaterally with opaque contact lenses. Four of the monkeys received drops of 1% apomorphine HCl 2-3 times/day in the occluded eye; 4 controls

received vehicle only. Axial lengths were determined (A-scan ultrasonography) at birth and 5-7 months of age. Occlusion increased axial growth in 3 of the 4 control monkeys by 1.3 mm on average. In contrast, growth of the occluded and non-occluded eyes of the apomorphine treated monkeys was equivalent, except in 1 monkey whose non-occluded eye failed to develop normally. At 6.5 - 9 months of age, 3 of 4 controls had myopic refractive errors (-3 to -7 diopters) in the occluded eyes; 3 of the 4 apomorphine-treated monkeys had slightly hyperopic refractive errors (+1 to +3 diopters) in their occluded eyes, with the 4th subject's eye being only -0.5 diopters myopic. Thus, apomorphine may retard excessive axial elongation and development of myopia in nonhuman primates, and further suggest that similar treatments may be useful in treatment of certain types of juvenile progressive myopia in humans.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Long-term Recording of Neural Signals from Monkey

AXIS I: 1a, 21

AXIS II: 48, 52

PRC UNIT: Neurobiology

INVES1: Kennedy, Philip R.
DEGREE1: Ph.D.
DEPT1: Bioengineering Center
STAFF1: O

INVES2: Tigges, Johannes
DEGREE2: Ph.D.
DEPT2: Neuroanatomy
STAFF2: C

INVES3: Bakay, Roy A. E.
DEGREE3: M.D.
DEPT3: Neurological Surgery
STAFF3: O

SPECIES1: Macaca mulatta
NUM1: 5

NON-HOST INSTITUTION: Georgia Institute of Technology (PRK)

ABSTRACT: Objectives: Determine [1] if a new long-term recording electrode (the Cone Electrode) developed in rats was also operable in monkeys. If so, then [2] how long would it continue to monitor neural signals, [3] how discrete would the signals be (single or multi-units), [4] what would their signal-to-noise ratios be, and [5] what behavioral correlations could be made?

The significance of this research in primates was that it will allow monitoring of neural signals over long time periods for the study of motor control, sensory responses, sensorimotor integration, plasticity experiments in the motor and sensory systems with its attendant questions of learning and memory, and, not least, its possible role as a neural prosthetic controller.

Results: [1] The first monkey was used solely for histology and this showed silver stained neuronal processes in the tissue in the cone, and, using fluorescent tracer dyes, a connection to cortical neurons. EM studies in rat show myelinated neuronal processes growing into each end of the cone. These studies continue. Monkeys implanted with the cone electrode show that neural signals can be recorded. [2] The longevity of the recordings continues to be assessed. Recordings continue at 10 months in one monkey. Another monkey produced signals until destruction of the implant at 5 months. [3] Signals consist of a number of single units firing together during movements thereby constituting a burst of multi-unit activity. New digital processing techniques show that units persist for the duration of the recordings. [4] Signal-to-noise ratios are consistent at over 2:1, usually 3 or 5:1 depending on the individual unit. This is similar to the rat. [5] The neural signals are associated with hand and finger movements. In sum, all objectives are being met.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Correction of Monocular Aphakia in Monkeys with IOLs

AXIS I: 1a, 25b

AXIS II: 60, 82

PRC UNIT: Neurobiology

INVES1: Lambert Scott R.
DEGREE1: M.D.
DEPT1: Ophthalmology and Pediatrics
STAFF1: O

INVES2: Tigges, Margarete
DEGREE2: Ph.D.
DEPT2: Neural Ultrastructure
STAFF2: C

INVES3: Boothe, Ronald G.
DEGREE3: Ph.D.
DEPT3: Neuropsychophysics
STAFF3: C

SPECIES1: Macaca mulatta
NUM1: 2

ABSTRACT: For human infants born with monocular cataracts, visual outcome is usually poor even after early removal of the cataract. The postoperative correction of the resulting aphakia is the limiting factor in visual rehabilitation of these eyes. Correcting the aphakic eyes with contact lenses, epikeratoplasty or spectacles, magnifies the image in the aphakic eye, thereby creating a disparity in the image size between the 2 eyes, resulting in amblyopia. Intraocular lens (IOL) implantation is a promising new approach to this problem with the potential to optimize vision in the aphakic eye. Although IOL are routinely used in adult human patients, their efficacy and safety in an eye that is still growing is not known. Therefore, a pilot study was initiated using newborn rhesus monkeys as an animal model to evaluate the efficacy and safety of IOL. Two neonatal monkeys underwent monocular lensectomies with the implantation of a posterior chamber intraocular lens.

A detailed histopathological study of the pseudophakic eye of the second monkey revealed that a posterior chamber IOL can be implanted safely. We also achieved a better visual acuity in the pseudophakic eye than in an aphakic eye corrected with an extended-wear contact lens. Examination of the striate cortex with neuroanatomical methods revealed that a pseudophakic eye can compete successfully with an unmanipulated fellow eye for cortical territory. There was only a slight shift in ocular dominance columns in favor of the unmanipulated eye. Since congenital cataracts are one of the most common causes of impaired vision during childhood, our animal model will be important for the design and testing of treatment methods to preserve good visual functions in human infants with congenital visual system disorders.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Aging and the Primate Nervous System

AXIS I: 1a, 21

AXIS II: 30

PRC UNIT: Neurobiology

INVES1: Moss, Mark B.
DEGREE1: Ph.D.
DEPT1: Anatomy
STAFF1: 0

INVES2: Rosene, Douglas L.
DEGREE2: Ph.D.
DEPT2: Anatomy
STAFF2: 0

SPECIES1: Macaca mulatta
NUM1: 20

NON-HOST INSTITUTION: Boston University School of Medicine (MBM, DLR)

ABSTRACT: The objective is to determine the neural substrates of the cognitive decline that occurs during aging in primates. Since well-controlled studies of this cannot be conducted in humans we have chosen to investigate this in the aging rhesus monkey. We have previously characterized some of these cognitive deficits. During the past year we have begun to analyze brain tissue from some of these animals. These initial studies have focused on the cholinergic system of the forebrain because of abundant evidence implicating it in some aspects of age-related dementias in humans. We have processed tissues in two ways. In one set of experiments, we have utilized the histochemical enzyme procedure to demonstrate the cholinergic catalytic enzyme, acetylcholinesterase (AChE) and have assessed the number of AChE containing neurons that provide cholinergic innervation of the cerebral cortex. These results demonstrate an age-related decline in neuron number from age 5 through age 35 that approaches 50%. In a second approach we have processed tissue using in vitro autoradiography to demonstrate the density and localization of radioactively labeled ligands that bind to the high affinity choline uptake site (a marker for presynaptic cholinergic fibers) and others that bind to various subtypes of the muscarinic receptors. The results of these studies are still being analyzed but preliminary observations suggest that this approach will be more sensitive and specific than the AChE methodology.

(Tissues obtained from aged monkeys are being shared with several investigators and will be used in a number of studies in a concerted effort to develop the rhesus monkey as a model for human aging.)

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Aging in the Primate Nervous System

AXIS I: 1a, 21

AXIS II: 30

PRC UNIT: Neurobiology

INVES1: Peters, Alan
DEGREE1: Ph.D.
DEPT1: Anatomy
STAFF1: 0

SPECIES1: Macaca mulatta
NUM1:

NON-HOST INSTITUTION: Boston University School of Medicine

ABSTRACT: The study is concerned with the effects of aging on the neurons and neuroglial cells of the cerebral cortex of the rhesus monkey (Macaca mulatta). In the past, these studies have shown that there is no significant loss of neurons with age from either the visual or the primary motor cortices. It has also been shown that while some neurons, such as those in the visual cortex, including Meynert cells, have little lipofuscin accumulation, other cortical neurons such as Betz cells can become loaded with this material. These studies have had to be discontinued due to lack of funding, but a Program Project application entitled "Neural Substrates of Cognitive Decline in Aging Monkeys" has been submitted to the National Institute on Aging to meet the February 1, 1990 submission deadline. If funding is restored, these studies will continue.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Perikaryal Inclusions in Betz Cells of Area 4

AXIS I: 1a, 21

AXIS II: 30

PRC UNIT: Neurobiology

INVES1: Tigges, Johannes
DEGREE1: Ph.D.
DEPT1: Neuroanatomy
STAFF1: C

INVES2: Tigges, Margarete
DEGREE2: Ph.D.
DEPT2: Neural Ultrastructure
STAFF2: C

INVES3: Peters, Alan
DEGREE3: Ph.D.
DEPT3: Anatomy
STAFF3: O

SPECIES1: Macaca mulatta
NUM1: 8

NON-HOST INSTITUTION: Boston University School of Medicine (AP)

ABSTRACT: During an electron microscopic investigation to determine the effect of age on somal synapses, relatively large inclusion bodies (IB) were seen in Betz cells. Research on these IBs was intensified for two reasons. 1) IBs were seen only in the two oldest rhesus monkeys (28 and 35 years). 2) This type of IB has never been described before. In some fortuitous electron micrographs the IB appears to consist of 3 sets of parallel sheets of material. In trying to explain the 3-dimensional configuration of the IBs a comparison with the device in a carton to protect bottles during shipping may be helpful. The protective device usually consists of 2 sets of parallel and equidistant sheets of corrugated paper and intersect each other at right angles; viewed edge-on the intersecting sheets form squares, to protect the bottles on all 4 sides. The IBs are more complicated in that they consist of 3 sets of parallel and equidistant sheets of material. These 3 sets of sheets intersect each other in such a way (60° angle) that when an IB is viewed edge-on, a regular geometric pattern is seen, the basic unit of which has the form of the star of David. In a 3-dimensional view, the star of David would be actually a hexagonal tube with equal sides (like a cell of a honeycomb) plus 6 triangular tubes with equal sides. Each triangular tube shares one wall with the hexagonal tube. At present the material components and the function of the IBs are unknown.

(Tissues obtained from aged monkeys are being shared with several investigators and will be used in a number of studies in a concerted effort to develop the rhesus monkey as a model for human aging.)

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Parvalbumin in the Lateral Geniculate Nucleus (LGN) of Rhesus Monkeys

AXIS I: Ia, 21

AXIS II: 60

PRC UNIT: Neurobiology

INVES1: Tigges, Margarete
DEGREE1: Ph.D.
DEPT1: Neurobiology/Neural Ultrastructure
STAFF1: C

INVES2: Tigges, Johannes
DEGREE2: Ph.D.
DEPT2: Neurobiology/Neuroanatomy
STAFF2: C

SPECIES1: Macaca mulatta
NUM1: 2

ABSTRACT: GABAergic interneurons are common in the LGN, but their exact role in the processing of visual information from retina to striate cortex is still obscure. According to recent immunocytochemical studies on various cortical areas of rat, cat, and monkey, the calcium-binding protein parvalbumin (PV) is confined almost exclusively to GABA positive (+) interneurons. Using an antibody to PV, we observed a close correlation of the distribution of PV positive (+) and GABA+ neurons in area 17 of an adult rhesus monkey. We studied the relationship between PV+ and GABA+ neurons in the LGN. We found a PV labeling pattern strikingly different from that of GABA. While GABA+ interneurons are small and comprise only a fraction of all LGN neurons, PV labels a much greater number of cells in all layers of the LGN, including the large neurons in layers 1 and 2. Thus, it appears that in the LGN of monkeys PV is not exclusive to interneurons, but is present in projection neurons, too. Neurons with high PV content have been associated with a high level of cytochrome oxidase, a metabolic marker sensitive to denervation. After long-term enucleation of one eye in an adult monkey, somata in the denervated layers, although severely shrunken, are still PV+ and indistinguishable in density of label from somata in layers connected to the remaining eye. Only PV immunoreactivity in the neuropil of the denervated layers appears reduced. Our results lead us to propose that PV+ neurons in the LGN have a specific as yet undetermined role in the circuitries of the LGN, not directly related to inputs from the retina and only partially overlapping with the influence of GABAergic interneurons. How this influences the output of information to striate cortex needs to be established by future experiments.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Effects Of Aphakia, Combined With Occlusion, on Area 17 of Infant Rhesus Monkeys

AXIS I: 1a, 21

AXIS II: 60

PRC UNIT: Neurobiology

INVES1: Tigges, Margarete
DEGREE1: Ph.D.
DEPT1: Neurobiology/Neural Ultrastructure
STAFF1: C

INVES2: Tigges, Johannes
DEGREE2: Ph.D.
DEPT2: Neurobiology/Neuroanatomy
STAFF2: C

INVES3: Wilson, James R.
DEGREE3: Ph.D.
DEPT3: Neurobiology/Neurophysiology
STAFF3: C

INVES4: Boothe, Ronald G.
DEGREE4: Ph.D.
DEPT4: Neurobiology/Neuropsychophysics
STAFF4: C

SPECIES1: Macaca mulatta
NUM1: 5

ABSTRACT: The rationale for work pursued in this laboratory is twofold. One is a neuroanatomical inquiry into basic organizational principles underlying information processing in the brain and the influence of environmental factors during postnatal development by using the developing visual system of rhesus monkeys as a model. The second aim using the same primate model is to gain a better understanding of causes underlying visual system disorders like congenital cataracts, myopia, strabismus and amblyopia. Our monkey model uses newborn rhesus monkeys. Unilateral lensectomies were performed and the aphakic eyes corrected with contact lenses. In 2 monkeys, the fellow eye was occluded continuously with opaque occluder lenses up to 2 years. In 3 monkeys, the fellow eye was occluded partially for short periods per day. When the monkeys were between 19 and 42 months old, 1 eye was enucleated; 4-14 days later, area 17 was reacted for cytochrome oxidase (CO) as a marker for deprivation-induced changes in the ocular dominance system. In all monkeys, layer 4C in the representation of the central visual field of area 17 exhibited darkly and lightly reacted CO stripes. In all partially occluded monkeys, stripes connected to the occluded eyes were wider than stripes connected to the aphakic eyes. After continuous occlusion, the dark and light stripes in one monkey appeared to be of approximately equal width. In the second monkey, stripes related to the aphakic eye were slightly wider. These

data demonstrate that an occluded eye is capable of maintaining a considerable amount of cortical territory when competing against an aphakic eye. Because of close similarities between the visual systems of monkeys and humans, this information will help to design, test and implement better clinical treatment methods for the correction of visual impairments and for the prevention of blindness in humans.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Brainstem Afferents to the Macaque's LGN

AXIS I: 1a, 21, 25b

AXIS II: 92, Neuroscience

PRC UNIT: Neurobiology

INVES1: Wilson, James R.
DEGREE1: Ph.D.
DEPT1: Neurophysiology
STAFF1: C

INVES2: Hendrickson, Anita E.
DEGREE2: Ph.D.
DEPT2: Ophthalmology
STAFF2: O

INVES3: Sherk, Helen
DEGREE3: Ph.D.
DEPT3: Biological Structure
STAFF3: O

SPECIES1: Macaca fascicularis
NUM1: 4

NON-HOST INSTITUTION: University of Washington (AEH, HS)

ABSTRACT: In order to determine the possible functions of the lateral geniculate nucleus (LGN), it is necessary to know all of its connections. Obviously, to closely relate such findings to human functioning, monkeys must be used. In this study, horseradish peroxidase was injected into the LGN and the areas of the brainstem having retrogradely-labeled neurons were observed. The parabrachial region, pretectum, parabigeminal, superior colliculus, and dorsal raphe nucleus all contained labeled neurons. The locus coeruleus had six labeled neurons observed in the brain of one monkey. This monkey had the largest W-HRP injection into the LGN. None of the other three monkeys contained W-HRP-labeled neurons in the locus coeruleus. The areas of the brainstem described have the capability of influencing retinal signals, passing through the LGN, probably in a gating manner. This research has been in collaboration with Drs. Anita Hendrickson and Helen Sherk. By joining up with this Seattle group, we have shared the use of monkeys, leading to fewer required animals. The results have now been written up and will be submitted to a prominent neuroscience journal for publication.

DIVISION OF PATHOBIOLOGY AND IMMUNOLOGY

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T. Dodson	Department of Surgery, Emory University
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M. Eberhard	Parasitic Diseases, Centers for Disease Control
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R. Hester	Department of Surgery, Emory University
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R. Hunter	Department of Pathology, Emory University
P. Johnson	Department of Microbiology, Georgetown University
H. Keyserling	Department of Pediatrics, Emory University
L. Klein	Department of Gyn. & Obstet., Emory University
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S. Mirra	Department of Pathology, Emory University
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P. Nguyen-Dinh	Malaria Branch, Centers for Disease Control
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J. Ribas	Armed Forces Institute of Pathology
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M. Smith	Department of Periodontology, Emory University
R. Smith	Department of Vascular Surgery, Emory University
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M. Isahakia	Institute of Primate Research, Kenya
M. Otsyula	Institute of Primate Research, Kenya
F. Villinger	Division of Pathobiology and Immunobiology

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B. Eriksson	Department of Virology, Karolinska Institute
K. Hanna	Ophthalmology, Hotel-Dieu Hospital, Paris

Consultants:

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J. Richardson	Consultant in Biosafety, Emory University
R. Weaver	Consultant in Microbiology, Ctrs for Disease Control

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Natural SIV Infection in Stumptail Macaques

AXIS I: 1a, 7b

AXIS II: 31, 56, 64, 66, 77

PRC UNIT: Pathobiology & Immun

INVES1: Anderson, Daniel C.
DEGREE1: D.V.M.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVES2: McClure, Harold M.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVES3: Ansari, Aftab A.
DEGREE3: Ph.D.
DEPT3: Pathology
STAFF3: C

INVES4: Fultz, Patricia N.
DEGREE4: Ph.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

INVES5: Klumpp, Sherry A.
DEGREE5: D.V.M.
DEPT5: Pathobiology and Immunobiology
STAFF5: O

SPECIES1: Macaca arctoides
NUM1: 21

ABSTRACT: A naturally occurring SIV infection has recently been documented in a stumptail macaque (Macaca arctoides) colony at the Yerkes Center. This colony was formed at the Yerkes Center in 1964, and has been maintained as a closed colony except for the introduction of 4 animals in 1981. One of these animals died shortly after arrival due to fight wounds at the time of introduction. Two of the other three animals remained within the colony until their deaths at 7 and 8 years after introduction into the colony; one of the three animals is currently alive. In 1986 we became aware that the animals introduced into the colony in 1981 were from an SIV positive colony. Sera from 16 of 31 animals in the colony were checked for antibodies to SIV. Only two SIV seropositive animals were detected and both of these were animals introduced into the colony in 1981. In mid-1988, the colony (32 animals) began showing an increased incidence of clinical disease and an increased mortality rate. Due to a continued high incidence of clinical disease and high mortality rate, the entire colony (now only 21 animals) was checked for antibodies to SIV in August, 1989. This serologic survey revealed that all

animals except one infant, born in 1988, were seropositive for antibodies to SIV. Twelve of 17 deaths that occurred from mid-1988 through 1989 were seropositive for antibodies to SIV; the serologic status of 4 of these animals was unknown. The only known seronegative animal that died during this period was a 10 month old infant. The major finding at necropsy of these 17 animals was severe weight loss; a considerable number of the animals had oral and esophageal candidiasis and some animals had intestinal mycobacteriosis. A lentivirus, designated SIVstm, was subsequently isolated from a number of animals in this colony. Preliminary immunologic evaluations on a small number of animals removed from this colony due to clinical disease have revealed significant reductions in lymphocyte counts, reduced numbers of $CD4^+$ cells and decreased $CD4^+/CD8^+$ cell ratios. It is clear that naturally transmitted SIV infection is widespread in this colony; that this infection is causing significant immunosuppression in infected animals; and that the increased incidence of clinical disease and mortality is due to this naturally occurring SIV infection.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Amyloidosis in Nonhuman Primates

AXIS I: 1a, 28 (All systems)

AXIS II: 46, 56, 64, 77

PRC UNIT: Pathobiology & Immun

INVES1: Anderson, Daniel C.
DEGREE1: D.V.M.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVES2: McClure, Harold M.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVES3: Klumpp, Sherry A.
DEGREE3: D.V.M.
DEPT3: Pathobiology and Immunobiology
STAFF3: O

SPECIES1: Macaca mulatta
NUM1: 111

SPECIES2: Macaca nemestrina
NUM2: 19

SPECIES3: Macaca nigra
NUM3: 3

SPECIES4: Macaque hybrids
NUM4: 3

SPECIES5: Saimiri sciureus
NUM5: 2

SPECIES6: Cercocebus atys
NUM6: 1

SPECIES7: Macaca arctoides
NUM7: 1.

ABSTRACT: The occurrence of a high incidence of spontaneous amyloidosis (140 cases in 15 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 (111 rhesus, 19 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 30 years of age. A significant number of the animals with amyloidosis have a history of arthritis.

Efforts are currently underway to more effectively diagnose amyloidosis early in the course of the disease. This will be accomplished primarily by rectal, small intestine or liver biopsy in animals with clinical signs of amyloidosis. Animals with early amyloidosis will then be monitored periodically by hemogram, blood chemistry and immunologic evaluations. The latter will include immunoglobulin determinations and phenotyping of the peripheral blood mononuclear cells. Evaluation of these parameters during various stages of the disease may provide data which can be used to suggest possible treatment modalities.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Novel Approaches for the Diagnosis of SIV Infections

AXIS I: 1a, 1d, 6, 17, 19

AXIS II: 31, 64, 66

PRC UNIT: Pathobiology & Immun

INVES1 Ansari, Aftab A.
DEGREE1: Ph.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: C

INVES2: Cohen, Tamar Jehuda
DEGREE2: Ph.D.
DEPT2: Pathobiology & Immunobiology
STAFF2: O

INVES3: McClure, Harold H.
DEGREE3: D.V.M.
DEPT3: Pathobiology & Immunobiology
STAFF3: C

INVES4: Powell, Jonathan D.
DEGREE4: B.S.
DEPT4: Pathobiology & Immunobiology
STAFF4: O

SPECIES1: Cercocebus atys
NUM1: 25

SPECIES2: Macacca mulatta
NUM2: 12

ABSTRACT: Peripheral blood mononuclear cells (PBMC) from SIV seropositive and seronegative (by ELISA, RIPA, and Western blot analysis) sooty mangabeys and rhesus macaques were cultured in vitro with pokeweed mitogen (PWM). Supernatant fluids were assayed for antibody against SIV/SMM using routine ELISA and Western blot assays. Not unexpectedly, the supernatant fluids from PWM stimulated cultures of 10 uninfected rhesus macaques were all negative for anti SIV antibodies whereas supernatant fluids from 8 rhesus macaques experimentally infected with SIV/SMM and 12 naturally infected, clinically asymptomatic SIV/SMM seropositive sooty mangabeys were all positive for antibodies against SIV/SMM. Of great interest was our finding that supernatant fluids of PWM stimulated cultures from 10 SIV/SMM seronegative sooty mangabeys had significant antibody titers against SIV/SMM. These findings were highly reproducible upon repeated testing of each seropositive and seronegative monkey. In addition, depletion of $CD8^+$ T cells from PBMC from SIV seronegative mangabeys prior to culture in vitro with PWM resulted in marked increases in titers of antibodies against SIV/SMM (1-10 log fold increase in titers).

These findings prompted us to examine supernatant fluids from PWM stimulated cultures of PBMC from a random population of high risk human individuals. Preliminary data demonstrate significant levels of anti HIV-1 antibodies in supernatant fluids of PWM stimulated cultures from 10 - 15% of humans who are classified as high risk individuals and whose sera, upon repeated testing, showed negative antibody titers by both commercial ELISA and Western blot assays. Aliquots of PBMC from both SIV/SMM seronegative and HIV-1 seronegative mangabeys and humans respectively, whose PWM stimulated cultures show antibodies to SIV and HIV-1 are currently being subjected to PCR analysis using appropriate primer pairs.

Results of these studies have important implication on the current classification of AIDS infection.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Cell Lineage Tropism of SIV *in vitro*

AXIS I: 1a, 1d, 6, 17, 19

AXIS II: 31, 64, 66

PRC UNIT: Pathobiology & Immun

INVES1: Ansari, Aftab A.
DEGREE1: Ph.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: C

INVES2: Villinger, Francois V.
DEGREE2: D.V.M.
DEPT2: Pathobiology & Immunobiology
STAFF2: O

INVES3: Cohen, Tamar Jehuda
DEGREE3: Ph.D.
DEPT3: Pathobiology & Immunobiology
STAFF3: O

INVES4: McClure, Harold M.
DEGREE4: D.V.M.
DEPT4: Pathobiology & Immunobiology
STAFF4: C

SPECIES1: *Cercocebus atys*
NUM1: 25

SPECIES2: *Macacca mulatta*
NUM2: 12

ABSTRACT: Equal numbers of peripheral blood mononuclear cells (PBMC), enriched populations of $CD4^+$ T cells and monocytes from SIV/SMM infected clinically asymptomatic sooty mangabeys and rhesus macaques were incubated *in vitro* with live SIV/SMM. Supernatant fluids were monitored for RT activity over a 28 day period. While the RT activity in supernatant fluids of PBMC from mangabeys was significantly lower than rhesus macaques, supernatant fluids from enriched cultures of $CD4^+$ T cells from both species demonstrated equal RT activity. Of interest was our finding that supernatant fluids from monocyte cultures of sooty mangabeys incubated with SIV/SMM consistently gave a 5 - 10 fold higher RT level than similar cultures of monocytes from experimentally infected rhesus macaques. This dramatic difference was not secondary to high endogenous levels of SIV in mangabeys or due to STLV-1 infection. Of further interest was our observation that $CD8^+$ T cells from SIV infected sooty mangabeys induced 70 - 80% inhibition of RT activity in autologous monocyte cultures as compared to 25 - 30% inhibition induced by $CD8^+$ T cells in autologous cultures of monocytes from SIV infected rhesus macaques. Preliminary data indicate that $CD8^+$ T cells from SIV infected mangabeys predominantly inhibit SIV replication in autologous monocytes

whereas $CD4^+$ T cells appear to be the primary target of $CD8^+$ T cell regulation of SIV replication in rhesus macaques. The suppression in both species is MHC restricted and antigen specific since $CD8^+$ T cells from uninfected rhesus macaques fail to suppress replication of SIV/SMM in autologous cultures of $CD4^+$ T cells and/or monocytes.

These data on the increased susceptibility of monocytes from sooty mangabeys and relative different target cell specificity of $CD8^+$ T cells that regulate SIV replication in vitro may relate to the clinical asymptomatic state of sooty mangabeys and the disease susceptible state of rhesus macaques.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: SIV Specific Cellular Immunity in Nonhuman Primates

AXIS I: 1a, 1d, 6, 17, 19

AXIS II: 31, 64, 66

PRC UNIT: Pathobiology & Immun

INVES1: Ansari, Aftab A.
DEGREE1: Ph.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: C

INVES2: Powell, Jonathan D.
DEGREE2: B.S.
DEPT2: Pathobiology & Immunobiology
STAFF2: O

INVES3: Villinger, F. V.
DEGREE3: D.V.M.
DEPT3: Pathobiology & Immunobiology
STAFF3: O

INVES4: McClure, Harold M.
DEGREE4: D.V.M.
DEPT4: Pathobiology & Immunobiology
STAFF4: C

SPECIES1: Cercocebus atys
NUM1: 25

SPECIES2: Macacca mulatta
NUM2: 12

ABSTRACT: The exact nature, mechanism and consequences of humoral and cellular virus specific immune responses in human AIDS and experimental animal models of AIDS have yet to be elucidated. In addition to the characterization of both neutralizing and enhancing antibodies, virus specific and autoreactive cell mediated immunity (CMI) has been described in HIV-1 infected humans. Using the nonhuman primate SIV model of AIDS, our laboratory has established an assay whereby both humoral and CMI to the same viral peptides can be measured in vitro. Briefly, purified preparations of SIV/SMM are subjected to SDS-PAGE and transferred to nitrocellulose. Based on protein staining of one representative strip, individual bands are excised and transferred aseptically to 96 well microtiter wells and used as a source of antigen in a T cell proliferation assay. Serum from the same animal is used to detect SIV/SMM specific antibodies by routine Western blot assay using one strip of the same blot. Our results indicate that the predominant cellular response of both SIV/SMM seropositive sooty mangabeys and rhesus macaques appears to be directed against proteins of 41 and 14 kd. The T cell proliferation assay is highly antigen specific since T cells from uninfected animals do not respond to these protein bands. In addition, although T cells from SIV/SMM infected

monkeys of both species respond to the same protein bands, the peak proliferative response occurs on day 2 - 3 in T cells from naturally infected mangabeys and day 5 - 6 in T cells from experimentally infected rhesus macaques. The response is MHC restricted and appears to be mediated by phenotypically distinct T cell subpopulations. Electroelution of relevant peptides from the blot and limited proteolysis followed by HPLC may provide answers to the precise sequences that induce such proliferative responses. The requirement for antigen processing is currently under study. This cellular Western blot assay is being performed to sequentially monitor SIV specific humoral and CMI in rhesus macaques post experimental infection with SIV/SMM.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Immune Regulatory T Cells in Nonhuman Primates

AXIS I: 1a, 1d, 6, 17, 19

AXIS II: 31, 64, 66

PRC UNIT: Pathobiology & Immun

INVES1: Ansari, Aftab A.
DEGREE1: Ph.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: C

INVES2: Powell, Jonathan D.
DEGREE2: B.S.
DEPT2: Pathobiology & Immunobiology
STAFF2: O

INVES3: McClure, Harold M.
DEGREE3: D.V.M.
DEPT3: Pathobiology & Immunobiology
STAFF3: C

SPECIES1: Cercocebus atys
NUM1: 25

SPECIES2: Macacca mulatta
NUM2: 12

ABSTRACT: It has been shown that $CD8^+$ T cells from HIV-1 and SIV/mac infected humans and rhesus macaques, respectively (but not from uninfected humans/monkeys) inhibit HIV and SIV replication in autologous cells. However, in spite of this $CD8^+$ T cell mediated regulation of virus replication, HIV-1 and SIV/mac infection of humans and rhesus monkeys invariably results in death. This prompted us to examine this phenomenon in sooty mangabeys which are chronically infected with SIV/SMM but, to date, remain clinically asymptomatic. Results of our studies, similar to those described for HIV and SIV/mac infected humans and rhesus macaques, demonstrate that $CD8^+$ T cells from SIV/SMM seropositive asymptomatic mangabeys also inhibit SIV/SMM viral replication in vitro. Furthermore, of great interest is our finding that $CD8^+$ cells from SIV^- mangabeys also are able to inhibit viral replication. These monkeys were initially characterized as being virus negative by ELISA and Western Blot, as well as by the absence of RT activity, after co-culture with human PHA-P blasts which regularly yields virus growth from SIV/SMM seropositive monkeys. Supernatant fluids from in vitro culture of peripheral blood mononuclear cells (PBMC) from such SIV seronegative mangabeys demonstrate significant endogenous SIV replication as measured by RT activity only after removal of $CD8^+$ T cells prior to culture. Preliminary studies indicate a prominent role for $CD8^+$ T cells bearing the gamma delta T cell receptor in this virus growth inhibition assay. In addition, our data show that $CD8^+$ T cells from HIV-2 infected rhesus macaques inhibit the replication of SIV/SMM in autologous cells in vitro. Studies are in progress to examine

the nature of this cross reactivity by examining the ability of $CD8^+$ T cells from HIV-1, SIV/Agm, and STLV-1 infected animals and HTLV-1 infected humans to suppress replication of HIV-2,SIV/SMM and HIV-1 in vitro. Such studies may shed light on the specificity of $CD8^+$ T cell mediated suppression of virus replication in vitro. In addition, our data concerning seronegative mangabeys suggest that, among high risk individuals, there may exist seronegative individuals who are infected with HIV-1. These individuals who are currently not detected due to negative serology not only are infected, but may in fact possess potent protective immunity to the virus.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Phenotype and Function of Natural Immune Effector Cells in Nonhuman Primates

AXIS I: 1a, 1d, 6, 17, 19

AXIS II: 31, 64, 66

PRC UNIT: Pathobiology & Immun

INVES1: Ansari, Aftab A.
DEGREE1: Ph.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: C

INVES2: McClure, Harold M.
DEGREE2: D.V.M.
DEPT2: Pathobiology & Immunobiology
STAFF2: C

INVES3: Powell, Jonathan D.
DEGREE3: B.S.
DEPT3: Pathobiology & Immunobiology
STAFF3: O

SPECIES1: Cercocebus atys
NUM1: 25

SPECIES2: Macacca mulatta
NUM2: 12

ABSTRACT: Greater than 75% of the sooty mangabey monkeys at the Yerkes Regional Primate Center are naturally infected with SIV without any apparent clinical symptomology. On the other hand, experimental infection of rhesus macaques with SIV results in a clinical syndrome similar to human AIDS. These differences with regard to SIV infection prompted us to examine the natural immunosurveillance system of peripheral blood mononuclear cells (PBMC) from SIV-infected and uninfected monkeys of these two species. Phenotypic and functional studies of precursor and effector NK and LAK cells in the PBMC from these two species were carried out using monoclonal reagents, flow microfluorometry (FMF) and the standard in vitro ^{51}Cr release assay against prototype K562 (NK sensitive) and RAJI (NK resistant, LAK susceptible) target cell lines. Data indicate that both NK and LAK cell activities in the PBMC or sooty mangabeys were significantly ($P<0.01$) greater than those in rhesus macaques. The predominant NK effector cells and LAK cell precursors were shown to be $Leu19^{-}$ $CD8^{+}$ in the PBMC of sooty mangabeys and $Leu19^{+}$ $CD8^{-}$ in the PBMC of rhesus macaques as determined by panning depletion techniques and FMF analysis. On the other hand, predominant LAK effector cells were found to be dual marked $Leu19^{+}$ $CD8^{+}$in rhesus macaques and $Leu19^{-}$ $CD8^{+}$ in sooty mangabeys. These qualitative and quantitative differences were not due to SIV infection of these two species since PBMC from both SIV-seropositive and virus-positive and SIV-seronegative and virus-negative monkeys gave similar results. Moreover, of importance is the finding that the functional NK and LAK

precursor cells are $CD8^+$ and $CD8^-$ in sooty mangabeys and rhesus macaques respectively. These data may have implications for the natural SIV/SMM virus-positive asymptomatic state of sooty mangabeys and may provide useful tools for tracing the ontogeny and lineage derivation of NK and LAK cells.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Macrophage Function of Nonhuman Primates

AXIS I: 1a, 1d, 6, 17, 19

AXIS II: 31, 64, 66

PRC UNIT: Pathobiology & Immun

INVES1: Ansari, Aftab A.
DEGREE1: Ph.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: C

INVES2: Cohen, Tamar Jehuda
DEGREE2: Ph.D.
DEPT2: Pathobiology & Immunobiology
STAFF2: O

INVES3: McClure, Harold H.
DEGREE3: D.V.M.
DEPT3: Pathobiology & Immunology
STAFF3: C

SPECIES1: Cercocebus atys
NUM1: 25

SPECIES2: Macacca mulatta
NUM2: 12

ABSTRACT: Highly purified $CD4^+$ and/or $CD8^+$ T cells from the PBMC of mangabeys naturally infected with SIV or macaques experimentally infected with SIV/SMM failed to proliferate when cultured in vitro with varying doses of UV and psoralen (UV/P) inactivated SIV. However, pulsing of autologous monocytes with the UV/P SIV for 3 hours followed by co-culture with autologous T cells or purified $CD4^+$ and/or $CD8^+$ T cells induces significant proliferation. The proliferation is antigen specific. Optimal results were obtained using 5×10^4 virus pulsed antigen presenting cells (APC) and 2×10^5 T cells incubated for 5 days. Treatment of APC's with 0.1% paraformaldehyde (PF) after virus pulsing did not appreciably alter their ability to present antigen. However, treatment with (PF) prior to virus pulsing or pulsing of untreated APC's at 0°C did not permit efficient antigen presentation. Addition of chloroquine or leupeptin to APC during virus pulsing diminished their ability to present antigen. Thus, SIV specific T cell proliferation require typical antigen processing by APC's and that lysosomal degradation is an obligate requirement for the measurement of antigen specific T cell proliferative responses.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Comparative Pharmacokinetics of AZddU and AZT in Monkeys

AXISI: 1a, 7b

AXIS II: 31, 50a, 50b, 66

PRC UNIT: Pathobiology & Immun

INVES1: Boudinot, F. Douglas
DEGREE1: Ph.D.
DEPT1: Pharmacology
STAFF1: O

INVES2: Schinazi, Raymond F.
DEGREE2: Ph.D.
DEPT2: Pediatrics
STAFF2: O

INVES3: Gallo, J.M.
DEGREE3: Ph.D.
DEPT3: Pharmacology
STAFF3: O

INVES4: McClure, Harold M.
DEGREE4: D.V.M.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

INVES5: Anderson, Daniel C.
DEGREE5: D.V.M.
DEPT5: Pathobiology and Immunobiology
STAFF5: C

INVES6: Chu, C.K.
DEGREE6: Ph.D.
DEPT6: Pharmacology
STAFF6: O

NON-HOST INSTITUTION: College of Pharmacy, University of Georgia (FDB, JMG, CKC).

SPECIES1: Macaca mulatta
NUM1: 6

ABSTRACT: The objective of this study was to characterize and compare the pharmacokinetics and bioavailability of AZddU and AZT in rhesus monkeys. In separate studies, the experimental animals were administered either AZddU or AZT as follows: 60 mg/kg intravenously, 60 mg/kg orally, 200 mg/kg orally and 33 mg/kg subcutaneously. Serial blood samples were collected during the first 24 hours for drug level determinations. Cerebrospinal fluid and urine samples were taken 1 hour after drug administration for drug level determinations. Drug levels were assayed by HPLC.

After AZddU administration, total clearance averaged 0.91±0.05 L/h/kg and volume of distribution was 0.89±0.14 L/kg. After AZT administration, total clearance and volume of distribution were 1.57 L/h/kg and 1.07 L/kg, respectively. Oral absorption of AZddU and AZT was virtually complete ($F>0.90$) after 60 mg/kg, however, bioavailability of both nucleosides was markedly lower ($F<0.50$) after 200 mg/kg. Both nucleosides appeared to be well absorbed after subcutaneous administration. Both AZddU and AZT penetrate the cerebrospinal fluid with CSF:serum concentration ratios ranging between 0.05-0.25 one hour after drug administration. The similar pharmacokinetic characteristics and lower toxicity of AZddU compared to AZT suggest that clinical trials of AZddU are warranted.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Pharmacokinetics of FDT, D4T and AZddMeC in Monkeys

AXISI: 1a, 7b

AXIS II: 31, 50a, 50b, 66

PRC UNIT: Pathobiology & Immun

INVES1: Boudinot, F. Douglas
DEGREE1: Ph.D.
DEPT1: Pharmacology
STAFF1: O

INVES2: Schinazi, Raymond F.
DEGREE2: Ph.D.
DEPT2: Pediatrics
STAFF2: O

INVES3: Doshi, K.J.
DEGREE3: Ph.D.
DEPT3: Pharmacology
STAFF3: O

INVES4: McClure, Harold M.
DEGREE4: D.V.M.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

INVES5: Qin, Y.X.
DEGREE5: Ph.D.
DEPT5: Pharmacology
STAFF5: O

INVES6: Chu, C.K.
DEGREE6: Ph.D.
DEPT6: Pharmacology
STAFF6: O

NON-HOST INSTITUTION: College of Pharmacy, University of Georgia (FDB, KJD, YXQ, CKC).

SPECIES1: Macaca mulatta
NUM1: 9

ABSTRACT: The objective of this study was to characterize the pharmacokinetics and bioavailability of FDT, D4T and AZddMeC in rhesus monkeys. In separate studies, the experimental animals were administered 60 mg/kg of FDT, D4T or AZddMeC intravenously or orally, or 33.3 mg/kg of FDT or D4T subcutaneously. Serial blood samples were subsequently collected during the first 24 hours for drug level determinations. Cerebrospinal fluid (CSF) and urine samples were collected one hour after dosing for drug level determinations. Drug levels were assayed by HPLC.

After FDT administration, total clearance averaged 0.88±0.11 L/h/kg and volume distribution was 0.90±0.05 L/kg. After D4T administration, clearance and volume of distribution were 0.69±0.15 L/h/kg and 1.03±0.08 L/kg, respectively. Following AZddMeC administration, clearance was 2.19±0.12 L/h/kg and volume of distribution was 1.20±0.53 L/h/kg. Oral bioavailability of FDT, D4T and AZddMeC was incomplete, averaging 0.58±0.37, 0.42±0.15 and 0.21±0.08, respectively. A similar extent of absorption was seen after subcutaneous administration of FDT and D4T. FDT and D4T penetrate the cerebrospinal fluid, with CSF:serum concentration ratios ranging between 0.09-0.18 one hour after drug administration. AZddMeC did not penetrate the cerebrospinal fluid, however, a major metabolite did. These studies show that FDT, D4T and AZddMeC exhibit similar disposition characteristics.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Induction of Plasmodium Infections to Support Malaria Vaccine Studies

AXIS I: 1a, 3, 4, 7c, 17

AXIS II: 64, 66

PRC UNIT: Pathobiology & Immunology

INVES1: Collins, William E.
DEGREE1: Ph.D.
DEPT1: Pathobiology & Immunology
STAFF1: O

INVES2: McClure, Harold M.
DEGREE2: D.V.M.
DEPT2: Pathobiology & Immunology
STAFF2: C

SPECIES1: Pan troglodytes
NUM1: 6

NON-HOST INSTITUTION: Centers for Disease Control

ABSTRACT: Animals are infected with malarial parasites to obtain blood-stage parasites 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 tests, (5) infection of mosquitoes through membrane feeding to produce sporozoites for (a) genetic engineering studies, (b) production of monoclonal antibodies, and (c) to infect Aotus and Saimiri monkeys and to test the efficacy of experimental vaccines, and (6) production of immune sera. The following parasites and animals were inoculated: Plasmodium ovale - BRENT (C-415), MARY (C-202); Plasmodium vivax - MORT (C-423), JEANIE (C-494), HEPPIE (C-400); Plasmodium malariae - TEPPIE (C-384), JEANIE (C-494). We will continue these studies in support of the development of vaccines for human malarias.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: AIDS and Opiates: A Monkey Model

AXIS I: 1a, 2, 4, 7b, 17, 19

AXIS II: 31, 36, 50b, 64, 66, 77

PRC UNIT: Pathobiology and Immun

INVEST1: Donahoe, Robert M.
DEGREE1: Ph.D.
DEPT1: Psychiatry
STAFF1: O

INVES2: McClure, Harold M.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVES3: Byrd, Larry D.
DEGREE3: Ph.D.
DEPT3: Behavioral Biology
STAFF3: C

INVES4: Fultz, Patricia
DEGREE4: Ph.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

INVES5: Ansari, Aftab A.
DEGREE5: Ph.D.
DEPT4: Pathology
STAFF5: C

SPECIES1: Macaca mulatta
NUM1: 22

NON-HOST INSTITUTION: Georgia Mental Health Institute (RMD)

ABSTRACT: Intravenous drug addiction remains a serious threat for the spread of AIDS. There is certain knowledge that transmission of HIV, the viral cause of AIDS, by intravenous drug abusers relates to their needle-sharing habits, but there is also indirect evidence to suggest that the immunomodulatory properties of addicting drugs may be material to the outcome of HIV infection. This project is aimed at testing the latter possibility using SIVsmm-M9, a strain of simian immunodeficiency virus that induces AIDS-like symptoms. A group of 6 monkeys (Macaca mulatta) have been infected with SIVsmm-M9 for nearly 2 years during which time they also have been kept opiate-dependent. Evidence from study of these animals suggests that the opiate-dependence has not altered the course of viral infection in terms of onset of AIDS-like pathology. However, it was observed that brief withdrawal of opiates (2 days) from these animals exacerbated infection with SIVsmm. This suggests that the physiological changes of withdrawal in HIV-infected, human, heroin addicts

could, indeed, exacerbate development of AIDS since street addicts are frequently subject to withdrawal from opiates. Results from nearly two years of study of a larger group of opiate-dependent (10) and control monkeys (10) that have not yet been infected with SIVsmm confirmed that withdrawal from opiates does cause immune disturbances. In fact, the preliminary data collected so far indicate that the immune effects of opiates are mediated through their central influence over the entire neuroimmune network which is probably true of all behaviorally active substances with immunomodifying properties. Experiments are continuing to complete documentation of the role of opiates and withdrawal from opiates in activation of latent SIVsmm infection and alteration of immune status in monkeys dependent on morphine.

P51RR00165-29 1/1/89 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Characterization of Onchocerca Antigens and Animal Model Development

AXIS I: 1a, 7c, 14, 17

AXIS II: 39, 64, 66, 77

PRC UNIT: Pathobiology & Immun

IVEST1: Eberhard, Mark L.
DEGREE1: Ph.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: 0

INVES2: Tsang, Victor C.W.
DEGREE2: Ph.D.
DEPT2: Pathobiology & Immunobiology
STAFF2: 0

INVES3: McClure, Harold M.
DEGREE3: D.V.M.
DEPT3: Pathobiology & Immunobiology
STAFF3: C

INVES4: Zea Flores, Guillermo
DEGREE4: M.D.
DEPT4:
STAFF4: 0

SPECIES1: Pan troglodytes
NUM1: 3

SPECIES2: Cercocebus atys
NUM2: 3

SPECIES3: Erythrocebus patas
NUM#: 7

NON-HOST INSTITUTION: Centers for Disease Control

ABSTRACT: This study, which terminated this year, had as its main goal to evaluate the response of primates infected with O. volvulus to the responses detected in humans residing in endemic areas. Although chimpanzees were the primary primate species because of their known susceptibility to the parasite, other primates were studied as well. One chimpanzee, which became microfilaria positive 21 months postinoculation, developed recognition of two low molecular weight antigens (22 & 14 KD) at 9.5 and 13 months, respectively. Two mangabey monkeys also developed recognition of these antigens, but in addition also recognized one or two other low molecular weight antigens. One of these, a 20 KD antigen, was recognized by both animals at 3.5 and 5 months postinoculation. One mangabey went on to develop a patent infection first detectable at 17 months postinoculation. Comparison to human profiles provided several very interesting and potentially useful

discoveries. First, through the longitudinal evaluation of experimental infections, we now have an understanding of when in the course of infection these different antigen bands are first recognized, and some idea of what they may be in response to. Several of the recognized antigens are candidates for development in diagnostic tests as markers of early infection. Second, and possibly more important, the recognition in mangabey monkeys of an antigen band (20 KD) also recognized in "immune" individuals may open the door for understanding resistance and development of potential vaccines.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Primates as Host for Onchocerca volvulus

AXIS I: 1a, 7c, 14, 17

AXIS II: 64, 66, 77

PRC UNIT: Pathobiology & Immun

INVES1: Eberhard, Mark L.
DEGREE1: Ph.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: O

SPECIES1: Pan troglodytes
NUM1: 7

Species2: Cercocebus atys
NUM2: 8

NON-HOST INSTITUTION: Centers for Disease Control

ABSTRACT: The purpose of this study is to determine what minimum dose of O. volvulus infective larvae are necessary to consistently establish a patent infection in chimpanzees, and to more fully evaluate mangabey monkeys as a primate model for study of this infection. The availability of both parasite material and primates are limited, consequently, the need to be able to consistently establish infection is crucial before further experimental studies, such as candidate vaccines trials, can be conducted. Groups of chimpanzees inoculated with graded doses of L3 (200, 300, or 400) will be monitored parasitologically and immunologically over the course of the infection to determine which inocula size results in consistent, predictable infections. The search for a primate, other than chimpanzees, which could serve as hosts for O. volvulus was rewarded recently with our success in establishing the parasite in mangabey monkeys. Because the number of animals initially studied was small, follow-up studies aimed at determining relative susceptibility, range of responses, etc. are currently underway in a larger number of animals. It is especially interesting that preliminary studies indicate that immunological responses in mangabey monkeys more closely mimic those detected in human populations exposed to and infected with O. volvulus. The recognition of a similar antigen in mangabeys and putatively "immune" people may play a key role in developing a candidate vaccine as well as understanding the nature of resistance versus infection.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Isolation of a Lentivirus from Sykes Monkeys

AXIS I: 1a, 7b

AXIS II: 31, 66, 77

PRC UNIT: Pathobiology & Immun

INVES1: Emau, Peter
DEGREE1: Ph.D.
DEPT1: Virology
STAFF1: O

INVES2: McClure, Harold M.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVES3: Fultz, Patricia N.
DEGREE3: Ph.D.
DEPT3: Pathobiology and Immunobiology
STAFF3: C

INVES4: Isahakia, Mohamed
DEGREE4: Ph.D.
DEPT4: Director
STAFF4: O

SPECIES1: Cercopithecus mitis
NUM1: 9

NON-HOST INSTITUTION: Institute of Primate Research, Kenya (PE, MI)

ABSTRACT: Initial serologic surveys of various nonhuman primate species in Kenya revealed a high prevalence (62%) of antibodies to SIV in Sykes monkeys (Cercopithecus mitis). Six seropositive and 3 seronegative Sykes monkeys were subsequently shipped from the IPR, Kenya, to the Yerkes Center for use in virus isolation attempts. A lentivirus was subsequently isolated from 5 of 6 seropositive Sykes monkeys and efforts are currently underway to characterize the in vitro properties of this isolate. The Sykes monkey isolate, designated SIVsyk, will grow in CEMx174 and SupT-1 cells, but will not grow in U937, CEM or Molt4 clone 8 cell lines. SIVsyk also does not appear to replicate in PBMC from rhesus or pig-tailed macaques, mangabeys, chimpanzees or humans. Additional in vitro characterization studies, including cloning and sequencing, are in progress and the pathogenicity of this isolate in rhesus and pig-tailed macaques will be evaluated.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Isolation of a Lentivirus from Stump-tailed Macaques

AXIS I: 1a, 7b, 19

AXIS II: 31, 66

PRC UNIT: Pathobiology and Immun

INVEST1: Fultz, Patricia N.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

SPECIES1: Macaca arctoides
NUM1: 1

ABSTRACT: Peripheral blood mononuclear cells (PBMC) from a stump-tailed macaque found to be seropositive for antibodies to SIV in 1986 were obtained and cocultivated with PBMC from a normal human donor. A retrovirus, with Mg^{+2}-dependent reverse transcriptase activity and morphologically resembling a lentivirus, was isolated and characterized for biologic properties in vitro. The new virus, designated SIVstm, was compared to SIVsmm, HIV-1 and HIV-2 with respect to apparent molecular weights and cross-reactive epitopes of virus-specific proteins.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Effect of CD4H23 on Virus Load in SIVsmm-infected Macaques

AXIS I: 1a, 2, 7b, 17, 19

AXIS II: 31, 39, 50b, 66

PRC UNIT: Pathobiology and Immun

INVEST1: Fultz, Patricia N.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVEST2: Anderson, Daniel C.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVEST3: Gregersen, Jens P.
DEGREE3: Ph.D.
DEPT3:
STAFF3: O

INVEST4: Hilfenhaus, Joachim
DEGREE4: Ph.D.
DEPT4:
STAFF4: O

SPECIES1: Macaca mulatta
NUM1: 4

NON-HOST INSTITUTION: Behringwerke (JPG, JH)

ABSTRACT: To determine the therapeutic efficacy of a CD4-IgG1 fusion protein (CD4H23) in SIVsmm-infected macaques, animals persistently infected with the SIVsmm9 isolate were given intravenous injections of CD4H23 at doses of 1.5 mg/kg or 3 mg/kg. Animals were monitored for clinical evidence of disease, for changes in weight or hematologic parameters and for virus load. Two symptomatic animals with decreased levels of $CD4^+$ lymphocytes that had experienced weight loss were treated every other day with 1.5 mg CD4H23/kg for 20 days. One animal that had less than 200 $CD4^+$ cells and had lost 0.5 kg (12% body weight) over the preceding 6 months developed progressive AIDS-like disease and died during the series of inoculations. Although the second animal experienced a twofold increase in number of $CD4^+$ cells (from 450 to 910) during the 3 months following the start of treatment and began to gain weight, no change in virus load was detected. The second phase of the study, in which two SIV-infected macaques received 3 mg CD4H23/kg every other day for 30 days, has just been completed, and results are currently being evaluated. None of the surviving animals experienced any obvious ill effects from the drug or the dosage regimen.

P5IRR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Role of Antibodies to Histone H2B in SIV-induced Disease

AXIS I: 1a, 2, 7b

AXIS II: 31, 64, 66

PRC UNIT: Pathobiology and Immun

INVEST1: Fultz, Patricia N.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVEST2: Stricker, Raphael B.
DEGREE2: Ph.D.
DEPT2:
STAFF2: O

INVEST3: Anderson Daniel C.
DEGREE3: D.V.M.
DEPT3: Pathobiology and Immunobiology
STAFF3: C

SPECIES1: Cercocebus atys
NUM1: 8

SPECIES2: Macaca mulatta
NUM2: 2

NON-HOST INSTITUTION: University of California, San Francisco (RBS)

ABSTRACT: The presence of serum antibodies that recognized histone H2B previously were found to correlate with clinical disease in HIV-infected people and in SIV- and SRV-infected macaques. To determine whether immunization of SIVsmm-infected monkeys with histone H2B would induce antibodies to the protein and facilitate disease progression or induce disease in asymptomatic SIV-infected macaques or mangabeys, respectively, animals were immunized by intradermal injection of histone H2B-RNA complexes in incomplete Freund's adjuvant on days 0, 7 and 14. On day 21, the animals were given an intravenous injection of H2B-RNA complexes; all inocula contained 500 ug histone. Experimental groups of two animals each were: (1) uninfected mangabeys immunized with H2B; (2) uninfected mangabeys immunized with H2B and inoculated with SIVsmm9 iv.; (3) uninfected mangabeys inoculated with SIVsmm9; (4) SIV-infected mangabeys immunized with H2B; and (5) SIV-infected rhesus macaques immunized with H2B. All immunized animals except those in group 4 produced detectable antibodies to histone H2B within 1 month of the first injection. The four uninfected mangabeys became readily infected with SIVsmm9. After 9 months of follow-up, none of the mangabeys nor the two SIVsmm9-infected macaques have developed clinical signs of disease or hematologic abnormalities. These data suggest that the presence of antibodies to histone H2B in AIDS patients and diseased macaques probably are a consequence of enhanced viral replication that occurs in late stages of disease and are unlikely to contribute significantly to disease progression.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Effect of a Somatostatin Analogue on Acute Infection by SIVsmmPBj14

AXIS I: 1a, 2, 7b, 16c

AXIS II: 31, 50, 66

PRC UNIT: Pathobiology and Immun

INVEST1: Fultz, Patricia N.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVEST2: Montagnier, Luc
DEGREE2: M.D.
DEPT2:
STAFF2: O

INVEST3: Anderson, Daniel C.
DEGREE3: D.V.M.
DEPT3: Pathobiology and Immunobiology
STAFF3: C

INVEST4: McClure, Harold M.
DEGREE4: D.V.M.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

SPECIES1: Macaca nemestrina
NUM1: 6

NON-HOST INSTITUTION: Institut Pasteur (LM)

ABSTRACT: Somatostatin is a neuropeptide of 14 amino acids that is secreted from the hypothalamus and inhibits release of somatotropin from the anterior pituitary. Although somatostatin has little therapeutic value, some analogues, including RC-160 (an octapeptide), are much more potent than somatostatin at inhibiting growth hormone release and, in addition, are therapeutic for secretory diarrhea. SMS 201-995, an analogue related to RC-160, has been used successfully to treat AIDS patients with chronic diarrhea. Because severe diarrhea is the first sign of clinical disease in macaques infected with SIVsmmPBj14 and these animals apparently die of dehydration, we tested RC-160 to determine whether it could alleviate the severe diarrhea associated with acute SIVsmmPBj14 infection and, if so, whether prevention of diarrhea was accompanied by survival and decreased viral replication. Six pig-tailed macaques were inoculated intravenously with 10^3 $TCID_{100}$ of SIVsmmPBj14, a dose that previously was shown to induce diarrhea by day 7 post-inoculation (PI). Four macaques received 200 ug RC-160 twice daily beginning on day 5, while two animals served as controls and received no drug. The animals were monitored daily for signs of illness. RC-160 had no apparent influence either on development of diarrhea or virus load since all animals developed severe bloody diarrhea, characteristic of SIVsmmPBj14 infection, and were sacrificed by day 11 PI due to deteriorating clinical condition.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Pathogenicity of Molecular Clones of SIVsmmPBj14

AXIS I: 1a, 7b, 17, 19

AXIS II: 31, 59, 66

PRC UNIT: Pathobiology and Immun

INVEST1: Fultz, Patricia N.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVEST2: Anderson, Daniel C.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVEST3: Mullins, James I.
DEGREE3: Ph.D.
DEPT3:
STAFF3: O

INVEST4: Dewhurst, Steven
DEGREE4: Ph.D.
DEPT4:
STAFF4: O

SPECIES1: Macaca nemestrina
NUM1: 6

SPECIES2: Macaca mulatta
NUM2: 2

NON-HOST INSTITUTION: Stanford University (JIM)
Harvard University (SD)

ABSTRACT: Infectious molecular clones of SIVsmmPBj14, a variant of SIVsmm that induces an acute disease syndrome and death within 2 weeks in pig-tailed macaques and mangabey monkeys, were generated by PCR amplification and cloning and were tested for pathogenicity in pig-tailed and rhesus macaques. Of three molecularly cloned viruses, all induced acute diarrhea in pig-tailed macaques within 1 week following IV inoculation of two animals each with 10^4 to 10^5 $TCID_{50}$. Three (including both animals that received the smmPBj-4.41 clone) of the pig-tailed macaques died in 8 days of disease that was indistinguishable clinically and histologically from that induced by the uncloned smmPBj14 virus pool. Two additional animals died on days 49 and 55 post-infection (PI), while one animal has survived 6 months. Because rhesus macaques appear less susceptible to the lethal effects of smmPBj14 than pig-tailed macaques, two rhesus were inoculated with 10^5 $TCID_{50}$ of smmPBj-4.41. In contrast to death within 6 days in the two pig-tailed macaques, neither rhesus developed diarrhea or other signs of disease and appear normal at 4 months PI. The availability of pathogenic molecular clones will provide a valuable tool for localizing pathogenic determinants of lymphotropic lentiviruses to specific

sites in the viral genome, which ultimately may be of benefit in devising effective therapies for treatment of AIDS.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Protective Efficacy in Chimpanzees of Candidate HIV Vaccines

AXIS I: 1a, 2, 7b, 19

AXIS II: 31, 39, 66, 91

PRC UNIT: Pathobiology and Immun

INVEST1: Fultz, Patricia N.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVEST2: Girard, Marc
DEGREE2: Ph.D., D.V.M.
DEPT2:
STAFF2: O

INVEST3: Muchmore, Elizabeth
DEGREE3: M.D.
DEPT3:
STAFF3: O

SPECIES1: Pan troglodytes (not Yerkes animals)
NUM1: 2

NON-HOST INSTITUTION: Pasteur Vaccins/Institut Pasteur (MG)
New York University, LEMSIP (EM)

ABSTRACT: In efforts to develop a vaccine that protects against infection by HIV-1, chimpanzees have been immunized with various HIV-1 antigen preparations. Two chimpanzees were immunized by different regimens. One animal received four injections of whole inactivated HIV formulated with the Syntex adjuvant (SAF) over 6 months, followed by booster injections with purified gp160 env in an effort to increase neutralizing antibody titers. When this failed, the chimpanzee was boosted subsequently with a 24-mer oligopeptide representing the V3 region of gp120, which is the major neutralizing epitope, cross-linked to KLH. Following three injections of the peptide with SAF, sustained neutralizing titers were obtained. A second chimpanzee, primed with a recombinant vaccinia virus expressing gp160 env, followed by immunization with purified recombinant gp160, p18 gag, p27 nef and p23 vif in SAF, also was boosted with the V3 oligopeptide-KLH conjugate. Five weeks after the last injection of V3 peptide, the two chimpanzees were challenged with 100 $TCID_{50}$ of the HTLV-111b isolate of HIV-1. Through 6 months of follow-up, both animals have had decreases in total HIV-specific antibodies, and HIV has not been recovered from PBMC or lymph node tissue of either animal at any time post-challenge. Because a naive chimpanzee inoculated in parallel with an equivalent dose of virus readily became infected, as evidenced by seroconversion and isolation of virus from PBMC, these data strongly suggest that the two vaccinated chimpanzees were protected against HIV infection.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Evaluation of Small Vessel Prostheses

AXIS I: 1a, 3, 13, 17

AXIS II: 48, 50, 52, 86

PRC UNIT: Pathobiology and Immuno

INVES1: Hanson, Stephen R.
DEGREE1: Ph.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: 0

SPECIES1: Papio Anubis
NUM1: 12

ABSTRACT: Since relocating to Emory University on July 1, 1989, a major study has been initiated to test the hypothesis that chronic inhibition of angiotensin converting enzyme by an oral agent (cilazapril) decreases the intimal proliferative response induced by mechanical arterial injury in baboons. In these studies we are measuring vascular healing, intimal thickening (intimal hyperplasia), and endothelial cell integrity after 1) surgical placement of aorto-iliac vascular grafts, 2) carotid artery endarterectomy, and 3) balloon catheter injury of the superficial femoral artery. Findings in five control animals will be compared with results obtained in baboons given oral daily cilazapril beginning five days prior to arterial injury and maintained through the period of study (3 months). All animals have now been entered into the study.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Platelet-Adhesive Glycoprotein Interactions In Vivo

AXIS I: 1a, 1d, 2, 13, 17

AXIS II: 50, 63

PRC UNIT: Pathobiology and Immun

INVES1: Hanson, Stephen R.
DEGREE1: Ph.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: 0

SPECIES1: Papio Anubis
NUM1: 8

ABSTRACT: We have also continued our studies with specific anti-thrombins for anti-thrombotic therapy (hiruden, anti-thrombin peptides) as well as with agents which specifically inhibit platelet function (synthetic peptides, monoclonal antibodies). These studies have shown that thrombus formation induced by thrombogenic stimuli (Dacron vascular graft) placed acutely into femoral arteriovenous shunts in baboons may be abolished by such therapy given prophylactically, and that the growth of established thrombus may be permanently interrupted by short-term intravenous or local administration of thrombin inhibitors. These studies implicate thrombin in both the initiation and later development of thrombosis, and suggest a potent strategy for intervention.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Endarterectomy:Prevention of Thrombosis and Restenosis

AXIS I: 1a, 13, 17

AXIS II: 50b, 63g,h, 86

PRC UNIT: Pathobiology and Immun

INVES1: Harker, Laurence A.
DEGREE1: M.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: O

INVES2: Kelly, Andrew
DEGREE1: D.V.M.
DEPT2: Pathobiology & Immunobiology
STAFF2: C

SPECIES1: Papio Anubis
NUM1: 10

ABSTRACT: To evaluate thrombus formation by metallic mesh endovascular stents 111In-platelet deposition has been measured by gamma camera imaging and compared for two different endoprostheses placed inside 3 mm expanded polytetrafluorethylene grafts incorporated into chronic arteriovenous silicone rubber shunts in baboons. Platelet deposition was substantial on stented grafts compared with untreated grafts ($p = 0.003$) and was unchanged by systemic heparin therapy ($p > 0.5$). In contrast, infusion of the synthetic antithrombin, D-phenylalanyl-L-prolyl-L-arginyl-chloromethyl ketone (D-FPRCH2Cl) interrupted platelet accumulation by stents. Thus, stainless steel endovascular stents induce platelet-dependent, heparin-resistant thrombosis under high flow conditions that is abolished by systemic infusion of D-FPRCH2Cl.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Effect of Cilazapril on Intimal Hyperplasia in Baboons

AXIS I: 1a, 2, 13, 17

AXIS II: 48, 50b, 86

PRC UNIT: Pathobiology and Immun

INVES1: Harker, Laurence A.
DEGREE1: M.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: 0

INVES2: Hanson, Stephen R
DEGREE1: Ph.D.
DEPT2: Pathobiology & Immunobiology
STAFF2: 0

SPECIES1: Papio Anubis
NUM1: 10

ABSTRACT: The overall purpose of this proposal which began in late 1989 was to test the hypothesis that chronic inhibition of angiotensin converting enzyme by oral cilazapril decreases the intimal proliferative response induced by mechanical arterial injury in baboons. Results are currently being analyzed.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Antithrombotic Therapy in Experimental Thrombosis

AXIS I: 1a, 2, 13, 17

AXIS II: 39, 48, 50b, 86

PRC UNIT: Pathobiology and Immun

INVES1: Harker, Laurence A.
DEGREE1: M.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: O

INVES2: Kelly, Andrew
DEGREE1: D.V.M.
DEPT2: Pathobiology & Immunobiology
STAFF2: C

SPECIES1: Papio Anubis
NUM1: 4

ABSTRACT: We studied the effects of anti-vWF MoA (BB3 BD5; inhibitor of ristocetin-induced vWF-dependent platelet aggregation), and anti GPIIb/IIIa MoA (CP8; inhibitor of adhesive protein interaction with GPIIb/IIIa) in baboons. Thrombus formation was assessed by measuring 111In-platelet accumulation and 125Ifibrinogen (F) incorporation on collagen-coated tubing segments (CS) inserted into arteriovenous shunts and exposed to blood for 40 min at high (750-1,000 sec-1) and low (100 sec-1) shear rates. Both MoAs markedly prolonged the bleeding time from 4.0 ± 0.3 min to > 26 ± 4 min. However, CP8 was markedly more potent in preventing P and F deposition on CS at both shear rates (PD and FD in Table, mean ± SE; *p<0.05).

		Control	BB3 BD5	CP8
High	:PD(x10-8)	24.2 ± 3.8	13.7 ± 3.0	1.6 ± 0.9*
	FD(mg)	0.5 ± 0.1	0.4 ± 0.1	0.1 ± 0.1*
Low	:PD(x10-8)	17.7 ± 2.6	13.3 ± 1.4	2.1 ± 0.6*
	FD(mg)	0.6 ± 0.1	0.5 ± 0.1	0.3 ± 0.1*

Thus, in this model, inhibition of vWF-dependent platelet recruitment produces equivalent antihemostatic effects, but has lesser antithrombotic efficacy than inhibition of GPIIb/IIIa-dependent platelet recruitment.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Omega 3 Fatty Acids, Thrombosis & Vascular Healing

AXIS I: 1a, 2, 13, 17

AXIS II: 48, 50b, 74F, 78

PRC UNIT: Pathobiology and Immun

INVES1: Harker, Laurence A.
DEGREE1: M.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: O

INVES2: Kelly, Andrew
DEGREE1: D.V.M.
DEPT2: Pathobiology & Immunobiology
STAFF2: C

SPECIES1: Papio Anubis
NUM1: 10

ABSTRACT: To measure the effects of omega-3 FA on thrombosis and hemostasis, dietary supplementation to 8 baboons was administered (1 Gm EPA and 0.5 Gm DHA/kg per day) for 12 weeks. This regimen produced marked increases in omega-3 FA content in plasma, platelets, monocytes and arteries, a modest prolongation of template bleeding times (9.6 ± 1.3 min vs 4.0 ± 0.9; $p<0.01$), and decreased sensitivity to collagen-induced platelet aggregation (ED50 8.7 ± 4.1 μg/mL vs 5.1 ± 2.9; $p<0.05$). Tissue factor expression by monocytes after endotoxin stimulation was impaired (1.7 ± 0.14 units/1000 cells vs 6.5 ± 1.2; $p<0.005$). The deposition of platelets onto segments of Dacron vascular graft and endarterectomized homologous normal aorta was reduced when measured as accumulation of ^{111}In-labeled platelets using gamma camera imaging of these segments inserted as extension pieces in exteriorized femoral arterio-venous shunts (14.4 ± 4.4 platelets x 109 vs 17.5 ± 1.9; $p<0.01$; and 2.1 ± 0.36 vs 4.0 ± 2.2; $p<0.01$, respectively). Platelet deposition was more profoundly reduced by omega-3 FA at sites of carotid endarterectomy (1.07 ± 0.36 platelets x 109 vs 4.0 ± 2.2; $p<0.001$). Concordantly, treated endarterectomized aortic segments tested in normal animals showed a marked decrease in platelet deposition (1.5 ± 0.29 platelets x 109 vs 4.4 ± 0.90). We conclude that dietary omega-3 FA interrupts arterial thrombus formation by decreasing the thrombogenicity of vascular wall cells and blood monocytes while producing lesser effects on hemostatic function.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Pathogenicity of Group 2 Aerotolerant Campylobacter

AXIS I: 1a, 7a

AXIS II: 66, 77

PRC UNIT: Pathobiology & Immun

INVES1: Klumpp, Sherry A.
DEGREE1: D.V.M.
DEPT1: Pathobiology and Immunobiology
STAFF1: O

INVES2: Choi, Gwen
DEGREE2: D.V.M.
DEPT2: Veterinary Medicine
STAFF2: O

INVES3: Kiehlbauch, Julie A.
DEGREE3: Ph.D.
DEPT3: Microbiology
STAFF3: O

INVES4: McClure, Harold M.
DEGREE4: D.V.M.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

SPECIES1: Macaca mulatta
NUM1: 8

SPECIES2: Macaca arctoides
NUM2: 1

SPECIES3: Macaca nemestrina
NUM3: 1

SPECIES4: Macaca fascicularis
NUM4: 1

NON-HOST INSTITUTION: Centers for Disease Control (JAK)

ABSTRACT: A new species of Campylobacter, designated group 2 aerotolerant Campylobacter (Grp2AC) but as yet unnamed, has been identified recently. This species is distinct from Campylobacter jejuni and Campylobacter coli. Although organisms belonging to the Grp2AC have been phenotypically identified as Campylobacter cryaerophilia, less than 30% homology by DNA hybridization has shown the Grp2AC to be a separate species. Unlike the better known species of Campylobacter which grow on either Campy-BAP and Campy-CVA plates at 42°C, the Grp2AC generally is not capable of growing at 42°C or on Campy-BAP.

The pathogenicity of Grp2AC is currently unknown. A total of 49 isolates have been obtained, to date, from human patients (31 from the U.S., 15 from Thailand, 2 from Canada and 1 from Australia). The isolates from Thailand

were obtained from children with diarrhea. Clinical histories available for 21 of the remaining 34 isolates indicated that 3 patients had appendicitis, 3 had bacteremias and the remaining 15 had diarrhea. Ten of the 15 patients with diarrhea had persistent diarrhea lasting for more than one month.

Recognition that a June 1986 isolate from a rhesus monkey with diarrhea at the Yerkes Center belonged to the newly defined Grp2AC prompted the culturing of 308 routine enteric specimens from primate cases of diarrhea for Grp2AC. This Campylobacter species was isolated from 10 additional nonhuman primates; all of the nonhuman primates were macaques and included 8 rhesus monkeys and 1 each of stumptail macaque, pig-tailed macaque and a cynomolgus macaque. These monkeys ranged in age from 2 months to 17 years, with a mean of 7.5 years. Biopsy or necropsy specimens were available for histologic examination from 6 of the 8 rhesus monkeys from which Grp2AC was cultured; colitis or typhlitis was diagnosed in all 6 animals. However, of these 6 macaques, 3 had a concomitant infection with either Campylobacter jejuni or Campylobacter coli. Plans are underway to conduct experimental infection studies to more precisely define the pathogenicity of this group of organisms for nonhuman primates.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Intravesical Injection of Teflon for Vesicoureteral Reflux

AXIS I: 1a, 27

AXIS II: 48, 62, 86

PRC UNIT: Pathobiology and Immun

INVES1: Malizia, Anthony A.
DEGREE1: M.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: O

INVES2: Woodard, John R.
DEGREE2: M.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: O

INVES3: Newton, Nancy E.
DEGREE3: M.D., Ph.D.
DEPT3: Pathobiology and Immunobiology
STAFF3: O

INVES4: Anderson, Daniel C.
DEGREE4: D.V.M.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

INVES5: Wyly, J. Bradley
DEGREE5: M.D.
DEPT5: Radiology
STAFF5: O

SPECIES1: Macaca mulatta
NUM1: 5

SPECIES2: Macaca nemestrina
NUM2: 5

ABSTRACT: Intravesical/subureteric injection of Polytef paste has been used to treat vesicoureteral reflux in over 1,000 children worldwide. This treatment has been used without FDA approval and only limited animal studies have been performed. Our studies in non-refluxing monkeys demonstrates not only distant migration of Polytef particles from the injection sites, but also the development of huge foreign body granulomas at all intravesical injection sites. We have also demonstrated that these granulomas can be clearly imaged radiologically. CT scanning and magnetic resonance imaging at intervals up to three years have shown a six fold increase in the average volume of the intravesical granulomas. It appears, however, that their growth does stabilize at 18 to 24 months. We have also found that ultrasound (the most common method used to follow human children) poorly defines granuloma size. Finally, at three years post injection, neovascularity has been identified within intravesical granulomas.

We injected 0.4 cc (1/2 of human dosage) of Polytef paste transurethrally into the intravesical/subureteric space of ten monkeys. Five monkeys were sacrified at six months and two monkeys at 32 months. The injection sites, pelvic and par-aortic nodes, kidneys, liver, lungs, and brain of each animal were studied by standard and polarized light microscopy. Local and distant migration of Polytef particles from the injection site were confirmed in all animals. A voluminous local granulomatous response was found at all intravesical injection sites. In addition, at 32 months these granulomas have developed a neovascularity which allows for their growth. In three living monkeys, the granulomatous reaction has been followed radiologically by both CT scanning and magnetic resonance imaging, allowing documentation of change in size over time.

We belive that until the long-term effects in humans are known, Polytef paste should not be used in children with a normal life expectancy. Our work has been instrumental in stopping FDA approval for the use of this material in children, and to our knowledge we have the only long-term living animal model for continued study.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Improved Technique for Radical Prostate Surgery

AXIS I: 1a, 9, 23, 27

AXIS II: 62, 86

PRC UNIT: Pathobiology and Immun

INVES1: Malizia, Anthony A.
DEGREE1: M.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: 0

INVES2: Woodard, John R.
DEGREE2: M.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: 0

INVES3: Newton, Nancy E.
DEGREE3: M.D., Ph.D.
DEPT3: Pathobiology and Immunobiology
STAFF3: 0

INVES4: Anderson, Daniel C.
DEGREE4: D.V.M.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

INVES5: Wyly, J. Bradley
DEGREE5: M.D.
DEPT5: Radiology
STAFF5: 0

SPECIES1: Macaca mulatta
NUM1: 5

SPECIES2: Macaca nemestrina
NUM2: 5

ABSTRACT: From autopsy studies performed on the primates which received subureteric injection of Polytef, an additional project has arisen with direct human application. It was noted that the prostate gland in the monkey could be removed without disrupting the bladder neck and proximal prostatic urethra. This led to human autopsy studies which have confirmed the same results. Thus, from our primate work we had chanced upon an entirely new idea, the possibility of preserving the internal sphincter mechanism while performing radical prostate surgery.

From the human autopsy studies confirming the same result, we have subsequently applied the technique to human patients with excellent surgical results. The new technique preserves both the internal and external sphincters, enhancing postoperative urinary continence following radical prostate surgery by increasing functinal urethral length, maintaining the normal configuration of the bladder neck with its oblique and circular muscle

fibers, and by leaving undisturbed most of the external striated urethral sphincter. In the future, we hope to continue studying and advancing this technique in primates.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Study of Refractive Keratoplasty

AXIS I: 1a, 25b

AXIS II: 62, 86

PRC Unit: Pathobiology & Immun

INVES1: McCarey, Bernard E.
DEGREE1: Ph.D.
DEPT1: Ophthalmology
STAFF1: 0

SPECIES1: Macaca mulatta
NUM1: 20

ABSTRACT: Refractive keratoplasty is a classification of corneal techniques that alter the refractive power of the eye. Our laboratory has developed the use of hydrophilic polymer (hydrogel) lenticules surgically implanted to the mid-thickness of the cornea. The implants are referred to as hydrogel intracorneal lenses. Currently there are 19 human patients with hydrogel intracorneal lenses in a limited clinical trial study. Our laboratory is interested in exploring the possible alterations in the corneal physiology caused by the hydrogel implant. The specific aims of our studies are: first, the nutritional safety margin of the implant, and, second, the anatomical healing response to the implant. Ophthalmic surgical and examination techniques, as well as laboratory sciences of biochemistry, immunohistochemistry, anatomy, and biomechanics, are being utilized in these studies.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: AIDS Drug Development and Testing in the SIV Infected Macaque Model

AXIS I: 1a, 2, 7b

AXIS II: 31, 50b, 66, 77

PRC UNIT: Pathobiology & Immun

INVES1: McClure, Harold M.
DEGREE1: D.V.M.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVES2: Anderson, Daniel C.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVES3: Klumpp, Sherry A.
DEGREE3: D.V.M.
DEPT3: Pathobiology and Immunobiology
STAFF3: O

INVES4: Ansari, Aftab A.
DEGREE4: Ph.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

INVES5: Schinazi, Raymond
DEGREE5: Ph.D.
DEPT5: Pediatrics
STAFF5: O

SPECIES1: Macaca mulatta
NUM1: 25

ABSTRACT: The overall objective of these ongoing studies is to use the SIV-infected macaque model to determine the prophylactic or therapeutic efficacy of newly developed antiretroviral drugs. Prior to drug testing in SIV-infected animals, the macaque monkey is used for pharmacokinetic studies, following various drug doses and routes of administration.

A recently completed study was designed to determine whether antiretroviral drugs can prevent infection when animals are treated shortly before and for a short period of time after exposure to SIVsmm. In this study, 25 rhesus macaques were divided into 5 groups and treated with either CS-87, AZT, D4T, FDT or PBS (control group). All 25 animals were inoculated intravenously with 100 $TCID_{50}$ of SIVsmm 24 hours after drug treatment was initiated. The drugs were administered subcutaneously at a dose of 100 mg/kg/day, divided into three doses and administered at 8:00 a.m., 4:00 p.m. and 12:00 a.m. Drug treatment was initiated 24 hours prior to virus exposure and continued for 14 days after virus exposure. The experimental animals were monitored by daily observations, with physical examinations and body weights recorded prior to and at 2, 4, 6 and 8 weeks post-exposure. Blood was collected at the same intervals for CBCs, immunology, virology and serology. All animals except two

in the FDT treatment group had seroconverted by six weeks post-exposure and the other animals had seroconverted at 10 weeks post-exposure. This study indicated that none of the drugs tested were effective in preventing infection with SIVsmm, even when the drugs were administered up to 24 hours prior to virus exposure.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: SIVsmm Protects Against Infection with SIVsmmPBj

AXIS I: 1a, 7b

AXIS II: 31, 64, 66, 77, 91

PRC UNIT: Pathobiology and Immun

INVES1: McClure, Harold M.
DEGREE1: D.V.M.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVES2: Anderson, Daniel C.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVES3: Fultz, Patricia N.
DEGREE3: Ph.D.
DEPT3: Pathobiology and Immunobiology
STAFF3: C

INVES4: Ansari, Aftab A.
DEGREE4: Ph.D.
DEPT4: Pathology
STAFF4: C

SPECIES1: Macaca nemestrina
NUM1: 12

SPECIES2: Cercocebus atys
NUM2: 6

Abstract: Preliminary studies indicated that infection with SIVsmm in the mangabey provided protection to a subsequent challenge with SIVsmmPBj, an acutely lethal variant of SIVsmm. In these preliminary studies, 3 of 4 seronegative mangabeys developed acute clinical disease and died within 12 days of challenge with SIVsmmPBj, whereas seropositive mangabeys remained clinically normal following challenge with the PBj isolate. As a follow-up to these preliminary observation, studies were initiated to determine whether prior infection with SIVsmm provides any protection to a subsequent challenge with SIVsmmPBj in pig-tailed macaques. In this study, 9 pig-tailed macaques were infected with SIVsmm and subsequently challenged with SIVsmmPBj at 3 weeks, 3 months and 7 months following infection with SIVsmm. Three control pigtails (not SIVsmm infected) were challenged with SIVsmmPBj at the same time as the SIVsmm-infected macaques. Following the SIVsmmPBj challenge, all 3 control animals developed acute clinical disease and died within 12 days. However, none of the 9 SIVsmm-infected macaques developed any evidence of acute disease following the SIVsmm PBj challenge. One of these 9 macaques died 17 days following the PBj challenge (7.5 months following infection with SIVsmm). However, this animal did not have any clinical or pathologic evidence of acute disease associated with the PBj challenge. This animal had shown longstanding, severe immunosuppression, chronic diarrhea and weight loss

associated with the initial SIVsmm infection. This study clearly showed that prior infection with the less virulent strain of virus (SIVsmm) provides protection (100%) to a subsequent challenge with the acutely lethal strain (SIVsmmPBj) of virus. These findings have important implications with respect to efforts to develop retrovirus vaccines. Efforts are currently underway in our laboratory to evaluate the immune response in these animals in an attempt to identify specific responses that were protective. Efforts will also be made, utilizing PCR techniques, to determine if this protection prevented infection with the PBj isolate, or if infection occurred and only the clinical course of the disease was altered.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Serological Survey of Nonhuman Primates in Africa

AXIS I: 1a, 7b

AXIS II: 31, 64, 66, 77

PRC UNIT: Pathobiology and Immun

INVES1: McClure, Harold M.
DEGREE1: D.V.M.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVES2: Anderson, Daniel C.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVES3: Fultz, Patricia N.
DEGREE3: Ph.D.
DEPT3: Pathobiology and Immunobiology
STAFF3: C

INVES4: Ansari, Aftab A.
DEGREE4: Ph.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

INVES5: Isahakia, Mohamed
DEGREE5: Ph.D.
DEPT5: Director
STAFF5: O

SPECIES1: Cercopithecus mitis
NUM1: 87

SPECIES2: Cercopithecus aethiops
NUM2: 141

SPECIES3: Papio cynocephalus
NUM3: 136

NON-HOST INSTITUTION: Institute of Primate Research, Kenya (MI)

ABSTRACT: In ongoing studies, serological surveys are being conducted on serum samples provided from feral nonhuman primates (baboons, Sykes monkeys, African green monkeys) in Kenya. These samples are checked for antibodies to SIV, HIV and STLV-1. Analyses done to date show a high prevalence of antibodies to SIV in Sykes (62% seropositive) and African green monkeys (47% seropositive). A somewhat lower prevalence of antibodies to STLV-1 has been observed (28% of Sykes monkeys and 33% of African green monkeys). These observations in feral Sykes and African green monkeys are remarkably similar to seroprevalence rates detected in the Yerkes mangabey breeding colony, suggesting that at least in these three African species of nonhuman primates,

SIV infection may be essentially universal. Additional observations in our laboratory using the recently developed Pokeweed Mitogen Assay and PCR to evaluate "seronegative" mangabeys support this possibility.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Natural SIV and STLV-1 Infection in Sooty Mangabeys

AXIS I: 1a, 7b

AXIS II: 31, 56, 64, 66, 77

PRC UNIT: Pathobiology and Immun

INVES1: McClure, Harold M.
DEGREE1: D.V.M.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVES2: Anderson, Daniel C.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVES3: Ansari, Aftab A.
DEGREE3: Ph.D.
DEPT3: Pathobiology and Immunobiology
STAFF3: C

INVES4: Fultz, Patricia N.
DEGREE4: Ph.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

INVES5: Gordon, Thomas P.
DEGREE5: M.S.
DEPT5: Behavioral Neuroendocrinology
STAFF5: C

SPECIES1: Cercocebus atys
NUM1: 118

ABSTRACT: A T-lymphotropic lentivirus has been isolated from a high percentage of mangabeys in the Yerkes mangabey breeding colony. This virus, designated SIVsmm, is morphologically identical to HIV by electron microscopy; serologically related to HIV by enzyme immunoassay (EIA), Western blot and radioimmunoprecipitation; and is cytopathic for human $CD4^+$ cells in vitro. To date, 118 mangabeys in the Yerkes breeding colony have been tested (serology and virus culture) for SIVsmm infection and 104 have been tested for antibodies to STLV-1. Seventy-three of 118 (62%) were seropositive and virus positive for SIVsmm and 45 of 104 (43%) were positive for antibodies to STLV-1. The frequency of SIVsmm infection in the mangabey colony increases with age of the animal; infection was documented in 94% (34 of 36) of mangabeys 9 years of age or older, in 83% (5 of 6) of animals 7-8 years of age, in 73% (11 of 15) of 5-6 years old animals, in 49% (17 of 35) of 3-4 year old animals, and in 23% (6 of 20) of animals 1-2 years of age. Although virus infection in the mangabey usually does not result in clinical disease, experimental infection of macaque monkeys results in a high incidence of an AIDS-like disease.

The high infection rate in mature animals and the occurrence of occasional

infections in infants suggest that transmission of SIVsmm may be comparable to the transmission of HIV (by sexual contract 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, for identification of cofactors that may be associated with the occurrence of clinical disease, and to evaluate immune responses that prevent the development of clinical disease.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Determination of Minimal Infectious Dose of SIVsmm

AXIS I: 1a, 7b

AXIS II: 31, 66, 77

ORG UNIT: Pathobiology and Immun

INVES1: McClure, Harold M.
DEGREE1: D.V.M.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVES2: Anderson, Daniel C.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVES3: Fultz, Patricia N.
DEGREE3: Ph.D.
DEPT3: Pathobiology and Immunobiology
STAFF3: C

INVES4: Ansari, Aftab A.
DEGREE4: Ph.D.
DEPT4: Pathology
STAFF4: C

SPECIES1: Macaca mulatta
NUM1: 8

ABSTRACT: In order to determine the minimal infectious dose of SIVsmm, eight young rhesus macaques were divided into 4 groups of 2 animals each and inoculated intravenously with 1 log dilutions of the standard SIVsmm inoculum (10^4 $TCID_{50}$), with the experimental groups receiving 0.1 to 100 $TCID_{50}$. All animals receiving the 10^{-2} or 10^{-3} dilutions (100 or 10 $TCID_{50}$) seroconverted and became virus positive; 1 of 2 animals receiving the 10^{-4} dilution (1 $TCID_{50}$) seroconverted and became virus positive; both animals receiving the 10^{-5} dilution (0.1 $TCID_{50}$) remained seronegative and virus negative. These data will be used to determine the virus challenge dose for drug or vaccine trials.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: SIV-Induced Disease in Naturally Infected Mangabey Monkeys

AXIS I: 1a, 7b

AXIS II: 31, 64, 66, 77

PRC UNIT: Pathobiology & Immun

INVES1: McClure, Harold M.
DEGREE1: D.V.M.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVES2: Anderson, Daniel C.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVES3: Klumpp, Sherry A.
DEGREE3: D.V.M.
DEPT3: Pathobiology and Immunobiology
STAFF3: O

INVES4: Ansari, Aftab A.
DEGREE4: Ph.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

INVES5: Ribas, Jorge L.
DEGREE5: D.V.M.
DEPT5: Genitourinary Pathology
STAFF5: O

SPECIES1: Cercocebus atys
NUM1: 2

NON-HOST INSTITUTION: Armed Forces Institute of Pathology (JLR)

ABSTRACT: Although it is generally believed that natural SIV infection in African species of nonhuman primates (e.g., African green monkeys and sooty mangabeys) does not result in clinical disease, we have previously noted occasional disease problems (e.g., CMV, Noma, amebiasis) in mangabeys that might have been associated with an immunosuppressive SIV infection. More recently, two adult mangabeys that died had histologic lesions characteristic of those seen in macaques experimentally infected with SIV. The first case, a 23-year-old female, wildborn mangabey (FH), was found to have diffuse lymphoid infiltrates in the lung (comparable to lymphoid interstitial pneumonia) with numerous syncytial giant cells throughout the lungs. Immunocytochemical stains are currently being done on these tissue sections to determine if SIV viral antigens can be demonstrated in the multinucleated cells. This animal had a clinical history of chronic lymphocytosis of seven years duration, with white blood cell counts ranging between 22,700 and 31,100 during that period.

The second case occurred in a 16-year-old colony-born mangabey (FGb) that developed a T cell leukemia during her last two years of life. During this

period, the animal's white blood cell count increased to 127,500; 94% of the WBC's were lymphocytes, with 98% of these T cells, 87% of which were $CD8^+$ T cells. The animal also had a lymphoreticular cell infiltrate in the skin, lymphadenopathy and hepatosplenomegaly. Approximately three months before death there was a marked decrease in WBC's, RBC's, hematocrit, hemoglobin and platelets. At necropsy the animal was found to have severe myelosclerosis with widespread myeloid metaplasia. The liver showed multifocal infiltrates that consisted of lymphoid elements and numerous multinucleated giant cells. This animal was positive for both SIV and STLV-1 and stains are currently being done to demonstrate SIV antigen in the syncytial cells.

In an attempt to determine whether T cell leukemia could be transmitted to other monkeys, blood was collected from FGb just prior to death and 10 ml of blood was given intravenously to each of two pig-tailed macaques, two rhesus macaques and two mangabeys; all recipients were seronegative for antibodies to SIV and STLV-1. The mangabeys and rhesus macaques are currently clinically normal six months following receipt of the blood transfusion. However, the pig-tailed macaques died at 4 and 5 months following receipt of the blood transfusion. These animals showed diarrhea and weight loss, severe progressive immunosuppression and clinical evidence of CNS disease. Histologically, lesions were limited predominantly to the brain and spinal cord and consisted of a severe, granulomatous meningoencephalomyelitis that contained large numbers of multinucleated giant cells. These observations indicate that the FGb virus is particularly neurotrophic in pig-tailed macaques.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Perinatal Transmission of SIVsmm in Rhesus Macaques

AXIS I: 1a, 7b

AXIS II: 31, 64, 66, 77

PRC UNIT: Pathobiology & Immun

INVES1: McClure, Harold M.
DEGREE1: D.V.M.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVES2: Anderson, Daniel C.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVES3: Ansari, Aftab A.
DEGREE3: Ph.D.
DEPT3: Pathology
STAFF3: C

INVES4: Fultz, Patricia N.
DEGREE4: Ph.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

INVES5: Nahmias, Andre
DEGREE5: M.D.
DEPT5: Pediatrics
STAFF5: O

SPECIES1: Macaca mulatta
NUM1: 15

ABSTRACT: Due to the increasing incidence of HIV infection in human infants and children, an appropriate animal model system is critically needed for the study of perinatal lentivirus infections. Such a model is needed to clarify mechanisms of in utero or perinatal transmission; time of infection during gestation, intrapartum or perinatally; frequency of infection; clinical outcome of infection in both the mother and offspring; and to evaluate preventive or therapeutic approaches to this increasing problem. These studies have, therefore, been initiated to develop the SIV-infected macaque as a model for study of perinatal transmission of an HIV-like lentivirus.

Studies to evaluate the perinatal transmission of SIVsmm in experimentally infected rhesus macaques were initiated during the past 18 months. These studies entailed the experimental infection of 15 timed pregnant rhesus macaques at various times during gestation and monitoring the offspring for evidence of virus infection. Five animals were infected between day 28-35 of gestation; five between day 71-78 of gestation; and five between day 146-150 of gestation. Offspring delivered by these experimentally infected macaques included two stillbirths and 13 livebirths that were clinically normal. The stillbirths did not appear to be related to SIV infection and PBMC from the

other infants and milk samples from the mothers have been virus negative, to date. These infants and mothers will continue to be monitored for 12 months for evidence of virus infection. In addition to conventional serology and virus culture, the Pokeweed Mitogen stimulation assay and PCR techniques will be used to evaluate the infants for evidence of infection. The SIV-infected adults will subsequently be returned to the timed breeding program to determine if pregnancy in animals that are SIV-infected at the time of conception alters the outcome with respect to perinatal transmission. These latter studies will also be designed to allow an assessment of sexual transmission of SIVsmm (male to female and female to male).

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Disease in Macaque Monkeys Chronically Infected with SIVsmm

AXIS I: 1a, 7b

AXIS II: 31, 64, 66, 77

PRC UNIT: Pathobiology and Immun

INVES1: McClure, Harold M.
DEGREE1: D.V.M.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVES2: Anderson, Daniel C.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVES3: Ansari, Aftab A.
DEGREE3: Ph.D.
DEPT3: Pathology
STAFF3: C

INVES4: Fultz, Patricia N.
DEGREE4: Ph.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

INVES5: Klumpp, Sherry A.
DEGREE5: D.V.M.
DEPT5: Pathobiology and Immunobiology
STAFF5: O

SPECIES1: Macaca mulatta
NUM1: 12

SPECIES2: Macaca nemestrina
NUM2: 1

ABSTRACT: In earlier studies, 12 rhesus and one pig-tailed macaque were inoculated intravenously with the SIVsmm isolate. These animals developed variable degrees of lymphadenopathy, splenomegaly, diarrhea, weight loss and hematologic abnormalities, including lymphopenia, neutropenia and thrombocytopenia. Eight of these 13 chronically infected macaques (61.5%) died from an AIDS-like disease between 14 and 43 months post-infection. One additional animal currently has an AIDS-like disease and is showing gradual deterioration of its clinical condition. All clinically ill animals have shown progressive decreases in $CD4^+$ cells and in their $CD4^+/CD8^+$ cell ratios. Sentinel animals housed in the same room or same cage with macaques chronically infected with SIVsmm have remained seronegative and virus negative. These observations indicate that the disease induced by SIVsmm, like HIV, is not transmitted by casual contact.

improvement, and this animal is currently showing normal hematologic values. During recent months, a second chimpanzee has shown a progressive decline in the number of $CD4^+$ cells and in the $CD4^+/CD8^+$ cell ratio (most recent determination revealed an absolute $CD4^+$ cell count of 863 and a $CD4^+/CD8^+$ cell ratio of 0.38. This animal, as well as all other animals in the study, continues to appear clinically normal.

Two chimpanzees exposed to a molecularly cloned HIV have remained antibody negative and virus negative, and one HIV-2 exposed chimpanzee seroconverted but has remained virus negative. We have demonstrated susceptibility to infection by way of IV inoculation of HIV, by way of blood transfusion from an infected chimpanzee, and by exposure of the vaginal mucosa to HIV. Infection did not occur following long-term cage contact with infected chimpanzees or by exposure to HIV by way of the oral mucosa.

Although HIV infected chimpanzees have not, to date, developed an AIDS-like disease, some long-term infected chimpanzees are showing serologic and/or hematologic changes comparable to changes that have been associated with progression to AIDS in HIV-infected humans. Based on these observations, it is possible that HIV-infected chimpanzees may yet develop AIDS. Even if clinical disease does not develop, chimpanzees are appropriate models for AIDS studies, especially for vaccine testing, due to their unique susceptibility to HIV infection.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Evaluation of the Long-term Effects of Irradiation in Rhesus Monkeys

AXIS I: 1a, 28 (All systems)

AXIS II: 30, 76a, 76b, 80a

INVES1: McClure, Harold M.
DEGREE1: D.V.M.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVES2: Anderson, Daniel C.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

SPECIES1: Macaca mulatta
NUM1: 76

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 33 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, 74 of the initial group of animals died. Thirty-five of the 74 (47.2%) animals which died had one or more neoplasms at the time of death. Tumors occurred in 30 of 54 (56.5%) irradiation-exposed animals which died, and in 5 of 20 (25.0%) non-exposed controls which died. Consequently, 30 of 35 (85.7%) tumor cases occurred in irradiation-exposed animals.

Tumors were diagnosed in 17 of 26 (65%) bomb-exposed animals which died; 7 of 16 (44%) Co^{60} exposed animals; and in 4 of 5 (80%) animals exposed to pure neutron irradiation. During the same time period, a tumor incidence of approximately 4% 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 adenocarcinomas 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), esophageal leiomyomas (2) and one each of glioblastoma of the brain, leukemia, seminoma, subcutaneous fibroma, subcutaneous lipoma, liver cell carcinoma, cholangiocarcinoma, salivary gland adenoma, hemangioma of the skin, squamous cell carcinoma of the mouth, and breast carcinoma. These observations suggest that irradiation exposure is cancerogenic in the rhesus monkey, and that tumors may occur many years following exposure.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Prophylactic Effects of AZT in the SIVsmmPBj Infected Macaque

AXIS I: 1a, 2, 7b

AXIS II: 31, 50b, 66, 77

PRC UNIT: Pathobiology and Immun

INVES1: McClure, Harold M.
DEGREE1: D.V.M.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVES2: Anderson, Daniel C.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVES3: Fultz, Patricia N.
DEGREE3: Ph.D.
DEPT3: Pathobiology and Immunobiology
STAFF3: C

INVES4: Ansari, Aftab A.
DEGREE4: Ph.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

SPECIES1: Macaca nemestrina
NUM1: 12

ABSTRACT: A variant of SIV, identified as SIVsmmPBj14, derived from a chronically infected pig-tailed macaque causes an acute clinical disease and death within 7 to 21 days in experimentally infected pig-tailed macaques. This animal model system, which should prove to be extremely useful in the rapid evaluation of newly developed antiretroviral drugs, was used in a preliminary study to evaluate the prophylactic effects of AZT when administered shortly after virus exposure.

In this study, four groups of three pig-tailed macaques were given 10 $TCID_{50}$ of SIVsmmPBj14. AZT at 100mg/kg/day, divided into 3 doses, was given subcutaneously for a period of 14 days. Treatment was initiated at 1 hour (group 1), 24 hours (group 2) or 72 hours (group 3) after virus exposure; group 4 animals served as untreated controls. All animals except one in group 1 were virus positive at 10 days post-inoculation. Three animals in group 1 and 2 remained clinically normal; all other animals developed clinical disease within 10-17 days of virus exposure. One death occurred in group 1, two deaths occurred in group 2, and each of the three animals in groups 3 and 4 died (two in each group died acutely and one animal in each group survived for 13 or 14 months). One animal in group 1 continues to be virus-negative and all 3 survivors in groups 1 and 2 continue to appear clinically normal. Animals in groups 3 and 4 had 30-fold higher antibody titers than animals in groups 1 and 2, suggesting that the former had more antigenic stimulation due to increased virus replication. Data derived from this study indicate that some protection is provided by AZT when treatment is initiated within 24 hours of exposure to an acutely lethal simian HIV-like virus.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Immunological and Molecular Studies of Primate Antigens

AXIS I: 1a, 2, 3, 4, 6, 9

AXIS II: 39, 60, 64, 74ah, 76ab, 91

PRC UNIT: Pathobiology & Immun

INVES1: Metzgar, Richard S.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

SPECIES1: Pan troglodytes
NUM1: 3

ABSTRACT: The overall goals of this project are to continue to define selected antigens of human cells and to use chimpanzees for evaluating potential human tumor vaccines. 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 nonprimate mammalian species. The antigenic focus during the current and continuation year is on peptide determinants of human tumor and normal cell apomucins. We have recently cloned the human pancreatic tumor mucin gene at Duke University and are currently evaluating in rodents, the immunogenicity of various synthetic peptides derived from the predicted amino acid sequence of the gene product. Peptides selected from the rodent studies, which have stimulated good antibodies to various regions of this large peptide (greater than 200,000 M.W.), and which show restricted specificity for normal or malignant mucin producing cells, will be evaluated for immunogenicity in chimpanzees. Preclinical and clinical studies currently being conducted at Duke University have indicated that mucin peptides may be important antigenic molecules for active immunotherapy of pancreatic cancer patients.

A chimpanzee that was immunized with a particially (95%) deglycosylated pancreatic tumor apomucin is currently being further stimulated with the most immunodominant synthetic peptide of the protein backbone. Lymphocytes from this animal are also being used to optimize conditions and generate hybridomas which produce chimpanzee monoclonal antibodies to peptide epitopes.

These immunological studies of human tumor antigens in higher apes are unique and important preclinial models to evaluate immunogenicity of selected tumor antigens and justify active immunotherapy trials with these antigens. In addition, the chimpanzee antibodies may be useful as diagnostic and/or clinical management aids for patients with certain types of mucin producing adenocarcinomas. There is considerable evidence that tumor mucins are aberrantly glycosylated compared to their normal cell couterparts so that antibodies to either carbohydrate or peptide determinant could detect the post-translational modifications of these tumor antigen molecules.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Documentation of Fetal Physiological Parameters by Radiotelemetry in Unrestrained Primates

AXIS I: 1a, 9, 13, 21

AXIS II: 48, 52, 70, 86

PRC UNIT: Pathobiology & Immun

INVES1: Patterson, C.A.
DEGREE1: M.D.
DEPT1: Pathobiology and Immunobiology
STAFF: 0

SPECIES: Macaca mulatta
NUM1: 20

ABSTRACT: Asphyxia and subsequent cerebral palsy continues to be a problem in the human infant. Cerebral palsy is thought to be associated with asphyxia that is sustained before labor begins. To address this problem, miniaturized radiotelemetry devices have been developed to transmit fetal heart rate and brain activity in the nonhuman primate fetus before, during and after parturition. This work is intended to extend current knowledge of fetal heart rate patterns and brain activity during the birthing process. The effects of hypoxia on these parameters is also assessed.

To accomplish these goals, timed breeding has been used to provide fetuses of known gestation age. The revised telemetry transmitter was implanted at fetal surgery in 14 animals. The liveborn infants were tested by studies assessing developmental performance and motor skills. The results in these infants were compared to 6 control infants born in the colony that had no intervention. We have shown that fetal surgery has no effect on motor skills or behavior in the rhesus.

To expose animals to hypoxia before birth, a special lexan box was devised to house the cage of the maternal animal. The O_2/N_2 environment was controlled by a modified anesthesia machine. Activity and oxygen concentration was continuously monitored. Infants born to mothers exposed to hypoxia were also assessed using the same tests for behavior and motor skills.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Immunohistochemical and Histologic Study of SIV-induced CNS Lesions in Nonhuman Primates

AXISI: 1a, 7b, 19

AXIS II: 31, 66, 77

PRC UNIT: Pathobiology & Immun

INVES1: Ribas, Jorge L.
DEGREE1: D.V.M.
DEPT1: Pathology
STAFF1: O

INVES2: McClure, Harold M.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

INVES3: Anderson, Daniel C.
DEGREE3: D.V.M.
DEPT3: Pathobiology and Immunobiology
STAFF3: C

SPECIES1: Macaca mulatta
NUM1: 8

SPECIES2: Macaca nemestrina
NUM2: 9

NON-HOST INSTITUTION: Armed Forces Institute of Pathology (JLR)

ABSTRACT: This study has three main objectives: a) neuropathologic description of SIV-induced lesions and related opportunistic infections in macaque monkeys, b) immunophenotyping of inflammatory cells and demonstration of SIV antigens in the central nervous system (CNS), and c) comparative neuropathology of SIV- and HIV-induced meningoencephalitis. During this reporting period we have characterized the lesions induced by SIV and have compared them to those present in HIV-infected human CNS. Briefly, CNS tissues from experimental macaque monkeys, which were chronically infected with SIVsmm or acutely infected with a lethal variant SIVsmmPBj14, were compared with autopsy CNS tissues from pediatric and adult patients dying with AIDS. A subacute meningoencephalomyelitis, characterized by randomly distributed perivascular collections of macrophages, glial cells and multinucleated giant (syncytial) cells, was present in both HIV- and SIV-infected CNS. Leptomeningeal lesions predominated in early stages of SIV-CNS infection, but with progression of disease the lesions were mainly parenchymal. In HIV-CNS infection lesions were primarily parenchymal and were localized in subcortical white and gray matter. Many concurrent opportunistic infections occurred in adult HIV-CNS, but cytomegalovirus reactivation was the main opportunistic infection present in pediatric HIV-CNS and SIV-CNS. Opportunistic neoplasms occurred in 5% of HIV-CNS and none were seen in SIV-

CNS. Vacuolar myelopathy was present in adult HIV-spinal cord only. Gross cerebrocortical atrophy occurred in 30% of HIV-infected brains, but it was not observed in SIV brains. Vascular and parenchymal calcification was seen in pediatric HIV-CNS, only. Infection with SIV appears to be more closely related to pediatric than adult HIV meningoencephalitis. We will continue these studies during the upcoming year and will emphasize the immunophenotyping of B and T lymphocytes present in the CNS of SIV infected macaques monkeys.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: National Cooperative Drug Discovery Group/AIDS

AXISI: 1a, 7b

AXIS II: 31, 50a, 50b, 66

PRC UNIT: Pathobiology & Immun

INVES1: Schinazi, Raymond F.
DEGREE1: Ph.D.
DEPT1: Pediatrics
STAFF1: O

INVES2: Eriksson, Bertil
DEGREE2: Ph.D.
DEPT2: Pediatrics
STAFF2: O

INVES3: McClure, Harold M.
DEGREE3: D.V.M.
DEPT3: Pathobiology and Immunobiology
STAFF3: C

INVES4: Anderson, Daniel C.
DEGREE4: D.V.M.
DEPT4: Pathobiology and Immunobiology
STAFF4: C

SPECIES1: Macaca mulatta
NUM1: 25

ABSTRACT: As a prelude to studies in humans, it is essential to evaluate new promising antiviral agents developed by our group for their ability to have favorable pharmacokinetic properties, low toxicity and activity in monkeys inoculated with simian immunodeficiency virus (SIV). Activity of the compounds against SIV in culture is ascertained prior to studies in monkeys. Once the pharmacokinetic parameters of the drugs using the preferred route of drug administration are determined, then studies in SIV inoculated animals are performed. These critical monkey studies will allow us to develop safe and effective new antiviral drugs for prophylaxis and treatment of infections caused by the human immunodeficiency virus. During the past year, the pharmacokinetics, toxicity and efficacy of four newly developed antiretroviral drugs have been evaluated in the macaque model.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Metabolism and Biochemical Pharmacology of AZddMeC

AXISI: 1a, 7b

AXIS II: 31, 50a, 50b, 66

PRC UNIT: Pathobiology & Immun

INVES1: Schinazi, Raymond F.
DEGREE1: Ph.D.
DEPT1: Pediatrics
STAFF1: 0

INVES2: Chu, C.K.
DEGREE2: Ph.D.
DEPT2: Pharmacology
STAFF2: 0

INVES3: Eriksson, B.F.
DEGREE3: Ph.D.
DEPT3: Pediatrics
STAFF3: 0

INVES4: Sommadossi, Jean-Pierre
DEGREE4: Ph.D.
DEPT4: Pharmacology
STAFF4: 0

INVES5: Gallo, J.M.
DEGREE5: Ph.D.
DEPT5: Pharmacology
STAFF5: 0

INVES6: Boudinot, F.D.
DEGREE6: Ph.D.
DEPT6: Pharmacology
STAFF6: 0

INVES7: Anderson, Daniel C.
DEGREE7: D.V.M.
DEPT7: Pathobiology and Immunobiology
STAFF7: C

INVES8: McClure, Harold M.
DEGREE8: D.V.M.
DEPT8: Pathobiology and Immunobiology
STAFF8: C

NON-HOST INSTITUTION: College of Pharmacy, University of Georgia (CKC, JMG, FDB), University of Alabama at Birmingham (J-PS).

SPECIES1: Macaca mulatta
NUM1: 6

ABSTRACT: 3'-Azido-2', 3'-dideoxy-5-methylcytidine (CS-92, AzddMEC) is an antiviral nucleoside analogue structurally related to 3'-azido-3'-deoxythymidine (AZT). We have determined that CS-92 is a potent and selective inhibitor of HIV reverse transcriptase and viral replication in human lymphocytes and macrophages in vitro. CS-92 was non-toxic to human bone marrow cells in vitro. Th compound was not a substrate for cytidine-deoxycytidine deaminase derived from HEp-2 cells. Metabolic studies show that the mono-, di and triphosphate of the drug were formed in human lymphocytes in culture. Pharmacological studies in mice indicate that CS-92 is not deaminated to AZT. However, in rhesus monkeys, a compound with a retention time similar to AZT was found. The mean half-life in rhesus monkeys for CS-92 was 1.52 and 1.74 hours after intravenous and oral administration, respectively. The oral bioavailability was about 21%. The favorable pharmacological and metabolic profile of CS-92 make it a potentially useful antiviral agent for the treatment of HIV infections.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Antiviral, Cytotoxic, Biochemical, and Pharmacokinetic Properties of CS-92 (AzddMeC)

AXISI: 1a, 7b

AXIS II: 31, 50a, 50b, 66

PRC UNIT: Pathobiology &" Immun

INVES1: Schinazi, Raymond F.
DEGREE1: Ph.D.
DEPT1: Pediatrics
STAFF1: 0

INVES2: Chu, C.K.
DEGREE2: Ph.D.
DEPT2: Pharmacology
STAFF2: 0

INVES3: Eriksson, B.F.
DEGREE3: Ph.D.
DEPT3: Pediatrics
STAFF3: 0

INVES4: Sommadossi, Jean-Pierre
DEGREE4: Ph.D.
DEPT4: Pharmacology
STAFF4: 0

INVES5: Gallo, J.M.
DEGREE5: Ph.D.
DEPT5: Pharmacology
STAFF5: 0

INVES6: Boudinot, F.D.
DEGREE6: Ph.D.
DEPT6: Pharmacology
STAFF6: 0

INVES7: Anderson, Daniel C.
DEGREE7: D.V.M.
DEPT7: Pathobiology and Immunobiology
STAFF7: C

INVES8: McClure, Harold M.
DEGREE8: D.V.M.
DEPT8: Pathobiology and Immunobiology
STAFF8: C

NON-HOST INSTITUTION: College of Pharmacy, University of Georgia (CKC, JMG, FDB), University of Alabama at Birmingham (J-PS).

SPECIES1: Macaca mulatta
NUM1: 9

ABSTRACT: 3′-Azido-2′, 3′-dideoxy-5-methylcytidine (CS-92) is a potent and selective anti-HIV-1 compound. The median effective concentration (EC_{50}) for CS-92 in HIV-1 infected human peripheral blood mononuclear cells was between 0.08 and 0.22 uM. The compound was effective against HIV-2 and SIV in human lymphocytes. CS-92 was not toxic to PBM or Vero cells when tested up to 200 uM. The compund appears to be selective for human retroviruses and was not active against HSV-1 or coxsackievirus B4 and weakly active against a Friend murine retrovirus (EC_{50} = 36 uM). It was also active in human macrophages infected with HIV-1 (EC_{50} = 0.006 uM). CS-92 was about 100 times less toxic to granulocyte, macrophage and erythroid precursor cells than AZT. The interaction of CS-92-5′-triphosphate with HIV-1 reverse transcriptase indicated competitive inhibition with an affinity 31 fold greater than that for ddCTP. Metabolic and pharmacokinetics studies of CS-92 in culture, rodents, and rhesus monkeys are in progress.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Immunogenicity of Human Melanoma Antigens in Non-Human Primates and Production of Monoclonal Antibodies to Human Melanoma TAA.

AXIS I: 1a, 1d

AXIS II: 64, 76b

PRC UNIT: Pathobiology and Immun

INVES1: Seigler, Hilliard F.
DEGREE: M.D.
DEPT: Surgery, Immunology
STAFF1: C

SPECIES1: Pan troglodytes
NUM1: 4

SPECIES2: Macacca mulatta
NUM2: 2

ABSTRACT: The objectives of this study are: (1) to determine the immunogenicity of human melanoma tumor associated antigens (TAA) in non-human primates in an effort to design immunization protocols which may provide protective immunity in humans, and (2) to use lymphocytes from the immune primates in fusion protocols to generate monoclonal antibodies against human melanoma TAA. Sera from four chimpanzees and two monkeys were evaluated for anti-GD3 antibody activity by solid phase RIA. Both monkeys demonstrated a serological response and sera from one of the animals had a titer greater than 2500. One chimp responded, but with lower titer. One chimp was immunized with a preparation of GD3 bound to Salmonella minnesota R595. This animal responded and has, with repeated immunizations, increasing serum titers against both purified GD3 and GD3-expressing melanoma lines. Lymph node cells from a chimpanzee immunized with GD3 were immortalized by EBV transformation. Ig-producing B-cells were expanded, and then fused with SP2\0 murine myeloma. Four weeks after fusion 10% of the seeded cultures grew, and four hybrids which produced melanoma-reactive Igs were cloned twice and expanded. These clones are stable in culture for 4 months, and produce .5-5 ug/ml/day of Igs as detected by human reagents. Initial characterization shows that these antibodies are strongly reactive with human melanoma and neuroectodermal tumors, and exhibit moderate reactivity to other tumors. The monoclonals lack reactivity to human PBL,B and T cells and fibroblasts. Two of these antibodies react with GD3. Over the next year, we intent to examine the role for immune response modifiers IL-1, IL-2 and IL-4 in modulating response of non-human primates to selected melanoma TAA. We will also continue the evaluations of the TAA recognized by the responding animals and defined by the current monoclonals, and any new monoclonals produced.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Toxicity of anti-AIDS Drugs on the Bone Marrow

AXIS I: 1a, 17

AXIS II: 31, 50, 74c

PRC UNIT: Pathobiology & Immun

INVES1: Sommadossi, Jean-Pierre
DEGREE1: Ph.D.
DEPT1: Pharmacology
STAFF1: O

INVES2: McClure, Harold M.
DEGREE2: D.V.M.
DEPT2: Pathobiology & Immunobiology
STAFF2: C

SPECIES1: Macaca mulatta
NUM1: 15

NON-HOST INSTITUTION: University of Alabama at Birmingham (J.-P.S.)

ABSTRACT: The objective of this research is to evaluate the toxicity and/or immunosuppressive effects of novel drug combinations with assessment of transport and metabolic disposition. In particular, effects of selected modulting agents (such as BAU) on anti-HIV drugs will be studied in an attempt to prevent or alleviate bone marrow toxicity associated with chronic treatment with certain anti-HIV nucleoside analogs. Efficacy of selected drug combinations (anti-HIV and modulating agent) will be assessed in SIV-infected rhesus monkeys.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Detection of Occult SIV Infection in Nonhuman Primates by PCR

AXIS I: 1a, 7b, 17, 19

AXIS II: 31, 39, 59, 66, 83,

PRC UNIT: Pathobiology & Immun

INVES1: Villinger, Francois
DEGREE1: DVM
DEPT1: Pathobiology & Immunobiology
STAFF1: 0

INVES2: Yehuda-Cohen, Tamar
DEGREE2: Ph.D.
DEPT2: Pathology
STAFF2: 0

INVES3: Powell, Jonathan D.
DEGREE3: B.S.
DEPT3: Pathology
STAFF3: 0

INVES4: Ansari, Aftab A.
DEGREE4: Ph.D.
DEPT4: Pathobiology & Immunobiology
STAFF4: C

INVES5: McClure, Harold M.
DEGREE5: DVM
DEPT5: Pathobiology & Immunobiology
STAFF5: C

INVES6: De, Barun K.
DEGREE6: Ph.D.
DEPT6: Centers for Disease Control
STAFF6: 0

SPECIES1: Cercocebus atys
NUM1: 25

SPECIES2: Cercopithecus mitis
NUM2: 3

SPECIES3: Macaca arctoides
NUM3: 13

NON-HOST INSTITUTION: Centers for Disease Control (BKD)

ABSTRACT: This study will develop the polymerase chain reaction (PCR) as a highly sensitive detection method for the presence of simian immunodeficiency

virus (SIV) sequences and therefore infection of the animal despite a lack of antibodies. Such occult infections have been suggested in the SIV seronegative mangabeys by the detection of memory B cells sensitized to SIV in their circulating PBMCs. Infection has been confirmed so far in 6 seronegative mangabeys by PCR, using a primer pair in highly conserved areas of the gag region of the SIV. A positive response however, was only observed after the PBMCs had been stimulated in vitro, highlighting the impact of cell cultivation on the replication activation of this and related retroviruses. Similarly, the 3 seronegative sykes were found to harbor SIV sequences among their PBMCs.

We will develop a whole panel of oligonucleotides for the amplification and detection of segments from various regions of the SIV genome (e.g., pol, env and LTR). The overall goal will be to optimize the sensitivity of the method in order to detect SIV sequences directly from PBMC DNA and screen the various susceptible nonhuman primates at Yerkes and from abroad for SIV infection.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Comparison of SIV *in vivo* Sequences from Naturally Infected *Cercocebus atys* and Experimentally Infected *Macaca mulatta*

AXIS I: 1a, 7b, 17, 19

AXIS II: 31, 39, 59, 66, 83,

PRC UNIT: Pathobiology & Immun

INVES1: Villinger, Francois
DEGREE1: DVM
DEPT1: Pathobiology & Immunobiology
STAFF1: O

INVES2: Yehuda-Cohen, Tamar
DEGREE2: Ph.D.
DEPT2: Pathology
STAFF2: O

INVES3: Powell, Jonathan D.
DEGREE3: B.S.
DEPT3: Pathology
STAFF3: O

INVES4: Ansari, Aftab A.
DEGREE4: Ph.D.
DEPT4: Pathobiology & Immunobiology
STAFF4: C

INVES5: McClure, Harold M.
DEGREE5: DVM
DEPT5: Pathobiology & Immunobiology
STAFF5: C

INVES6: De, Barun K.
DEGREE6: Ph.D.
DEPT6: Centers for Disease Control
STAFF6: O

SPECIES1: Cercocebus atys
NUM1: 4

SPECIES3: Macaca mulatta
NUM2: 3

NON-HOST INSTITUTION: Centers for Disease Control (BKD)

ABSTRACT: This study will attempt to delineate major sequence differences in SIV sequences of naturally infected and disease resistant *Cercocebus* and experimentally infected and disease susceptible *Macaca* using the polymerase chain reaction (PCR) as an amplification tool for these sequences present only in low copy numbers *in vivo*. Substantial differences have been assessed in a

selected area of the gag fragment using various oligonucleotide probes and PCR aided sequencing reaction.

We will try to detect similar divergent genomic fragments, in particular in the gag and env regions. We will then analyse their sequence and derive the resulting polypeptide variations. These peptides will then be synthesized according to their antigenic profile and tested for their immune response in Cercocebus and Macaca T-cells. We hope to shed some light on the differences of immune response and disease susceptibility of both monkey species.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Infection of Macaques with HIV-1

AXIS I: 1a, 7b, 17, 19

AXIS II: 31, 50, 66, 74f, 83,

PRC UNIT: Pathobiology & Immuno

INVES1: Villinger, Francois
DEGREE1: DVM
DEPT1: Pathobiology & Immunobiology
STAFF1: O

INVES2: Ansari, Aftab A.
DEGREE2: Ph.D.
DEPT2: Pathobiology & Immunobiology
STAFF2: C

INVES3: McClure, Harold M.
DEGREE3: DVM
DEPT3: Pathobiology & Immunobiology
STAFF3: C

INVES4: Zimmer, P
DEGREE4: MD
DEPT4: Bernhard Nocht Institut
STAFF4: O

SPECIES1: Macaca mulatta
NUM1: 3

SPECIES2: Macaca nemestrina
NUM2: 3

NON-HOST INSTITUTION: Bernhard Nocht Institut, Hamburg (FRG)(PZ)

ABSTRACT: This study will attempt to infect nonhuman primates with HIV-1, for the possible development and testing of a new virus/animal model comparable to the infection of humans with HIV-1. Preliminary experiments indicate that PBMCs from monkeys can be infected in vitro under particular culture conditions. It is our goal to try to create such conditions in the animal. Such cellular characterisitics can be obtained by submitting the animal to a diet abnormally high in cholesterol and rich in unsaturated fatty acids. We are currently ascertaining the results in vitro by testing various infection protocols before submitting the animals to the projected diet. Their PBMCs will then be tested in vitro for increased sensitivity to HIV-1 infection, following that attempts will be made to infect the similarly conditioned animals with HIV-1.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Laser Corneal Myopic Keratomileusis: Histopathology of Wound Healing

AXIS I: 1a, 25b

AXIS II: 62, 70, 86

PRC UNIT: Pathobiology and Immun

INVES1: Waring, George O.
DEGREE1: M.D.
DEPT1: Ophthalmology
STAFF1: O

INVES2: Hanna, Khalil
DEGREE2: M.D.
DEPT2: Ophthalmology
STAFF2: O

INVES3: Thompson, Keith
DEGREE3: M.D.
DEPT3: Ophthalmology
STAFF3: O

INVES4: Fantes, Francisco
DEGREE4: M.D.
DEPT4: Ophthalmology
STAFF4: O

SPECIES1: Macaca mulatta
NUM1: 15

ABSTRACT: Laser corneal myopic keratomileusis was performed in 30 eyes of 15 rhesus macaques and the animals were followed by slit lamp biomicroscopy for evidence of corneal scarring. At different intervals postoperatively, animals were sacrificed and the corneas prepared for light microscopy, transmission electron microscopy, and immunohistochemistry. Slit lamp examinations showed all corneas epithelialized within 7 days. The corneas remained clear by slit lamp examination until approximately 4-6 weeks postoperatively. Varying degrees of corneal scarring was then noted to develop in over two-thirds of the eyes treated. Histopathologic examination revealed the cause of the scarring to be subepithelial fibroplasia. Abnormalities were also present in the basal epithelial layer in some specimens. Immunohistochemistry revealed that the subepithelial scar was composed of Type III collagen, consistent with a normal corneal wound healing response to injury.

P5RR00165-29 1/1/89 - 12/31/89 Yerkes Regional Primate Research Center

TITLE: Pre-chemotherapy Marrow Priming with Recombinant CSF's

AXIS I: 1a, 1d, 2, 17

AXIS II: 50a, 76b, 88

PRC UNIT: Pathobiology and Immun

INVES1: Winton, Elliott F.
DEGREE1: M.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: O

SPECIES1: Macaca mulatta
NUM1: 12

ABSTRACT: We have developed methodology for in vitro clonogenic assays and FACS analysis to be used in experiments in which rHuIL-3 or rHuGM-CSF are administered to rhesus monkeys, and established normal range and variance of the assays in untreated rhesus monkeys. Experiments involving the animals were conducted in which marrow and peripheral blood samples were obtained before, during and after administration HGF or saline (control). The effects of the factors on number, cell lineage, and cell-cycle kinetics of progenitor cells, and the effect on megakaryocyte ploidy were quantified. A marked effect on megakaryocyte ploidy was observed within 48 hours of rHuGM-CSF administration. In addition, we have documented that the sequential administration of rHuIL-3 and rHuGM-CSF produced a highly significant elevation of peripheral blood progenitor cells, particularly megakaryocyte colony and burst forming cells (BFU-meg, CFU-meg). Extension of the above observations through additional experiments to be performed should lead to better definition of the potential roles of these factors in ameliorating the post-chemotherapy or post bone marrow transplant thrombocytopenia.

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P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Conditions Required for Detection of Specimen-Specific SE-I Secondary Electrons in an Analytical SEM

AXIS I: 1a, 1d, 9, 17, 23

AXIS II: 70

PRC UNIT: Reproductive Biology

INVES1: Apkarian, R.P.
DEGREE1: MA
DEPT1: SEM Facility/Repro. Bio. Yerkes
STAFF1: 0

SPECIES1: Ratus ratus
NUM1: 1

SPECIES2: Pan troglodytes
NUM2: 1

ABSTRACT: An analytical SEM equipped with an above-the-lens detector, an in-the-lens specimen stage and a high brightness LaB_6 emitter was used to produce a specimen-specific, secondary electron-I (SE-I) signal for recording edge brightness contrast with high intensity on small particles at high magnification (200,000). The SE-I edge brightness contrast produced from 20-40 nm colloidal gold on silicon wafers was useful for estimating instrument resolution since the edge brightness is the sum of the SE-I signal range (appox. 1 nm) and the beam diameter. LaB_6 crystal saturation and gun conditions were determined in order to minimize the probe diameter at the first cross-over position. Ferritin particles also on the silicon wafers were imaged by adjustments of the gun bias voltage conditions. Establishment of these conditions was useful for high resolution SEM studies of appropriately coated bulk biological specimens.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Condenser/Objective Lens SE-I Imaging of Chromium-Coated Biological Specimens Using a Schottky Field Emission Source

AXIS I: 1a, 9, 12a, 22, 23

AXIS II: 70

PRC UNIT: Reproductive Biology

INVES1: Apkarian, R. P.
DEGREE1: MA
DEPT1: SEM Facility/Repro. Bio. Yerkes
STAFF1: 0

SPECIES1: Homo sapiens
NUM1: 1

SPECIES2: Pan troglodytes
NUM2: 1

NON-HOST INSTITUTION: International Scientific Instruments Avon CT

ABSTRACT: We have had experience with high resolution SE-I enriched imaging of chromium (Cr) coated soft and hard, biological tissue. SEMs equipped with condenser/objective (c/o) lens stages and LaB_6 (ISI DS-130) or cold cathode field emission (CFE) (Hitachi S-900) sources operated at high voltage (15-30 KeV) were assessed by the comparison of emission properties and image contrasts generated from ferritin test specimens. Practical source performance during the imaging of metal coated bulk biological tissues is subject to the metal film quality which is responsible for generating accurate topographic contrasts at high magnifications of biologically significant structures in the 1-10 nm range. Recently a thermionically assisted Schottky field emission source (SFE) has been designed for the c/o lens optics of the ISI DS-130 SEM. A practical consideration for the imaging of biological microdomains at high magnification must be: how does the SFE source compare with the LaB_6 emitter on the same optical column and can the SFE compare with the CFE for producing quality ultrahigh magnification (500,000x) topographic contrasts in the nanometer range.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Correlative Light, Transmission, and High Resolution (SE-I) Scanning Electron Microscopy Studies of Rhesus Adrenocortical Vascular Morphology

AXIS I: 1a, 9, 12a, 13, 15

AXIS II: 74e, 74f, 77

PRC UNIT: Reproductive Biology

INVES1: Apkarian, R. P.
DEGREE1: MA
DEPT1: SEM Facility, Repro. Bio. Yerkes
STAFF1: O

INVES2: Hernault, L
DEGREE2: MA
DEPT2: Ophthalmology
STAFF2: O

SPECIES1: Macaca mulatta
NUM1: 4

ABSTRACT: A detailed correlative morphologic description using light microscopy (LM), transmission electron microscopy (TEM and high resolution SE-I scanning electron microscopy (SEM was conducted on the capillary endothelium of the zona-fasciculata (Z-F) in juvenile male rhesus monkeys. The glucocorticoid synthesis and release phenomena, associated with stress stimulated release of the adrenocorticotropic hormone (ACTH) via the hypothalamic-pituitary axis, intimately involves capillaries of the Z-F. A comprehensive study of all the ultrastructural features implicated in the transendothelial uptake of steroidogenic precursors and release of glucocorticoids in perfused rhesus adrenals has not previously been made. This report presents correlative images of transendothelial openings that include previously described single diaphragmed fenestrae and plasmalemma vesicles, and double diaphragmed transendothelial channels. New observations of endothelial cell pockets, tight junctional complexes and membrane filled ghost sacs were recorded from perfused rhesus adrenal. Membranous ghosts associated with adrenocortical endothelium were reported in a previous TEM study of perfused rat, however, the potential argument existed that ghosts were artifactual. Their role as steroid hormone releasing structures remains an open question, yet their structural characteristics appear justified based on imaging of identical profiles observed in perfused rhesus adrenocortical specimens. These structural features are considered for the potential of gating and sorting of metabolites , and release of glucocorticoids in response to ACTH stimulated stress events.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: A High Resolution SE-I SEM Assessment of Diimidoester Fixed Chimpanzee Sperm

AXIS I: 1a, 15, 23
AXIS II: 74e

PRC UNIT: Reproductive Biology

INVES1: Apkarian, R.P.
DEGREE1: MA
DEPT1: SEM Facility/Repro. Bio.
STAFF1: O

INVES2: Young, L.G.
DEGREE2: PhD
DEPT2: Physiology
STAFF2: O

INVES3: Gould, K.G.
DEGREE3: DVM, PhD
DEPT3: Reproductive Biology.
STAFF3: C

SPECIES1: Pan troglodytes
NUM1: 3

ABSTRACT: Diimodester (DIE) fixation was introduced in 1970. Although its merits for preserving the morphologic and antigenic structure of the cell are well known, its use has been minimal. We developed a DIE fixation procedure for chimpanzee sperm which preserves macromolecular domains imaged in the high resolution SE-I signal mode of scanning electron microscope (SEM).

Chimpanzee semen samples were obtained from adult males (Pan troglodytes) housed in AAALAC approved facilities at the Yerkes Research Center. Populations of swim-up sperm were suspended in the DIE, i.e. 2% dimethyl suberimidate dihydrochloride (DMS) (C_6 Anatrace, Maumee, OH) in 0.1M Na-cacodylate, final pH 8.5, for 1 h. The sperm were sedimented at 300g, washed 5 x in 0.1M Na-cacodylate, pH 8.5, for 5 min. at 20°C, resuspended in 1% OsO_4 in 0.1M Na-cacodylate, pH 7.4 for 30 min. at 20°C and rinsed in distilled deionized water. A drop of sperm was placed on a 5mm x 5mm silicon chip in an inverted embedding capsule dehydrated in an ascending gradient of ethanol, and critical point dried using delicate handling procedures. The silicon chips were degassed to 3×10^6 Pa in a Denton DV 602 turbo pump system and subsequently sputter coated with an ultrathin fine grain 2 nm chromium film at 1×10^1 Pa. All micrographs were taken with the specimen staged in-the-lens of an ISI DS-130 SEM using Schottky field emission emitter operated at 25 kV.

Diimidoester fixed sperm were imaged in their entirety for regional integrity. Sperm heads imaged at intermediate magnification, revealed intact acrosome, equatorial segment, and neck regions. The termination of the apical segment of the acrosome, which delineates the anterior margin of the equatorial segment, contains enriched SE-I particle contrast 5-10 nm range. The

posterior margin of the equatorial segment at the acrosomal terminus also displayed 5-10 nm particulate features. The junction between the principal and end piece of the osmotically sensitive sperm flagellum was well preserved and contained all SE-I contrasts. These SE-I contrasts include particle contrast of minute (3nm) macromolecular membrane, ectodomains, attesting to the ultrastructural preservation of the chimpanzee sperm with DIE fixation. This preservation was comparable to that demonstrated with glutaraldehyde fixation of chimpanzee sperm. The superiority of DIE fixation lies in the potential to maintain antigenic reactivity important for immunological labelling studies while providing excellent preservation of morphology.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: High Resolution SE-I SEM Study of Enamel Crystal Morphology

AXIS I: 1a, 1d, 4, 9, 22

AXIS II: 70, 74b

PRC UNIT: Reproductive Biology

INVES1: Apkarian, R. P.
DEGREE1: MA
DEPT1: SEM Facility/Repro. Bio. Yerkes
STAFF1: 0

INVES2: Gutekunst, M. D.
DEGREE2: BS
DEPT2: Dentistry
STAFF2: 0

INVES3: Joy, D. C.
DEGREE3: PhD
DEPT3: Analytical E.M. Facility
STAFF3: 0

SPECIES1: Homo sapiens
NUM1: 1

NON HOST INSTITUTION: University of Tennessee (DCJ)

ABSTRACT: Until recently high resolution TEM was the only imaging mode capable of probing the atomic lattice structure of crystals composing tooth enamel. Studies designed to determine the polyhedral shape of normal enamel crystals and initiation of carious lesions in enamel crystals were hampered and limited by interpretation of two-dimensional TEM images from thin section and freeze fracture replica specimens lacking depth of field. The newly developed SE-I signal mode for SEM (SE-I/SE-II ratio) can produce images of enamel crystals approaching beam diameter dimensions (0.7 - 2.0 nm) rivaling the resolution of the TEM technique and generating topographic contrasts for three dimensional imaging at a very high magnification (~1,000,000x). Ultrathin chromium (Cr) films generate enriched high resolution SE-I contrasts of enamel crystal surfaces and when imaged using an immersion lens field emission SEM operated at high voltage (20 - 30 KeV) produced unsurpassed topographic contrasts. Since the grain size of Cr is below the resolution of any SEM and is ultrathin (~1 nm) then SE-I images can provide a more accurate representation of enamel crystal structure than TEM methodologies.

Our SE-I SEM observations of normal human enamel crystals reveal fractured spicules which contain angled flat surfaces delineated by a prominent 2 nm wide SE-I edge brightness contrast. Although microscopic observations often show crystals which are hexagonal in cross-section, in both SEM and TEM many other growth habits, including rectangular or irregular crystals (30-40 nm in width) which contain "notches", are also observed. More detailed

morphological studies are therefore required to determine the most likely habit planes and their relevance to the function of the enamel crystals. The granular appearing fine structural contrast imposed onto <100> lattice planes of sectioned enamel in TEM micrographs is also resolved with topographic contrasts in SE-I micrographs. These granules probably represent one or both of the enamel protein classes.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Neurobehavioral responsivity of neonatal nursery-reared chimpanzees.

AXIS I: 1a, 21, 25, 36

AXIS II: 60, 65, 71

PRC UNIT: Reproductive Biology

INVES1: Bard, Kim A.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: O

INVES2: Platzman, Kathleen A.
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF2: O

INVES3: Suomi, Stephen J.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: O

INVES4: Swenson, R. Brent
DEGREE4: D.V.M.
DEPT4: Veterinary Medicine
STAFF4: C

INVES5: Lester, Barry M.
DEGREE5: Ph.D.
DEPT5:
STAFF5: O

SPECIES 1: Pan troglodytes
NUM1: 7

NON-HOST INSTITUTION: NICHD, Laboratory of Comparative Ethology, Bradley Hospital and Brown University.

ABSTRACT: From January 1989 through December 31 1989, 7 chimpanzee infants were placed in the nursery due to inadequate maternal care. The neurobehavioral integrity of these infants has been assessed with the Brazelton Neonatal Behavioral Assessment Scale (BNBAS) (Brazelton, 1984). When comparisons are made with human infants striking similarities are found in the following areas: capacity for attention to visual and auditory, social and nonsocial stimuli; motor activity, coordination, and muscle control; autonomic nervous system stress. Significant differences between the species were found in two clusters of behavior related to infant state. Human infants reach a higher level of arousal and undergo more behavior state changes during the course of the examination than do chimpanzee neonates. Chimpanzee infants maintain a quiet alert state throughout the examination. Moreover, chimpanzee neonates utilize their own behaviors, or those of the examiner, to regulate their state to a greater extent than do human infants.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Attachment in nursery-reared chimpanzees: Ainsworth Strange Situation.

AXIS I: 1a, 36

AXIS II: 60, 71

PRC UNIT: Reproductive Biology

INVES1: Bard, Kim A.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: O

INVES2: Platzman, Kathleen A.
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF2: O

INVES3: Suomi, Stephen J.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: O

INVES4: Swenson, R. Brent
DEGREE4: D.V.M.
DEPT4: Veterinary Medicine
STAFF4: C

SPECIES 1: Pan troglodytes
NUM1: 5

NON-HOST INSTITUTION: NICHD, Laboratory of Comparative Ethology.

ABSTRACT: The quality of attachment in five nursery-reared chimpanzees have been assessed using the Ainsworth Strange Situation. This research is ongoing. Each individual was tested with his or her favorite caregiver as the 'mother', a completely unknown female as the stranger, and the research team of the primary investigator and 3 research assistants participating as the experimenter, videotaper, companion for the nontested individuals, and observer. Analyses have begun to document (1) the use of the attachment figure as a secure base from which to explore a novel and interesting room; (2) behavioral distress to brief separations from the caregiver; and (3) differential responses to the caregiver and the stranger, including immediate and sustained clinging to the caregiver upon reunion and behavioral avoidance when alone with the stranger. When analyses are completed a comparison of the classification of security of attachment for chimpanzees and humans will be possible.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Social learning of tool use in chimpanzees.

AXIS I: 1a, 36

AXIS II: 41, 60

PRC UNIT: Reproductive Biology

INVES1: Bard, Kim A.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: 0

INVES2: Tomasello, Michael
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: 0

INVES3: Suomi, Stephen J.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: 0

INVES4: Visalberghi, Elisabetta
DEGREE4: Ph.D.
DEPT4: Behavioral Biology
STAFF4: 0

INVES5: Fragaszy, Dorothy
DEGREE5: Ph.D.
DEPT5: Behavioral Biology
STAFF5: 0

SPECIES 1: Pan troglodytes
NUM1: 4

NON-HOST INSTITUTION: NICHD, Laboratory of Comparative Ethology, CNR, Instituto di Psicologia.

ABSTRACT: This study was designed to investigate 1) the development of the ability to use a simple tool; 2) the cognitive substrate necessary for tool use; 3) and a comparison of the learning process when the task is learned by individual trial-and-error and when the task is learned through social observation. To date 2 chimpanzees have been used for pilot testing and 2 chimpanzees have been tested. This is research in progress. The 3-1/2-year-old learned to use a tool through trial-and-error learning in 25 trials. Subsequent errors lead to the conclusion that he lacked a mental representation of the characteristics necessary to solve the task. The second chimpanzee, a 2-year-old, learned to use a tool through trial-and-error learning in over 150 trials and also demonstrated a lack of mental representation with regard to solving the tool task.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Foundations of parenting in chimpanzees: Intuitive parenting.

AXIS I: 1a, 36

AXIS II: 60, 71

PRC UNIT: Reproductive Biology

INVES1: Bard, Kim A.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: 0

INVES2: Papousek, Hanus
DEGREE2: M.D.
DEPT2:
STAFF2: 0

INVES3: Suomi, Stephen J.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: 0

SPECIES 1: Pan troglodytes
NUM1: 4

NON-HOST INSTITUTION: NICHD, Laboratory of Comparative Ethology, Center for Social Pediatrics, Munich FRG.

ABSTRACT: In order to investigate the foundations of intuitive parenting, 4 additional mother-reared chimpanzees have been videotaped from birth through 3 months of age. Mutual eye gaze between mother and infant chimpanzee has been documented. Interactions which lead to infant smiles have been observed at 14 days of age and infant laughter is heard between 6 and 8 weeks of age. Chimpanzee mothers do engage their infants in interactive contexts; they provide stimulation which is similar in content to that provided by human mothers to their babies.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Conservation of Non-Human Primates in Belize, Central America

AXISI: 1a, 23

AXISII: 34, 78

PRC UNIT: Reproductive Biology

INVES1: Dahl, J.F.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: 0

SPECIES1: A. pigra
NUM1: (non-captive)

SPECIES2: A. geoffroyi
NUM2: (non-captive)

ABSTRACT: The objectives of this on-going project concern three related areas of effort: (1) The in-field training of Belizean Nationals in the methods of techniques of primate habitat evaluation, surveying, and censusing; (2) Censusing the population of Baatz, areas totalling 55 sq. km., and surveying the same areas for the occurrence of Spider Monkeys (Alouatta pigra luctuosa); (3) Obtaining preliminary data and materials on the reproductive behavior and physiology of the Baatz pertinent to a long-term, detailed study of reproduction. Data on the daily activity pattern of the Baatz are being collected as an adjunct to the results of previous work showing that this species of ceboid is active during the night as well as the day. This is of significance to a better understanding of New World Monkey biology and primate evolution, but is particularly relevant to the design of a study of reproductive behavior as this work will necessitate an ability to monitor the animals' sexual activities at night as well as the day. One practical aim is to evaluate our identified adult females for which the variable program was designed for Forest Officers of the Belizean Government; relatively new deforestation pressures, of both a legal and illegal nature, require that Forest Officers acquire new skills in order to enforce regulations.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Freeze Preservation of Primate Semen

AXIS I: 1a, 2, 23

AXIS II: 60, 65

PRC UNIT: Reproductive Biology

INVES1: Gould, K.G.
DEGREE1: B.Vet.Med. Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

SPECIES1: Pan troglodytes
NUM1: 6

ABSTRACT: Semen from the human and a number of domestic species has been successfully cryopreserved for a number of years. However, application of this technology to nonhuman primate species has been less successful. We have used a number of freeze patterns and cryoprotectants in an empirical study designed to identify an effective method for cryopreservation of chimpanzee and gorilla sperm. Different methods have been compared by subjective, and computer assisted quantitative analysis of sperm motility and viability; by indirect measurement of potential fertilizing capacity using the hamster zona free oocyte penetration assay; and by the initiation of pregnancy using thawed chimpanzee sperm. Thus far, the best results have been obtained using a final concentration of 7.8% Glycerol in a medium of Ham's F10 plus 15% heat inactivated human cord serum. Semen frozen by this method has been used to initiate three pregnancies, two of which have gone to normal term.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Seasonal Change In Semen Parameters in the Chimpanzee Associated with Fertilizing Capacity

AXIS I: 1a, 2, 23

Axis II: 60, 65

PRC UNIT: Reproductive Biology

INVES1: Gould, K.G.
DEGREE1: B.Vet.Med. Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

SPECIES1: Pan troglodytes
NUM1: 4

ABSTRACT: The fertility, and productivity, of a male is related to the semen quality of that male. Fertility of a given male, as defined by the probability of successful impregnation of a female, resulting in pregnancy, is crucially important in the management of endangered or threatened species. Data was obtained from four proven fertile males over a 15 month period. Correlation was sought between the season of semen recovery and semen quality, and between semen quality and concurrent fertility as measured by birth rate in the total colony.

Semen was collected by use of an artificial vagina (AV) from four adult male chimpanzees of proven fertility (i.e., had sired offspring by natural mating). Semen was collected intermittently (>3 x / month) during the months of February to December. Fresh semen samples were collected, recovered from the AV, and prepared as described previously. After collection and preparation, semen samples were videotaped, and the videotape records analyzed using a Motion Dynamics VP100 system.

Measured semen parameters varied between individual males, and with season. There was no significant correlation between measured parameters, from potentially normal males, and seasonal fertility. Thus, the numbers obtained here demonstrate a minimal range to be considered "normal", as evidenced by fertility.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Identification of HIV in Chimpanzee Semen

AXIS I: 1a, 2, 23
AXIS II: 60, 65

PRC UNIT: Reproductive Biology

INVES1: Gould, K.G.
DEGREE1: B.Vet.Med. Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

INVES2: McClure H.M.
DEGREE2: DVM.
DEPT1: Pathology & Immunology
STAFF2: C

INVES3: Fultz P.
DEGREE3: Ph.D.
DEPT3: Pathology & Immunology
STAFF3: C

SPECIES1 Pan troglodytes
NUM1: 4

ABSTRACT: As a result of interest in the localization of HIV in semen, and in the route used for its entry to semen, a study is underway to determine the amount of HIV in the semen of HIV infected male chimpanzees, and the degree to which that virus enters the semen via accessory gland secretions vs. the epididymis. Semen is collected by standard RPE techniques and the amount of virus determined by coculture techniques. Subsequent to this baseline determination, the males are reversibly vasectomised by vas occlusion, and the presence of HIV in the semen reestablished. Correlation will be sought between the amount of virus in the semen, its location with regard to seminal components, and the alteration in virus concentration with fertility status of the male.

If positive correlations are detected, then micropuncture of the epididymis will be undertaken to establish the cells within the eppididymis associated with the HIV.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Artificial Breeding of Chimpanzees

AXIS I: 1a, 2, 23

Axis II: 60, 65

PRC UNIT: Reproductive Biology

INVES1: Gould, K.G.
DEGREE1: B.Vet.Med. Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

SPECIES1: Pan troglodytes
NUM1: 8

ABSTRACT: The overall objective of the program is to establish artificial breeding of chimpanzees as an effective method for increasing birth rates at facilities in the USA which house this species. Three specific goals have been set:

To improve the effectiveness of artificial insemination methodology by careful evaluation of hormonal treatments used to induce ovulation; by identification of optimum route for insemination; and by determination of the optimum sperm count and quality needed;

To improve methods for cryopreservation of chimpanzee semen as determined by direct and indirect methods for evaluation of semen fertilizing capacity;

To establish and maintain a semen bank for frozen specimens.
Once developed and ongoing, this artificial breeding program will: 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. Also important is the maintained integrity of the captive population by maintenance of the gene pool.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Blood Chemistries in the Western Lowland Gorilla

AXIS I: 1a, 2, 23

AXIS II: 60, 65

PRC UNIT: Reproductive Biology

INVES1: Gould, K.G.
DEGREE1: B.Vet.Med. Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

SPECIES1: Gorilla gorilla
NUM1: 73

ABSTRACT: A continuing problem with the application of sophisticated biomedical techniques to the maintenance of a healthy population of great apes is the paucity of relevant baseline data. The relevant values for a number of routinely assayed blood chemistry parameters as applicable to the lowland gorilla *(Gorilla gorilla gorilla)* have been collected and collated. The database was obtained from a total of 227 measurements from 73 animals in the North American Continent. When there was no apparent significant change with age or sex in a parameter it has been recorded as a mean ± S.D. in tabular form. When there was a significant relationship between age and/or sex with a measurement, the data has been preserved in a form which permits identification of the nature of the age and/or sex related variation. This data should not be interpreted as representative of the "ideal" chemistry for the captive gorilla. Rather it represents normative data for the successfully maintained captive population. This data remains to be duplicated in the wild population, and until such comparison is available, caution is required regarding relation of these values to the wild situation or to the 'natural' gorilla. The data presently available is derived from an apparently healthy population, and can be readily used for comparative purposes with regard to normal husbandry of the captive population.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Temperature Telemetry of the Pregnant Chimpanzee

AXIS I: 1a, 2, 23

AXIS II: 60, 65

PRC UNIT: Reproductive Biology

INVES1: Gould, K.G.
DEGREE1: B.Vet.Med. Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

SPECIES1: Pan troglodytes
NUM1: 4

ABSTRACT: There is still a significant neonatal loss of infant apes associated with prolonged and/or abnormal delivery. In addition, some inexperienced mothers do not care adequately for the newborn offspring. In order to reduce this problem we are developing an intravaginal radiotelemetry system for monitoring of the intravaginal temperature. At the time of delivery the temperature transmitter is expelled and the resulting drop in temperature is used to alert medical personnel that delivery is imminent. Micro transmitters, operating on 27.695MHz have been configured to provide up to a 50' transmission range. They have been encapsulated in sponge material of size and design suitable for retention in the vagina. Preliminary tests have been conducted using four non-pregnant animals. We are evaluating other methods for encapsulation of the transmitters, which will be tested in further non-pregnant and pregnant animals in the coming year.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Influence of Premarin and Somatotropin on Bone Loss in GnRH Agonist Treated Monkeys.

AXISI: 1a, 15, 23

AXISII: 60, 74e

PRC UNIT: Reproductive Biology

INVES1: Mann, David
DEGREE1: Ph.D.
DEPT1: Physiology
STAFF1: O

INVES2: Gould, Kenneth
DEGREE1: Ph.D., D.V.M.
DEPT2: Reproductive Biology
STAFF2: O

SPECIES1: Macaca fascicularis
NUM1: 37

ABSTRACT: We have been examining the feasibility of using the gonadotropin releasing hormone (GnRH) agonist-treated monkey as a primate model for postmenopausal bone loss. Thirty-seven female monkeys have been divided among five treatment groups, including vehicle, GnRH agonist, GnRH agonist plus Premarin, GnRH agonist plus somatotropin and GnRH agonist plus Premarin plus somatotropin. Animals are being maintained on a calcium diet which provides 10 mg/kg BW/day of calcium (equivalent to daily calcium intake/day in women). The effect of the various treatment regimes on bone mass and histology, and serum levels of calcium, osteocalcin, estradiol, progesterone and intact PTH are being monitored to assess the effect of the loss of ovarian function (induced by the GnRH agonist) on bone metabolism. It is hoped that the GnRH agonist-treated female monkey will serve as a model to test the efficacy of experimental approaches for treating postmenopausal bone loss.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Influence of a GnRH antagonist (Antide) on LH and Testosterone Secretion and Sexual Behavior in Adult Male Monkeys.

AXISI: 1a, 15, 23

AXISII: 60, 74e

PRC UNIT: Reproductive Biology

INVES1: Mann, David
DEGREE1: Ph.D.
DEPT1: Physiology
STAFF1: O

INVES2: Wallen, Kim
DEGREE2: Ph.D.
DEPT2: Psychology
STAFF2: C

SPECIES1: Macaca mulatta
NUM1: 7

ABSTRACT: We have been assessing the effect of a potent GnRH antagonist on LH and testosterone secretion, the response to GnRH and sexual behavior in seven adult male Macaca mulatta. Blood samples were taken twice weekly during the pretreatment period and over the 10-week period following Antide injection. Animals were treated with a single sc injection of 15 mg/kg BW of Antide. Animals were challenged with GnRH (50mg/kg BW) during the pretreatment period and at 2, 4 and 8 weeks after Antide administration.

Plasma levels of LH and testosterone are being correlated with changes in sexual behavior resulting from administration of the antagonist in an attempt to better understand the endocrine mechanism regulating male sexual behavior.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Neonatal Testosterone and Primate Sexual Development

AXISI: 1a, 15, 23

AXISII: 60

PRC UNIT: Reproductive Biology

INVES1: Mann, David
DEGREE1: Ph.D.
DEPT1: Physiology
STAFF1: O

INVES2: Wallen, Kim
DEGREE2: Ph.D.
DEPT2: Psychology
STAFF2: O

INVES3: Gould, Kenneth
DEGREE3: Ph.D., D.V.M.
DEPT3: Reproductive Biology
STAFF3: C

SPECIES1: Macaca mulatta
NUM1: 30

ABSTRACT: We have evidence suggesting that neonatal activation of the pituitary-testicular axis is a critical event in the process of sexual and behavioral maturation in male primates. Monkeys treated as neonates with a gonadotropin-releasing hormone (GnRH)-agonist to suppress testicular function exhibited differences in social behavior during the second year of life, a delay or retardation of testicular development during the peripubertal period and reduced male mountings during the non-breeding season of their third year of life. The proposed study is an effort to expand our understanding of the importance of neonatal testosterone as an organizational influence on sexual and behavioral processes in male primates. There are two components to this proposal: an adult component involving 5-year-old male monkeys treated as neonates with a GnRH-antagonist. With the adult component, we will determine whether the deleterious effects of suppressing neonatal pituitary-testicular function on sexual development are transient or permanent and assess whether adult sexual and aggressive behavior under conditions of high and low intermale competition are altered by neonatal treatment with a GnRH-analogue. Efforts will be made to define the site(s) (hypothalamus, pituitary or testis) of the physiological defect and determine whether the FSH-inhibin negative feedback loop is functionally normal in GnRH-agonist-treated monkeys. We will also perform a detailed evaluation of the fertility of these animals. In the infant component, we will attempt to confirm the effect of blocking neonatal activation of the pituitary-testicular on sexual maturation using a GnRH-antagonist. The importance of neonatal testosterone in this process will be assessed by treating one group of infants simultaneously with the GnRH-antagonist and testosterone. The effect of treatment on the developmental pattern of pituitary and gonadal hormone secretion, on growth and maturation of the skeletal system and on sexual maturation will be

determined. The development of male typical behavior and adult sexual behavior will be compared between animals treated with the GnRH-antagonist alone or in combination with testosterone therapy. The proposed study will with testosterone therapy. The proposed study will increase our understanding of developmental mechanisms that govern sexual and behavioral development in male primates and the role that neonatal testosterone plays in this process .

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Rehabilitation of Reproductive Function in Paraplegic Males

AXIS I: 1a, 5b, 9, 23, 27

AXIS II: 52, 70

PRC UNIT: Reproductive Biology

INVES1: Martin, David E.
DEGREE1: PhD
DEPT1: Reproductive Biology
STAFF1: 0

INVES2: Warner, Harold
DEGREE2: Emeritus Prof.
DEPT2: Biomedical Engineering
STAFF2: 0

INVES3: Perkash, Inder
DEGREE: MD
DEPT3: (V.A. Medical Center, Palo Alto)
STAFF3 0

SPECIES1: Pan troglodytes
NUM1: 3

SPECIES2: Homo sapiens
NUM2: 10 (V.A. Medical Center, Palo Alto)

NON-HOST INSTITUTION: V.A. Medical Center

ABSTRACT: This study has involved the development of a device to permit production of erection and semen collection through rectal probe electrostimulation (RPE). This technology was originally conceived for use in semen collection among great apes, but its efficacy of use in spinal cord injured human males, whose considerably reduced sensorium permits tolerance to electrical current delivery required for semen collection, has resulted in our efforts to refine the device for human use. A recent refinement has included the addition of a battery option to permit RPE without direct connection to the electrical mains. Another refinement has been the development of computer-driven circuitry. This provides consistently uniform stepwise increases in electrical stimulation. Previously, stimulus envelopes of gradually increasing intensity were created manually, with poorer repeatability. Extensive pre-testing of various RPE prototypes, using chimpanzees as animal models, increased the rapidity with which such design features could be visualized and implemented for use in the human patient setting. Favorable preliminary results have been forthcoming in at least two areas. The first is increased safety and ease of operation of the device. The second is the ability to hover for short time periods around selected submaximum current levels, just below the level of patient discomfort and/or spastic lower limb activity, which are adequate for stimulating ejaculation. Our success rate of producing seminal emissions has thus risen to virtually 100 percent. In turn, this has permitted greater opportunity to grapple with the continuing need to improve sperm motility (typically low) in collected

specimens if they are to be used successfully in artificial insemination.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Effects of Diet on the Oxidation of Estrogens in the Chimpanzee

AXIS I: 1a, 16, 23

AXIS II: 57, 74e, 78

PRC UNIT: Reproductive Biology

INVES1: Musey, P.I.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: O

INVES2: Collins, D.C.
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF2: O

INVES3 Gould, K.G.
DEGREE3: B.Vet.Med. Ph.D.
DEPT3: Reproductive Biology
STAFF3: C

SPECIES1: Pan troglodytes
NUM1: 4

NON-HOST INSTITUTION: Atlanta University, V.A. Medical Center

ABSTRACT: The oxidation of estrogens occurs primarily at Carbon-2 (C-2) and Carbon 16 (C-16) to produce catechol estrogens and estriols, respectively. We have studied the effects of diet on the relative rates of oxidation of 17ß-Estradiol at Carbon-2 and Carbon-16 in chimpanzees. The animals were studied longitudinally for a period of 12 weeks on each diet. The diets were a random sequence of normal laboratory monkey chow, high carbohydrate, high fat, high protein, high vegetable and high fiber diets. After 6-8 weeks on each diet, [16-^{3}H]-E_2 was injected intravenously and blood samples were taken at 0.5, 1, 2, 3, 4, 24, and 48 hr. The protocol was repeated 4 days later after injection of [2-^{3}H]-E_2. Blood samples were lyophilized and the ^{3}H released into body water was counted to assess the extent of E_2 metabolism at C-2 and C-16. The patterns of E_2 oxidation were similar in all the animals. Following exposure to high vegetable, high carbohydrate, and high fiber diets, oxidation at C-2 exceeded that at C-16. The rates of oxidation were reversed in all animals maintained on a high fat or a high protein diet. These data support the hypothesis that diet has a profound effect on the relative rates of oxidation of estrogens at C-2 and C-16. Oxygenation at C-2 is thought to reduce peripheral estrogen action (protective factor) while C-16 oxygenation maintains estrogen action (risk factor). Oxygenation at C-2 was used to calculate the relative protective factor (C-2 oxygenation of test diet/C-2 oxygenation of normal diet). The relative protective factors were 0.94 for high vegetable; 0.75 for high carbohydrate; 0.50 for high protein; and 0.40 for high fat diets. Oxygenation at C-16 was similarly used to calculate the relative risk factors (C-16 oxygenation of test diet/C-16 oxygenation of normal diet). The relative risk factors were 1.5 for high vegetable; 2.5 for high carbohydrate; 6.0 for high protein; and 12.0 for high fat diets. Only

the fat content of each diet was correlated (r=0.95) with the risk factor.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Nonreproductive Mating of the Chimpanzee

AXIS I: 1a, 15, 23

AXIS II: 36

PRC UNIT: Reproductive biology

INVES1: Nadler, Ronald D.
DEGREE1: Ph.D.
DEPT1: Reproductive biology
STAFF1: C

INVES2: Dahl. Jeremy F.
DEGREE2: Ph.D.
DEPT2: Reproductive biology
STAFF2: 0

INVES3: Swenson, R. Brent
DEGREE3: D.V.M.
DEPT3: Veterinary medicine
STAFF3: C

SPECIES1: Pan troglodytes
NUM1: 4

ABSTRACT: The objective of the study is to determine the basis for mating in chimpanzees that serves no direct reproductive function, i.e., mating during the menstrual cycle that is temporally dissociated from the day of ovulation and mating during pregnancy. Two versions of the restricted-accesss test (RAT) are used, the RAT with male control over access (RATm) and the RAT with female control over access (RATf). The RATm is used to test the hypothesis that the male's mating initiative, both during the menstrual cycle and during pregnancy, is artificially stimulated by specific aspects of the conditions of testing in the traditional laboratory pair-test, the free-access test (FAT). The RATf is used to test the hypothesis that the female's mating during pregnancy in the FAT reflects acquiescence under duress from the male. Urine for hormone assay (estrone, pregnanediol and testosterone glucuronide and creatinine) is collected from the male and female to assess the hormonal correlates of behavior. Clarification of the basis for matng initiative in chimpanzees should suggest methods of breeding that are more compatible with the species' natural inclinations regarding mating. The use of more natural methods of breeding chimpanzees should improve their behavioral well-being and enhance their propagation in captivity.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Mother-Infant Relations and Lactational Amenorrhea in Gorillas.

AXIS I: 1a, 15, 23

AXIS II: 36, 60, 71

PRC UNIT: Reproductive Biology

INVES1: Nadler, Ronald D.
DEGREE1: Ph.D.
DEPT1: Reproductive biology
STAFF1: C

SPECIES1: Gorilla gorilla
NUM1: 8

ABSTRACT: The objectives of the research are to clarify several issues pertinent to the breeding and propagation of gorillas in captivity; 1) the critical parameters of suckling for the maintenance of lactational amenorrhea (LA) and determination of the interbirth interval, 2) maternal hormone patterns associated with LA, 3) the influence on mother-infant relations of age, parity and dominance rank of the mother and sex of the infant, 4) the changing social and spatial relationships among the mother, infant and others, especially the leading male, 5) the hormonal and/or behavioral basis for predicting maternal rejection or abuse of the infant, and 6) affiliative behavior and male parental investment. These issues are investigated using routine observational procedures and the analysis of urinary hormone levels. The research is conducted in relatively normal social groups living in the semi-natural habitats at Zoo Atlanta. Clarification of these issues should contribute to a broader comparative perspective on the regulation of mother-infant relations in primates and facilitate the breeding of gorillas in captivity.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Correlated Microscopic Observations of Arterial Responses to Intravascular Stenting

AXIS I: 1a, 3, 9, 12a

AXIS II: 46, 50, 52, 70, 74f, 86

PRC UNIT: Reproductive Biology

INVES1: Robinson, K. A.
DEGREE1: PhD
DEPT1: Interventional Cardiology E.U.
STAFF1: 0

INVES2: Roubin, G
DEGREE2: MD
DEPT2: Interventional Cardiology E.U.
STAFF2: 0

INVES3: King, S
DEGREE3: MD
DEPT3: Interventional Cardiology E.U.
STAFF3: 0

INVES4: Siegel, R
DEGREE4: MD
DEPT4: Clinical Pathology E.U.
STAFF4: 0

INVES5: Rodgers, G
DEGREE5: MD
DEPT5: Cardiology Baylor College of Medicine
STAFF5: 0

INVES6: Apkarian R.P.
DEGREE6: MA
DEPT6: SEM Facility/Repro. Bio. Yerkes
STAFF6: 0

SPECIES2: Oryctolagus caniculus
NUM2: 36

SPECIES3: Sus scrofa
NUM3: 16

SPECIES1: Canis familiarus
NUM1: 39

NON-HOST INSTITUTION: Baylor College of Medicine

ABSTRACT: Percutaneous catheter implantation of intravascular stent prostheses has emerged as a novel clinical adjunct to balloon angioplasty in the treatment of obstructive atherosclerotic vascular disease. We have examined the cellular and subcellular responses to stenting in the coronary

arteries of the dog and pig (both normal and atherosclerotic), and in the iliac arteries and aorta of the atherosclerotic rabbit, using scanning electron, transmission electron, and light microscopies. Stenting in these models resulted in a thrombotic reaction ranging from mild to severe, depending on species and antithrombotic therapy. Subsequent organization of thrombotic material with hyperplasia of smooth muscle and inflammatory cells, luminal recovering with endothelial and pseudoendothelial cells, and atrophy of the tunica media led to incorporation of the prosthesis into the arterial wall. Endothelial or pseudoendothelial cells were observed adherent to the prosthesis as early as one day after placement, and regeneration of a confluent periluminal cell layer occurred within 2 to 4 weeks. Persistent ultrastructural abnormalities of the periluminal cell layer were seen as late as 2 years after stenting, but the intimal hyperplastic response appeared limited.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Luminal Surface Ultrastructure of Porcine Coronary Artery Endothelium in Experimental Atherosclerosis

AXIS I: 1a, 13

AXIS II: 74f

PRC UNIT: Reproductive Biology

INVES1: Robinson K. A.
DEGREE1: PhD
DEPT1: Interventional Cardiology (Dept of Medicine)
STAFF1 0

INVES2: Apkarian, R. P.
DEGREE2: MA
DEPT2: SEM Facility Repro. Bio. Yerkes
STAFF2: 0

INVES3: King III, S.B.
DEGREE3: MD
DEPT3: Interventional Cardiology (Dept of Medicine)
STAFF3: 0

SPECIES1: Sus scrofa
NUM1: 8

ABSTRACT: Increased transport of macromolecules such as low-density lipoprotein cholesterol (LDL) by arterial endothelium is known to occur in atherogenesis. LDL uptake and transport by endothelial cells (EC) involves coated and uncoated pits and vesicles, respectively. Using transmission electron microscopy and high resolution scanning electron microscopy, we obtained morphologic evidence of a close spatial association between luminal surface pits (60-80 nm diameter) and EC surface-adherent chylomicron sized structures (260-380 nm) in native and regenerated (after arterial injury) coronary artery endothelium of hyperlipidemic swine. The adherent structures exhibited a particulate nature, with spheroidal subunits which ranged in size from 10 to 120 nm. Pits were more frequently observed in 4 week regenerated compared to native endothelium, as were other EC ultrastructural abnormalities such as elaborate cell junctions and surface microvilli. The interaction between these elements may represent a mechanism for arterial wall accumulation of lipid and/or cholesterol from circulating components in hyperlipidemia, which appears to be augmented by arterial injury.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Inhibition of Coronary Arterial Thrombosis in Swine by Infusion of Poloxamer 188

AXIS I: 1a, 2, 12a, 13, 17

AXIS II: 50,86

PRC UNIT: Reproductive Biology

INVES1: Robinson, K. A.
DEGREE1: PhD
DEPT1: Interventional /Cardiology
STAFF1: 0

INVES2: Hunter, R. L.
DEGREE2: MD, PhD
DEPT2: Pathology
STAFF2: 0

INVES3: Stack, J. E.
DEGREE3: BS, MT
DEPT3: Pathology
STAFF3: 0

INVES4: Hearn, J. A.
DEGREE4: MD
DEPT4: Interventional/Cardiology
STAFF4: 0

INVES5: Apkarian, R. P.
DEGREE5: MA
DEPT5: SEM Facility Repro. Bio. Yerkes
STAFF5: 0

INVES6: Roubin, G. S.
DEGREE6: PhD, MD
DEPT6: Medicine
STAFF6: 0

SPECIES1: Sus scrofa
NUM1: 35

NON HOST INSTITUTION: University of Alabama at Birmingham (GSR)

ABSTRACT: Coronary artery thrombosis is a potential complication of both percutaneous angioplasty and intracoronary stenting. We assessed the efficacy of infusion of a saline solution of the copolymer poloxamer 188 for the prevention of coronary arterial thrombosis after stenting in a porcine model. Twenty-two normal juvenile pigs received a bolus injection of heparin (100 u/kg) and wire coil stents in the LAD, and were randomized to infusion of poloxamer 188 (bolus of 50 mg/kg followed by infusion of 25mg/kg/hour) or equivalent volume of 0.9% NaCl. Poloxamer 188 significantly inhibited thrombosis as determined by morphometry of arterial specimens (p=0.001). Copolymer infusion did not affect bleeding time or platelet aggregation, but

did reduce blood viscosity ($p=0.014$) Dosing studies in 13 additional pigs showed a modest drop in white blood cell count with copolymer injection which may reflect intravascular leukocyte margination. In contrast to published studies with fluorocarbon emulsions containing poloxamer 188 a marked drop in neutrophil count attributable to activation of complement was not observed. These data suggest that poloxamer 188 may prove useful as a component of thrombopreventative therapy during coronary interventions.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: LM, TEM and SEM Observations on Deembedded, Osmium Macerated Biological Tissue Sections

AXIS I: 1a, 9, 12a
AXIS II: 70

PRC UNIT: Reproductive Biology

INVES1: Scala, C
DEGREE1: MD
DEPT1: Institute of Clinical Electroncroscopy
STAFF1: 0

INVES2: Cenacchi, G
DEGREE2: MD
DEPT2: Institute of Clinical Electron Microscopy
STAFF2: 0

INVES3: Apkarian, R.P.
DEGREE3: MA
DEPT3: SEM Facility, Repro. Bio. Yerkes
STAFF3: 0

INVES4: Preda, P
DEGREE4: MD
DEPT4: Institute of Clinical Electron Miscroscopy
STAFF4: 0

INVES5: Pasquinelli, G
DEGREE5: MD
DEPT5: Institute of Clinical Electron Microscopy
STAFF5: 0

SPECIES1: Ratus ratus
NUM1: 6

NON-HOST INSTITUTION: University of Bologna (CS, GC, PP, GP)

ABSTRACT: A method facilitating correlation of LM, SEM and TEM images has been developed. Rat kidney and heart were initially subjected to the osmium maceration procedure and them embedded in a mixture of acetone-soluble acrylic resin. Glass knife sectioning of the tissue blocks provided semithin sections for LM and ultrathin sections for TEM. After resin removal, both semithin and ultrathin sections were examined by SEM. The three dimensional images of intracellular organelles provided an informative adjunct to LM and TEM. Furthermore, sectioned materials were particularly suitable for continuous, thin metal film deposition by using fine-grained sputtered chromium.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Prolonged Lactational Infertility During Adolescence

AXISI: 1a, 2, 15, 23, 36

AXISII: 60, 71

PRC UNIT: Reproductive Biology

INVES1: Wilson, Mark E.
DEGREE1: PhD
DEPT1: Reproductive Biology
STAFF1: C

INVES2: Gordon, Thomas P.
DEGREE2: MS
DEPT2: Behavioral Biology
STAFF2: C

SPECIES1: Macaca mulatta
NUMBER1: 40

ABSTRACT: Adolescent rhesus monkey mothers experience a prolonged period of lactational infertility following their first parturition. Studies were designed to determine whether adolescent mothers were more sensitive to the inhibition of suckling on the reproductive system. Mothers and infants were housed socially in outdoor compounds. By 20 weeks of age, infants are capable of sustaining normal growth by ingesting monkey chow and fresh fruit. Nevertheless, infants at this age still nurse sufficiently to inhibit reproduction. In order to determine how a brief interruption in nursing would affect pituitary gonadotropin and gonadal steroid secretion in adolescent mothers, adult (MU; n = 12) and adolescent (PU; n = 11) which had nursing unrestricted were compared to adult (MR; n = 8) and adolescent (PR; n = 9) mothers which had nursing restricted for a two period. This was accomplished by the mothers wearing a denim vest which block infant's access to nursing. Infant growth rates were unaffected by the treatment. Nursing restriction significantly increased serum levels of estradiol in PR mothers, similar to those found in MU and MR mothers. In contrast, concentrations of estradiol and gonadotropins were significantly lower in PU mothers. These data suggest that nursing restriction at this point in lactation has no effect on the reproductive system in adult females. Furthermore, the data indicate that adolescent mothers are exquisitely sensitive to the inhibitory aspects of nursing on fertility. These studies will help describe the mechanism regulating contraceptive aspects of nursing and to define problems of infertility in adolescent females.

P5IRR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Hormonal and Seasonal Regulation of Puberty in Females

AXIS I: 1a, 2, 15, 23, 26

AXIS II: 54b, 60, 71

PRC UNIT: Reproductive Biology

INVES1: Wilson, Mark E.
DEGREE1: PhD
DEPT1: Reproductive Biology
STAFF1: C

INVES2: Gordon, Thomas P.
DEGREE2: MS
DEPT2: Behavioral Biology
STAFF2: C

SPECIES1: Macaca mulatta
NUMBER1: 48

ABSTRACT: Studies were completed during the current year describing how season influences reproductive maturation in female rhesus monkeys. Independent of environmental effects, the development of gonadotropin secretion is influenced by a nongonadal restraint mechanism followed in time by a decrease in hypersensitivity to estradiol negative feedback suppression. Following the suppression of gonadotropin secretion during the juvenile period in animals housed in a nonseasonal environment, concentrations increase in agonadal females significantly earlier than agonadal females treated with estradiol. The rise in gonadotropins in these estradiol treated females occurs at an age coincident with the age of menarche in gonadally intact females housed in a similar environment and is preceded in time by significant elevations in serum growth hormone (GH) and insulin-like growth factor-1 and skeletal growth. Treatment of females with GH advanced the decrease in hypersensitivity to estradiol negative feedback in gonadally-intact females but not agonadal, estradiol treated females, suggesting that some aspect of GH physiology may be the cue initiating the neuroendocrine changes regulating puberty.. These maturational events - elevation in serum gonadotropins, menarche, and first ovulation - is delayed in females housed outdoors in a seasonal environment. For outdoor housed females, these events are restricted to the fall months once the loss of nongonadal restraint has occurred. Furthermore, these events of puberty are restricted to the fall months regardless of the season of birth. Exposure to a "fall-day" melatonin pattern at an age when the reproductive system is seasonally inhibited, advances puberty, suggesting that the daily pattern of secretion of melatonin, in response to a changing photoperiod, may be the seasonal cue regulating these events. These studies have described how reproductive maturation and skeletal growth are linked and have provided insight into how puberty may be affected in children with growth disorders.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Growth Hormone Effects on Neonatal Growth

AXIS I: 1a, 2, 15, 17, 26
AXIS II: 60, 62, 65, 71, 77

PRC UNIT: Reproductive Biology

INVES1: Wilson, Mark E.
DEGREE1: PhD
DEPT1: Reproductive Biology
STAFF1: C

INVES2: Gordon, Thomas P.
DEGREE2: MS
DEPT2: Behavioral Biology
STAFF2: C

INVES3: Tanner, James M.
DEGREE3: MD
DEPT3:
STAFF3: O

INVES4: Rudman, Christopher G.
DEGREE4: PhD
DEPT4:
STAFF4: O

SPECIES1: Macaca mulatta
NUMBER1: 58

ABSTRACT: Low birth weight infants at extreme risk of not surviving. To alleviate this problem, treatments must be found to enhanced weight gains in utero and neonatally. The effects of growth hormone (GH) treatment to either mothers or nursing infants on neonatal growth in rhesus monkeys was determined in order to begin to address this critical question. In Experiment 1, growth rates of infants (n = 9; GHi) treated with GH (100g/kg, sc, M, W, F) were compared to infants administered saline (n = 10; CON) and infants (n = 5; GHm) of mothers who had been receiving GH (250 g/kg, sc, M, W, F) since immaturity. All infants were allowed to nurse ad lib throughout the study. Treatments were initiated for GHi and CON infants at birth whereas mothers of GHm infants had received GH throughout pregnancy. Birth weights were indistinguishable among the three groups. In contrast, weekly weight gains were accelerated in GHm infants such that at the completion of treatment at 12 weeks of age GHm infants were significantly heavier than GHi and CON infants. By 35 weeks of age, body weights were similar among all infants. Crown-rump, tibia and tail lengths, as well as abdominal skinfold thickness and skeletal maturity did not differ among the three groups. Serum concentrations of IGF-1 rose in all infants and predicted significantly the overall weight gain during the 12 week period. Experiment 2 further assessed the effects of GH treatment to mothers on neonatal growth rates. Growth rates of infants (CON; n = 9) whose mothers received physiological saline from the second trimester of pregnancy through 7 weeks postpartum were compared to infants (PRG; n = 8) of mothers which received GH during pregnancy only from the second trimester to parturition, infants (LAC; n = 9) of mothers which received GH during lactation only from

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Growth During Adolescence

AXIS I: 1a, 2, 15, 23, 26

AXIS II: 58, 60, 62, 71

PRC UNIT: Reproductive Biology

INVES1: Wilson, Mark E.
DEGREE1: PhD
DEPT1: Reproductive Biology
STAFF1: C

INVES2: Gordon, Thomas P.
DEGREE2: MS
DEPT2: Behavioral Biology
STAFF2: C

INVES3: Tanner, James M.
DEGREE3: MD
DEPT3:
STAFF3: O

INVES4: Rudman, Christopher G.
DEGREE4: PhD
DEPT4:
STAFF4: O

SPECIES1: Macaca mulatta
NUMBER1: 12

ABSTRACT: Administration growth hormone (GH) may be efficacious in the treatment of children with growth disorders but the long term effects are not known. In order to determine the long term effects of GH administration on the attainment of adult skeletal maturity and stature, female rhesus monkeys were treated with GH (250 g/kg given sc Mon, Wed, Fri; Genentech, Inc.) from 20 mo of age through 70 mo of age. Skeletal age was initially advanced in GH treated females (n = 6) compared to controls (n = 6) due to an earlier onset of puberty and consequent elevation of estradiol. Once the controls entered puberty, skeletal ages were similar and the incremental rate has not differed between the groups. Following 50 mo of GH treatment tibia lengths, as an index of long bone growth, were similar. Furthermore, 6/6 of GH treated females have reached adult skeletal maturity whereas 4/6 of the controls have reached that point at the same chronological age. In addition, crown-rump lengths in GH treated females were slightly yet significantly longer indicating that, even in these normal pituitary individuals, GH can enhance height. No adverse affect of GH treatment were observed on fertility, glucose metabolism, or blood chemistries. These data provide much needed information on the health effects of long term administration of GH.

P51RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Electrophoretic Studies of the Chimpanzee Sperm Surface

AXIS I: 1a, 23

AXIS II: 74, 83

PRC UNIT: Reproductive Biology

INVES1: Young, L.G.
DEGREE1: Ph.D.
DEPT1: Physiology
STAFF1: O

SPECIES1: Pan troglodytes
NUM1: 4

ABSTRACT: We used lactoperoxidase-catalyzed iodination and 1D-SDS-PAGE to characterize externally oriented macromolecules on the surface of intact chimpanzee sperm. Caput epididymal sperm showed nine, cauda epididymal sperm showed thirteen, and ejaculated sperm showed ten labeled proteins/glycoproteins with apparent molecular weights (Mr) between 92 and 11 Kd.

Six components labeled on caput sperm (Mr = 64, 57, 48, 38, 21, and 18 Kd) were detected on cauda sperm and on ejaculated sperm, and two (Mr = 0 and 15 Kd) were detected on cauda but not on ejaculated sperm. Of the five components labeled on cauda sperm, which were not labeled on caput sperm, two were detected on ejaculated sperm.

We used fluorescein isothiocyanate-labeled lectins (FITC-lectins), to visualize changes in the distribution and density of glycocomponents on the surface of chimpanzee sperm during epididymal maturation and after ejaculation. Pure suspensions of washed, unfixed sperm from the caput and cauda epididymis and from the ejaculate were labeled with FITC-Con A, -RCA-I, -DBA, or -WGA. Our studies demonstrate a wide variety of saccharide groups available for lectin binding on the sperm surface and this, together with the nonuniform distribution of these saccharide groups, suggest that a number of different domains exist within the chimpanzee sperm plasma membrane. Except for RCA-I, the pattern of carbohydrate residues exposed on the sperm remains relatively stable during epididymal transit.

We obtained additional information on chimpanzee sperm surface glycocomponents using peroxidase-labeled lectins to analyze the carbohydrate chain structures of ^{125}I-labeled membrane components separated in 1D-SDS-PAGE and transferred to nitrocellulose paper (Western Blots). It appears that Con A and WGA bind to 64, 57, 48, 34, and 27 Kd glycocomponents on cauda sperm and to 64, 57, 48, 38, 27, 18, and 13 Kd glycocomponents on ejaculated sperm and that DBA binds to a 57 Kd glycocomponent on cauda sperm and to 64, 57, 48, and 38 Kd glycocomponents on ejaculated sperm.

DIVISION OF ANIMAL RESOURCES

James G. Else, D.V.M., Head

Core Scientists

J.G. Else, D.V.M., Head of Animal Resources and Associate Research Professor

R.B. Swenson, D.V.M., Associate Research Professor and Chief of Veterinary Medicine, Yerkes Center

G.C. Choi, D.V.M., Assistant Veterinarian, Division of Veterinary Medicine and Research Associate of Pathobiology and Immunobiology, Yerkes Center.

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J.L. Orkin, D.V.M., Associate Veterinarian, Yerkes Center.

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Consultant

B.B. Gay, Jr., M.D., Consultant in Medicine, Yerkes Center; Professor of Radiology, Emory University.

E. Keener, M.D., Consultant in Medicine, Private Practice in Neurosurgery, Atlanta, Georgia

P5RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Tana River Primate Project

AXIS I: 1a, 8, 11

AXIS II: 34, 36, 54b

PRC UNIT: Animal Resources

INVES1: Else, James
DEGREE1: D.V.M.
DEPT1: Animal Resources
STAFF1: C

INVES2: Smith, Euclid O.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: C

INVES3: Struhsaker, Thomas
DEGREE3: Ph.D.
DEPT3:
STAFF3: O

INVES4: Tsingalia, Harrison
DEGREE4: Ph.D.
DEPT4: Zoology
STAFF4: O

INVES5: Njuguna, Stephen
DEGREE5: Ph.D.
DEPT5:
STAFF5: O

SPECIES1: Colobus badius
NUM1: 800 (wild)

SPECIES2: Cercocebus galeritus
NUM2: 1600 (wild)

SPECIES3: Papio cynocephalus
NUM3: 400

NON-HOST INSTITUTION: University of Florida (TS), University of Nairobi (HT), and National Museums of Kenya (SN)

ABSTRACT: The Tana River National Primate Reserve was gazetted in 1976 to protect the Lower Tana riverine (gallery) forests and two highly endangered primates, the Tana River Red Colobus (Colobus badius rufomitratus) and the Tana River Crested Mangabey (Cercocebus galeritus galeritus). When the primates were recensused in 1986 dramatic declines in both the colobus (80%) and mangabey (45%) were reported. Given the importance of the Tana Reserve, this resulted in immediately developing the Tana Primate Project to: (1)

determine the cause(s) for the decline in primate populations; (2) evaluate the status of the reserve in respect to its forest composition and effectiveness; and (3) recommend a management plan based on project findings.

The Tana Primate Project was spearheaded by the National Museums of Kenya (NMK), New York Zoological Society, Yerkes Primate Research Center and Emory University. Under the general direction of the Tana Management committee, a permanent camp was established in the reserve and a series of research projects were undertaken by scientists and students addressing the project aims.

P5RR00165-29 1/1/1989 - 12/31/1989 Yerkes Regional Primate Research Center

TITLE: Establishment of a Chimpanzee Breeding and Research Program

AXIS I: 1a, 23

AXIS II: 36, 60, 92 (breeding)

PRC UNIT: Veterinary Medicine

INVES1: Swenson, R. Brent
DEGREE1: D.V.M.
DEPT1: Veterinary Medicine
STAFF1: C

INVES2: Gould, Kenneth G.
DEGREE2: Ph.D., D.V.M.
DEPT2: Reproductive Biology
STAFF2: C

INVES3: Nadler, Ronald D.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: C

INVES4: Gordon, Thomas P.
DEGREE4: M.S.
DEPT4: Behavioral Neuroendocrinology
STAFF4: C

SPECIES1: Pan troglodytes
NUM1: 71

ABSTRACT: A dedicated breeding group of chimpanzees has been established that is expected to produce 8-12 healthy and behaviorally normal offspring per year which will be used to establish a stable, self-sustaining breeding population to guarantee future availability of these animals for behavioral and biomedical research programs. The breeding activities are conducted using an existing social group of chimpanzees, pair and harem matings, and artificial inseminations. Infants are managed in such a way as to maximize social experience, including mother-rearing, peer-group rearing when nursery care is required and fostering of nursery-reared infants onto competent mothers.

Research is also being done in areas that will promote improved reproductive success and improved behavioral outcome. This includes investigation of early detection of labor using telemetry; investigation of hormonal manipulation to shorten interbirth intervals without separating infants from their mothers; methods of gamete preservation to improve artificial breeding techniques; investigation of developmental criteria in infants that might be predictive of future reproductive performance and identification of early rearing techniques that are conducive to subsequent successful reproduction.

There were 9 chimpanzee births in 1989.

PART II, SECTION B1 GRANT NUMBER: P51RR00165-29

INVESTIGATORS WITH PUBLIC HEALTH SERVICE SUPPORT

CORE: X OTHER:

NAME	TYPE	AGENCY	GRANT/CONTRACT	TOTAL FUNDS	% RPRC USED
Ansari, Aftab A.	FED	NIH	AI-27057	$160,237	20
Boothe, Ronald G.	FED	NIH	EY-05975	119,987	100
Byrd, Larry D.	FED	NIDA	DA-01161	269,786	100
Fultz, Patricia N.	FED	NIH	AI-27136	140,086	100
Gould, Kenneth G.	FED	NICHD	HD-26076	75,611	100
	FED	DRR	RR-03587	79,437	100
	FED	DRR	RR-05102	15,000	100
	FED	BRSG	---	15,000	100
McClure, Harold M.	FED	NIH	AI-26055	71,519	100
	FED	NIH	RR00165-29S	1,564,657	100
	FED				100
Metzgar, Richard S.	FED	NIH	CA-32672	183,582	5
	FED	NIH	CA-47507	112,296	7
Swenson, R. Brent	FED	NIH	RR03591-04	341,449	100
Tigges, Johannes	FED	NIH	AG-00001	23,912	100
Wallen, Kim	FED	NIH	HD-26423	16,384	100
Wilson, James R.	FED	NIH	EY-04976	92,659	100
Wilson, Mark E.	FED	NIH	HD-16305	74,411	100
	FED	NIH	HD-18120	94,112	100
TOTAL PHS SUPPORT			This page:	$3,765,982	
			Grand Cumulative Total:	3,765,982	

INVESTIGATORS WITH PUBLIC HEALTH SERVICE SUPPORT

CORE: OTHER: X

NAME	TYPE	AGENCY	GRANT/CONTRACT	TOTAL FUNDS	% RPRC USED
Bakay, Roy A.E.	FED	VA	Merit Award	37,119	20
	FED	NIH	NS-24340	111,833	90
Berntson, Gary G. Ohio State Univ.	FED	NIH	MH-45460	32,000	25
Donahoe, Robert M.	FED	NIH	DA-04400	128,260	44
	FED	NIH	DA-04400-S1	30,620	44
Hanson, Stephen R.	FED	NIH	HL-31469	62,008	75
	FED	NIH	HL-31950	55,470	25
Harker, Laurence A.	FED	NIH	HL-31950	74,070	25
	FED	NIH	HL-41619	89,941	50
	FED	NIH	HL-41357	90,550	50
Howell, Leonard L.	FED	NIH	DA-05346	74,368	100
Iuvone, Michael	FED	NIH	EY-04864	125,850	5
Mann, David R. Morehouse School of Medicine	FED	NIH	HD-26423	115,042	50
Moss, Mark B. Boston University	FED	NIH	AG-04321	132,276	10
Peters, Alan Boston University	FED	NIH	AG-00001	44,542	20
Rumbaugh, Duane M. Georgia State Univ.	FED	NIH	HD-06016	681,325	100
Schinazi, Raymond F.	FED	NIH	AI-26055	456,587	18
Sommadossi, Jean-P. Univ. of Alabama	FED	NIH	HL-42125	164,986	1
Waring, George O.	FED	NIH	EY-07388	120,399	50

TOTAL PHS SUPPORT

This Page: $ 2,627,246
Grand (Cumulative) Total: $ 2,627,246

PART II, SECTION B2 GRANT NUMBER: P51RR00165-29

INVESTIGATORS WITH SUPPORT OTHER THAN PUBLIC HEALTH SERVICE

CORE: X OTHER:

NAME	TYPE	AGENCY	GRANT/CONTRACT	TOTAL FUNDS	%RPRC USED
Bernstein, Irwin Univ. of Georgia	FED	NSF	BNS-17650	70,000	100
Byrd, Larry D.					
Fultz, Patricia N.					
Gould, Kenneth G.	FED	IMS	IC-80042-88	26,500	40
Herndon, James G.					
King, Frederick A.					
McClure, Harold M.					
Metzgar, Richard S.					
Nadler, Ronald D.	FED	NSF	BNS-87-08406	74,000	100
Smith, Euclid O.					
Tigges, Johannes					
Tigges, Margarete					

TOTAL NON-PHS SUPPORT This page:
Grand (Cumulative) Total:

INVESTIGATORS WITH SUPPORT OTHER THAN PUBLIC HEALTH SERVICE

CORE: X (cont'd) OTHER:

NAME	TYPE	AGENCY	GRANT/CONTRACT	TOTAL FUNDS	%RPRC USED
Wallen, Kim	FED	NSF	BNS-86-07295	59,950	100
Wilson, James R.					
Wilson, Mark E.					

TOTAL NON-PHS SUPPORT This page:
Grand (Cumulative) Total:

PART II, SECTION B2

GRANT NUMBER:P5100165-29

INVESTIGATORS WITH SUPPORT OTHER THAN PUBLIC HEALTH SERVICE

CORE:

OTHER: X

NAME	TYPE	AGENCY	GRANT/CONTRACT	TOTAL FUNDS	%RPRC USED
Apkarian, Robert P.					
Boysen, Sally T. Ohio State Univ.	FED	NSF	BNS-8820027	100,000	25
Eberhard, Mark L. Centers for Disease Control					
Gouzoules, Harold T.	FED --	NSF	BNS-879230	100,000	100
Greene, Bruce M. Univ. of Alabama					
Harker, Laurence A.					
Iuvone, Michael					
Kennedy, Philip R. Georgia Tech.					
Malizia, Anthony A.					
Mann, David R. Morehouse School of Medicine					
Martin, David Ga. State University	FED	VA	V640P-4316	36,425	25
McCarey, Bernard E.					

TOTAL NON-PHS SUPPORT

This page: $

Grand (Cumulative) Total:$

INVESTIGATORS WITH SUPPORT OTHER THAN PUBLIC HEALTH SERVICE

CORE: OTHER: X (cont'd)

NAME	TYPE	AGENCY	GRANT/CONTRACT	TOTAL FUNDS	%RPRC USED
Waring, George					
Winton, Elliott F.					
TOTAL NON-PHS SUPPORT			This page:$ Grand (Cumulative) Total:$		

PART II, SECTION C BOOKS/PAPERS/ABSTRACTS GRANT NUMBER: P51RR00165-29

CORE: XXX

Number Published:	76	Books:	0	Papers:	41	Abstracts:	35
Number in Press:	26	Books:	0	Papers:	24	Abstracts:	2

*Anderson, D.C.: Infectious agents of man and nonhuman primates. Review of Agents Transmissible from Simians to Man, by M. Brock. Am. J. Primatol. 17:251-252, 1989.

*Anderson, D.C. and McClure, H.M.: Diseases and pathology of great apes at the Yerks Regional Primate Research Center. In: Scientific Program and Abstracts: Fertlity in the Great Apes, June 15-17, 1989, Atlanta, Georgia, p.10 (Abstract).

*Anderson, D.C., McClure, H.M., Ribas, J.L., Ansari, A., Fultz, P. and Mirra, S.: Neuropathological study of SIV-infected macaques. Proceedings of the Fifth International Conference on AIDS, Montreal, Canada, p.532, June 4-9, 1989 (Abstract).

*Ansari, A.A., Brodie, A.R., Fultz, P.N., Anderson, D.C., Sell, K.W. and McClure, H.M.: Flow microfluorometric analysis of peripheral blood mononuclear cells from nonhuman primates: Correlation of phenotype with immune function. Am. J. Primatol. 17:107-131, 1989.

*Ansari, A.A., Powell, J.D., Jehuda-Cohen, T., Villinger, F., Anderson, D. and McClure, H.M.: Delineation of peptide specific T cell immunity in SIV/SMM infected nonhuman primates using the Cellular Western Blot assay. Seventh Annual Symposium on Nonhuman Primate Models for AIDS, Portland, Oregon, October 11-13, 1989, p.70 (Abstract).

Bernstein, I.S.: Breeding colonies and psychological well-being. Am. J. Primatol. Suppl. 1:31-36, 1989.

Bernstein, I.S.: Cognitive explanation: Plausibility is not enough. Behav. Brain Sci. 12:593-594, 1989.

Bernstein, I.S.: Rhesus monkey colony management: A 1988 update - Yerkes Regional Primate Research Center. Lab. Primate Newsl. 28:9, 1989.

*Bernstein, I.S., Weed, J.L., Judge, P.G. and Ruehlmann, T.E.: Seasonal weight changes in male rhesus monkeys (Macaca mulatta). Am. J. Primatol. 18:251-257, 1989.

*Fultz, P.N.: The biology of human immunodeficiency viruses. In: The Epidemiology of AIDS: Expression, Occurrence and Control of the Human Immunodeficiency Virus Type 1 Infection, R.A. Kaslow and D.P. Francis, eds., Oxford University Press, New York, pp.3-17, 1989.

*Fultz, P.N.: Nonhuman primates and the acquired immunodeficiency syndrome: a union of necessity. J. Med. Primatol. 18:73-83, 1989.

*Fultz, P.N.: CD4 receptor binding and cytopathic effects of a lethal variant

of SIV/SMM. Annual Meeting of the Laboratory of Tumor Cell Biology, August 22-27, 1988, Bethesda, Maryland (Abstract).**

*Fultz, P.N., Anderson, D.C., McClure, H.M., Sonigo, P., Montagnier, L. and Stricker, R.B.: Virulence and variation of viruses: Coalition with cells, cytokines and simians. Annual Meeting of the Laboratory of Tumor Cell Biology, August 21-26, 1989, Bethesda, Maryland (Abstract).

*Fultz, P.N., Anderson, D.C., McClure, H.M., Stricker, R.B., Dewhurst, S. and Mullins, J.I.: SIVsmm infection of macaque and mangabey monkeys: Correlation between in vivo and in vitro properties of different isolates. In: Abstracts of the Twenty-First Congress of the International Association of Biological Standardization: Progress in Animal Retroviruses, October 4-6, 1989, Annecy, France, p.100 (Abstract).

*Fultz, P.N., Horaist, C., McClure, H.M., Steimer, K.S., Dina, D. and Mawle, A.C.: Postinfection immunization of human immunodeficiency virus-infected chimpanzees with recombinant HIV-1 env and gag antigens. In: Vaccines 89, R.A. Lerner, H.G. Ginsberg, R.M. Chanock and F. Brown, eds., Cold Spring Harbor Laboratory, New York, pp.225-231, 1989.

*Fultz, P., McClure, H. and Anderson, D.: Replication of a lethal variant of SIV/SMM in macaque PBMC in the absence of exogenous IL-2 or activation by mitogens. Proceedings of the Fifth International Conference on AIDS, Montreal, Canada, p.684, June 4-9, 1989 (Abstract).

*Fultz, P.N., McClure, H.M., Anderson, D.C., Siegel, R.L., Ansari, A. and Brodie, A.: Changes in antibody profiles and hematologic parameters associated with long-term HIV-1 infection in chimpanzees. International TNO Meeting on Animal Models in AIDS, Maastricht, The Netherlands, October 23-26, 1989, p.55-56 (Abstract).

*Fultz, P.N., McClure, H.M., Anderson, D.C. and Switzer, W.M.: Identification and biologic characterization of an acutely lethal variant of simian immunodeficiency virus from sooty mangabeys (SIV/SMM). AIDS Res. Hum. Retroviruses 5:397-409, 1989.

*Fultz, P.N., McClure, H.M., Swenson, R.B. and Anderson, D.C.: HIV infection of chimpanzees as a model for testing chemotherapeutics. Intervirology 30 (Suppl. 1):51-58, 1989.

*Fultz, P.N., Mullins, J.I., Dewhurst, S., McClure, H.M., Ansari, A. and Anderson, D.C.: Virus-host interactions in SIV/SMM infection of macaque and mangabey monkeys. Quatrieme Colloque des "Center Gardes," Marnes-La-Coquette, France, October 26-28, p.64, 1989 (Abstract).

*Fultz, P., Siegel, R., McClure, H., Steimer, K., Dina, D., Swenson, B. and Anderson, D. et al.: Evidence for progression to disease in chimpanzees chronically infected with HIV-1? Proceedings of the Fifth International Conference on AIDS, Montreal, Canada, p. 532, June 4-9, 1989 (Abstract).

*Fultz, P.N., Stricker, R.B., McClure, H.M., Anderson, D.C., Switzer, W. and Horaist, C.: The role of antibodies in protection from or potentiation of disease in SIV/SMM-infected mangabeys and macaques. Internation TNO Meetinng

on Animal Models in AIDS, Maastricht, The Netherlands, October 23-26, 1989, p.20-21 (Abstract).

*Fultz, P., Stricker, R., Montagnier, L., Sonigo, P., McClure, H. and Anderson, D.: Role of antibodies, cytokines, and virus variation in SIV/SMM induced disease. Proceedings of the Fifth International Conference on AIDS, Montreal, Canada, p.511, June 4-9, 1989 (Abstract).

*Fultz, P.N., Welch, T., Mullins, J. and Dewhurst, S.: Influence of cytokines and requirements for replication of SIV/SMM-PBj14 and an infectious molecular clone of SMM-PBj14. Seventh Annual Symposium on Nonhuman Primate Models for AIDS, p.86, Portland, Oregon, October 11-13, 1989 (Abstract).

*Gordon, T.P., Gust, D.A. and Wilson, M.E.: Ovarian and pituitary hormones during pregnancy and lactation in the mangabey monkey. Am. J. Primatol. 18:147, 1989 (Abstract).

*Gould, K.G.: Artificial breeding of nonhuman primaes. In: Comparative Reproduction in Mammals and Man, R.M. Eley, ed. Proceedings of a Conference of the National Centre for Research in Reproduction, Nairobi, November, 1987. Institute of Primate Research, National Museums of Kenya, pp.12-18, 1989.

*Gould, K.G.: Artificial breeding of chimpanzees. In: Scientific Program and Abstracts: Fertility in the Great Apes, June 15-17, 1989, Atlanta, Georgia, p.24 (Abstract).

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PART II, SECTION C BOOKS/PAPERS/ABSTRACTS GRANT NUMBER:P51RR00165-29

CORE: OTHER: XXX

Number Published:	154	Books:	3	Papers:	78	Abstracts:	73
Number in Press:	74	Books:	0	Papers:	67	Abstracts:	7

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* Center support acknowledged
** (Not previously reported)

PART II, SECTION C BOOKS/PAPERS/ABSTRACTS GRANT NUMBER: P51RR00165-29

PUBLICATIONS SUPPORTED BY RECEIPT OF SPECIMENS: X

Number Published:	34	Books:	1	Papers:	21	Abstracts:	12
Number In Press:	8	Books:	0	Papers:	8	Abstracts:	0

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IN PRESS:

*Djian, P. and Green, H.: The involucrin gene of the gibbon: the middle region shared by the hominoids. Mol. Biol. Evol. (In press).

*Duchin, L.E.: The evolution of articulate speech: Comparative anatomy of the oral cavity in Pan and Homo. J. Hum. Evol. (In Press).

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Sibley, C.G., Comstock, J.A., and Ahlquist, J.E.: DNA hybridization evidence of hominoid phylogeny: A reanalysis of the data. J. Mol. Evol. (In press).

* Center support acknowledged
** (Not previously reported)

PART III, SECTION A RPRC PROGRAM SPECIFIC DATA GRANT NUMBER:P5RR00165-29

ADMINISTRATIVE STATISTICS

1. PERSONNEL	NUMBER
A. CORE Personnel	178
Doctoral Level Scientists	27
Other Personnel	151
B. Collaborative or Affiliated Scientists	137
C. Visiting Scientists	5
D. Graduate Students	12

2. REGIONALITY	
A. Scientists Provided with Specimens	94
B. Number of Specimens Provided	6,043
C. Scientists Touring the Center	83
D. Other Visitors	802

3. PERCENT OF TOTAL FUNDS[1] FOR EACH RPRC UNIT

UNIT	PERCENT
Administration and Support Services	38%
Division of Animal Resources[2]	16%
Division of Behavioral Biology	5%
Division of Neuroscience	4%
Division of Pathobiology[3]	34%
Division of Reproductive Biology	3%
TOTAL YRPRC	100%

[1] Monies awarded in Base Grant, Improvement and Modernization Supplement and AIDS Animal Model Development Supplement.
[2] Reflects Base Grant and Improvement and Modernization supplemental funds.
[3] Reflects AIDS Animal Model Development supplemental funds.

CURRICULUM VITAE - JAMES G. ELSE
Updated March 1990

ADDRESS

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PERSONAL BACKGROUND

Birth date:
Birth place:
Nationality: American
Marital status:
Children:
S.S. #:

EDUCATION

B.S.	1967	Entomology, University of California
M.S.	1968	Entomology, University of California
D.V.M.	1973	College of Vet. Med., U.C. Davis
M.P.V.M.	1973	Epidemiology, University of California
Lab An Med	1977	California Primate Center, U.C.D.

CURRENT POSITION

Head, Animal Resources, and Associate Research Professor, Yerkes Regional Primate Research Center, Emory University, Atlanta, Georgia, USA.

PREVIOUS POSITIONS

1987 - 1989	Head, Biological Resources National Museums of Kenya P.O. Box 40658 Nairobi, Kenya
1984 - 1989	Head, Dept. Conservation/Ecology Institute of Primate Research National Museums of Kenya P.O. Box 24481 Nairobi, Kenya
1977 - 1987	Director Institute of Primate Research National Museums of Kenya Nairobi, Kenya
1975 - 1977	Resident Clinical Veterinarian California Primate Research Center University of California, Davis

PREVIOUS POSITIONS (cont.)

1973 - 1975	Fogarty Fellow Dept. of International Health San Francisco Medical Center, and Institute for Medical Research Kuala Lumpur, Malaysia
1968 - 1973	Research Associate II Department of Entomology University of California, Davis
1965 - 1968	Laboratory Assistant Department of Entomology University of California, Davis

CONSULTANT POSITIONS

Member, Consultation Group, Primates for Research in Human Reproduction Special Programme for Research in Human Reproduction, World Health Organization, Geneva (1980-82).

Member, Consultation Group, International Primate Resources Programme, World Health Organization, Geneva (1980-81).

Special Consultant, Yerkes Regional Primate Research Center, Emory University, Atlanta, GA (1981-86). Advise on development of research studies and field projects in Africa.

Consultant, World Health Organization (1985-87). Evaluation of current and proposed primate and laboratory animal facilities in China; determination of institutional strengthening requirements and assistance in the development of a research programme in reproductive biology.

Ecological Consultant, Gallmann Memorial Foundation, Nairobi, Kenya (1985 - 1989).

Member, World Health Organization Site Visit Team (1990). Evaluation of Kenya National Center for Research in Reproduction.

SPECIAL COMMITTEES OR APPOINTMENTS

Board of Directors, Kenya National Centre for Research in Reproduction (1979 - 85).

Member of Board, World Wildlife Fund - Kenya (1981 - 82).

Member, Scientific Program and Organization Committee, International Primatological Society IXth Congress (1981 - 82).

Member, Kenya Live Animal Sub-Committee, International Air Transport Association (1981 - 84).

Member, IUCN/SCC Primate Specialist Group (1982 - 87).

SPECIAL COMMITTEES OR APPOINTMENTS (cont.)

Member, XVIIth CIOMS Round Table Conference on Biomedical Research Involving Animals (1983).

Chairman, Xth Congress, International Primatological Society (1983 - 84) and Congress Organizer and Host (1984).

Secretary, IPR International Advisory Board (1984 - 89).

Founding Member, Kenya Guidelines Committee for the Establishment of Laboratory Animal Husbandry Standards (1985 - 87).

Vice President for Captive Care and Breeding and Executive Board Member, International Primatological Society (1985 - 88).

Project Coordinator, Tana River Primate Project, and Chairman, Tana Management Committee (1986 - 89).

Chairman, IPS Committee on the Standards and Ethics of Animal Care (1986 - 88).

Member, GMF Scientific Advisory Committee (1986 - present).

Member, Captive Care Committee, International Primatological Society (1986 - 89).

Member, Conservation Committee, International Primatological Society (1988 - present).

Review Editor, Primate Conservation (1988).

Member, Advisory Board, School for Field Studies, Kenya Program (1988 - 89).

Member, IUCN Species Survival Commission African Primate Specialist Group (1988 - present).

Member, Emory University Biosafety Subcommittee (1989 - 1990).

Member, Yerkes Executive Committee (1989 - present).

Ad Hoc Member, Emory University Institutional Animal Care Committee (1989).

Member, Yerkes Task Force on Revised USDA Regulations Implementation (1989 - 1990).

Member, Yerkes Animal Resources Committee (1989).

Member, Yerkes AAALAC Committee (1989 - present).

Member, Yerkes Resources and Science Review Committee (1990 - present).

Chair, Emory University IACUC Primate Subcommittee (1990 - present).

Member, Emory University Institutional Animal Care and Use Committee (1990 - present).

PROFESSIONAL SOCIETIES

American Association for Laboratory Animal Science

American Society of Laboratory Animal Practitioners

American Society of Primatology

Association of Primate Veterinary Clinicians

East African Wildlife Society

International Primatological Society

Kenya Museums Society

Kenya Natural History Society

National Society for Medical Research

PROFESSIONAL AND RESEARCH INTERESTS

Policy and program development and project management in developing countries.

Research design, implementation and application.

Conservation biology and wildlife management.

Captive animal care, propagation and ethics.

Infectious disease control, epidemiology and zoonoses.

PUBLICATIONS

'CIENTIFIC PAPERS

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CURRICULUM VITAE

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APPENDIX TO INSTRUCTIONS
DRR SCIENTIFIC CLASSIFICATION

AXIS I

Code Nos.	RESEARCH AREAS (Maximum 6 Codes)
1	Animals, Whole
	a. Vertebrates, Mammal
	b. Vertebrates, Non-Mammal
	c. Invertebrates
	Animals, Cells
	d. Vertebrates, Mammal
	e. Vertebrates, Non-Mammal
	f. Invertebrates
2	Biological/Chemical Compounds
3	Biomaterials
4	Human, Cells
5	Human, Adult
	a. Female b. Male
	Human, Infant/Child
	c. Female d. Male
6	Membrane/Tissue/Isolated Organ
7	Microorganisms
	a. Bacteria b. Viruses
	c. Parasites d. Other
8	Plants/Fungi
9	Technology/Technique Development
11	Facility Construction/Improvement
12	Clinical Trials
	a. Multicenter b. Single Center

ANATOMICAL SYSTEM/RESEARCH AREAS

13	Cardiovascular System
14	Connective Tissue
15	Endocrine System
16	Gastrointestinal System
	a. Esophagus b. Gallbladder
	c. Intestine d. Liver
	e. Pancreas f. Stomach
17	Hematologic System
18	Integumentary/Skin System
19	Lymphatic and Recticulo-Endothelial System
20	Muscular System
21	Nervous System
22	Oral/Dental
23	Reproductive System
24	Respiratory System
25	Sensory System
	a. Ear
	b. Eye
	c. Taste/Smell/Touch
26	Skeletal System
27	Urinary System
28	Other (SPECIFY)
30	Aging
31	AIDS, SAIDS
32	Anesthesiology
34	Anthropology/Ethnography
35	Arthritis
36	Behavioral Sci/Psychology/Social Sci

AXIS II

Code Nos.	RESEARCH AREAS (Maximum 6 Codes)
38	Bioethics
39	Biotechnology (cDNA, CDNA, hydridoma)
41	Cognition/Learning
40	Communication/Speech
42	Computer Science
44	Congenital Defects or Malformations
45	Deafness/Hearing
46	Degenerative Disorders
48	Device, Protheses, Intra/Extracorporeal
50	Drug/Therapeutic Agent Studies
	a. Toxic b. Other c. Orphan Drugs
52	Engineering/Bioengineering
54	Environmental Sciences
	a. Toxic b. Other
56	Epidemiology
57	Fitness, Physical
58	Genetics, Including Metabolic Errors
59	Genome
60	Growth and Development
62	Health Care Applications
63	Imaging
	a. CT e. PET
	b. Laser f. Spect
	c. MRI, MRS g. Radiography
	d. NMR h. Ultrasound
64	Immunology and Allergy
65	Infant Mortality
66	Infectious Diseases
68	Information Science
70	Instrument Development
69	International Hlth
71	Maternal & Child Hlth
72	Mental Disorders/Psychiatry
74	Metabolism and Biochemical Transport
	a. Carbohydrate e. Hormone
	b. Electrolyte/Mineral f. Lipid
	c. Enzymes g. Nucleic Acid
	d. Gases h. Protein & Amino Acid
75	Minority Hlth
77	Model Dvlmt
76	Neoplasms/Oncology/Cancer
	a. Benign b. Malignant
78	Nutrition
79	Pain
80	Radiology/Radiation Nuclear Medicine
81	Rare Disease
82	Rehabilitation
83	Sexually Transmitted Disease
85	Sleep Research
84	Statistics/Mathematics
87	Substance Abuse
86	Surgery
88	Transplantation
90	Trauma/Burns/Injury
91	Vaccine
93	Womens Health Research
92	Other (SPECIFY)