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

NATIONAL CENTER FOR RESEARCH RESOURCES
COMPARATIVE MEDICINE PROGRAM
REGIONAL PRIMATE RESEARCH CENTERS PROGRAM (RPRC)
ANNUAL PROGRESS REPORT

1. PHS GRANT NUMBER: P51RR00165-30

2. NAME OF RECIPIENT INSTITUTION: Yerkes Regional Primate Research Center

3. HEALTH PROFESSIONAL SCHOOL (If applicable): Emory University Woodruff Medical Center

4. REPORTING PERIOD:

   A. FROM (Month, Day, Year): 01-01-90

   B. TO (Month, Day, Year): 12-31-90

5. CENTER DIRECTOR:

   A. NAME: Frederick A. King, Ph.D.

   B. TITLE: Director and Professor, Yerkes Regional Primate Research Center; Professor, Department of Anatomy; Adjunct Professor, Department of Psychology; Associate Dean, Emory University School of Medicine

   C. SIGNATURE: Frederick A. King

6. DATE SIGNED (Month, Day, Year): April 11, 1991

7. TELEPHONE (Include Area Code): (404) 727-7707

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YERKES REGIONAL PRIMATE RESEARCH CENTER
EMORY UNIVERSITY

ORGANIZATIONAL CHART

President
Emory University

Vice President for Health Affairs
Woodruff Health Sciences Center

Director
Yerkes Center

Board of Scientific Advisors (External)

Executive Committee (Internal)

- Associate Director for Scientific Programs
- Chief of Public Affairs
- Associate Director for Animal Resources
- Administrative Associate & Manager, Computer Services
- Associate Director for Administration

Research Programs

Neurobiology

Behavioral Biology

Sections
Psychobiology and Behavioral Pharmacology

Behavioral Endocrinology and Social Behavior

Language, Cognition & Neuropsychology

Reproductive Biology

Pathobiology and Immuno-biology

Research Support Services

Pathology

Histo-pathology

Laboratory Pathology

Necropsy

Pathology Archives and Tissue Collection

Transmission Electron Microscopy

Scanning Electron Microscopy and X-ray Analysis Unit

Radioimmunoassay Lab

Yerkes Resources & Science Review Committee

Primate Care

Veterinary Services

Animal Husbandry

Animal Records

IACUC Sub-committee

Primate Health & Support Services

Medical Care

Surgery

Radiology

Experimental Procedures

Administrative Support Services

Business Office
- Budget & Accounts
- Payroll
- Purchasing
- Travel

Personnel

General Office Services

Library

Physical Plant
- Bldg./Grounds Maint.
- Security
- Vehicle Maintenance
- Telecommunications

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- General Shop
- Bioelectronics
- Bioinstrumentation

Photography

FACULTY OF THE YERKES REGIONAL PRIMATE RESEARCH CENTER

EMORY UNIVERSITY

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April 15, 1991

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.
Associate Director for Animal Resources and Associate Research Professor	J.G. Else, M.S., D.V.M., M.P.V.M.
Administrative Associate and Manager, Computer Services	R.W. Buddington, Ph.D.
Chief, Public Affairs and Administrative Associate for Special Projects	C.J. Yarbrough, A.B.J.

SPECIAL CONSULTANTS TO THE DIRECTOR

Special Consultant in Wildlife Conservation and Paleobiology	R.E. Leakey, Director, Kenya Wildlife Service; Adjunct Professor of Anthropology, Emory University.
Administrative Consultant	H.C. Lansdell, Ph.D., Health Scientist Administrator, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health.

DIVISION OF BEHAVIORAL BIOLOGY
L.D. Byrd, Ph.D., Chief

Section on Psychobiology and Behavioral Pharmacology
L.D. Byrd, Ph.D., Section Head

Core Scientist

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Collaborative Scientist

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DIVISION OF BEHAVIORAL BIOLOGY (CONTINUED)

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Core Scientists

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Associate Scientist

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DIVISION OF BEHAVIORAL BIOLOGY (CONTINUED)

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Collaborative Scientists

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E. Visalberghi, Ph.D. Collaborative Scientist in Behavioral Biology, Yerkes Center; Senior Research Scientist and Primate Laboratory Unit Chief, Istituto de Psicologia, CNR, Rome, Italy.

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D.M. Rumbaugh, Ph.D., Section Head

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DIVISION OF BEHAVIORAL BIOLOGY (CONTINUED)

Affiliate Scientist

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Collaborative Scientists

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Collaborative Scientists

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DIVISION OF NEUROBIOLOGY (CONTINUED)

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DIVISION OF PATHOBIOLOGY AND IMMUNOBIOLOGY (CONTINUED)

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Collaborative Scientists

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DIVISION OF PATHOBIOLOGY AND IMMUNOBIOLOGY (CONTINUED)

G.H. Campbell, Ph.D., Collaborative Scientist in Pathobiology and Immunobiology, Yerkes Center; Research Microbiologist, Centers for Disease Control.

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DIVISION OF PATHOBIOLOGY AND IMMUNOBIOLOGY (CONTINUED)

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DIVISION OF PATHOBIOLOGY AND IMMUNOBIOLOGY (CONTINUED)

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S. Toma, M.D., Collaborative Scientist in Pathobiology and Immunobiology, Yerkes Center; Chief, Canadian Yersinia Reference Center and Chief Bacteriologist, Ontario Department of Health, Toronto.

V.C.W. Tsang, Ph.D., Collaborative Scientist in Pathobiology and Immunobiology, Yerkes Center; Research Chemist, Division of Parasitic Diseases, Centers for Disease Control.

E.F. Winton, M.D., Collaborative Scientist in Pathobiology and Immunobiology, Yerkes Center; Associate Professor of Medicine, Emory University.

DIVISION OF PATHOBIOLOGY AND IMMUNOBIOLOGY (CONTINUED)

Visiting Scientists

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Consultants

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J.H. Richardson, D.V.M., Consultant in Pathobiology and Immunobiology, Yerkes Center; University Biosafety Officer, Emory University.

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DIVISION OF REPRODUCTIVE BIOLOGY
K.G. Gould, Ph.D., M.R.C.V.S., Chief

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Research Scientist

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Associate Scientist

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Research Associate

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Affiliate Scientists

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DIVISION OF REPRODUCTIVE BIOLOGY (CONTINUED)

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Collaborative Scientists

D.C. Collins, Ph.D., Collaborative Scientist in Reproductive Biology, Yerkes Center; Professor of Medicine and Director, Hormone Research Laboratory, Atlanta Veterans Administration Medical Center; Associate Professor of Biochemistry, Emory University.

B.T. Hinton, Ph.D., Collaborative Scientist in Reproductive Biology, Yerkes Center; Assistant Professor of Anatomy and Cell Biology, University of Virginia.

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.

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; Professor of Biophysics at Westfalische Wilhelms-Universitat, Munster, Germany.

Consultants

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; Director of Office of Sponsored Programs, University of Alaska, Fairbanks, Alaska.

DIVISION OF ANIMAL RESOURCES AND VETERINARY MEDICINE

James G. Else, D.V.M., M.P.V.M., Associate Director for Animal Resources
R. Brent Swenson, D.V.M., Chief of Veterinary Medicine and Senior Veterinarian

Core Scientists

J.G. Else, D.V.M., Associate Director for Animal Resources and Associate Research Professor, Yerkes Center.

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

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

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

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

Research Associate

K.S. Paul, D.V.M., Research Associate of Pathobiology and Immunobiology and Assistant 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 1990 include continued expansion and improvements in the physical plant and housing facilities, continuation of active research programs by both core and adjunct faculty members, and continued productive interactions with investigators at the host institution as well as other regional, national and international institutions.

Improvement of the physical plant and animal housing facilities is an ongoing effort at the Yerkes Center, and considerable progress was made in this area in 1990. This has resulted in improved and expanded animal housing facilities and in increased research space, and has strengthened our position and capabilities as a research institution, and has made it possible for the Yerkes Center to remain fully accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC). During 1990, major accomplishments in this area included completion of a 5,200 square foot virology/AIDS research facility that provides expanded virology laboratory facilities, offices and containment facilities for housing SIV or HIV-infected animals; renovation of an existing facility to provide runs for group housing of monkeys that will provide for increased socialization of the animals; assembly of a new facility that provides four animal housing rooms and five rooms for animal testing; renovation and terracing of the outdoor portion of five additional compounds at the Field Station; renovation of the indoor quarters of four Field Station compounds; installation of Stonhard flooring to several additional animal quarters; installation of a cage washer at the Field Station; installation of concrete feeding pads for all Field Station compounds where these did not exist; and purchase of a number of new cages to meet the cage size requirements for animals in the 10-15 kg and 15-25 kg weight range. In addition, construction was initiated in 1990 on a clinical medicine facility at the Field Station and a facility at the Main Station for housing HIV-infected chimpanzees. Both of these facilities should be completed and occupied in early 1991.

Continuation and expansion of the research programs conducted at the Yerkes Center by adjunct faculty members affiliated with either the host institution or other regional and national institutions continues to be a major strength of the Yerkes Center. Our adjunct faculty program contributes substantially toward fulfillment of the Center's commitment and responsibilities to serve as a regional, national and international resource for the conduct of behavioral and biomedical research using nonhuman

primates as the animal model system. During 1990, the number of adjunct faculty members at the Yerkes Center totalled 148; this included 141 affiliate and collaborative scientists and 7 visiting scientists. There is also continued and increasing utilization of Center resources by undergraduate, graduate and postdoctoral students from the host institution as well as other regional universities. As a result of these collaborative efforts, active and expanded research programs and student training programs are currently underway in the areas of cardiovascular research, vision research, AIDS research, and research on aging, parasitic diseases, behavior and reproductive biology. An additional contribution of the Yerkes Center to regional, national and international biomedical research is the provision of a variety of biological specimens from nonhuman primates. This important contribution of the Yerkes Center has increased substantially over the past several years, with 4,612 specimens provided to 110 investigators during 1990.

As has been noted for the past several years, a major weakness of the current program is our inability, due to fiscal constraints and decreasing base grant support, to adequately expand the number of core faculty and technical positions and to upgrade or replace major items of equipment that are needed to meet the increased demands of expanding research programs and increasing number of animals in the colony. Despite the considerable expansion and improvement of the physical plant and animal housing facilities, as summarized in this and previous annual reports, the Center is unable to provide sufficient personnel, research laboratory space and equipment and adequate housing space to accommodate the increasing research demands in a timely manner. Rather than having received increases commensurate with expanded research efforts, the Center has experienced continuing erosion of core grant funding, making it extremely difficult for the Center to provide an adequate infrastructure to support the advances that have otherwise been accomplished.

2) Changes in Professional Personnel

During 1990, Dr. Frans de Waal, noted primate behavioral scientist, was recruited. Dr. de Waal will join the Division of Behavioral Biology at the Yerkes Center and the Department of Psychology, Emory College in mid 1991.

3) Major Problems Encountered or Anticipated

As noted in the past several Annual Reports, the major problem faced by the Yerkes Center, as well as the Regional Primate Research Centers Program in general, is the continued progressive decrease in base grant funding support. Based on conservative estimates, the base grant support from NIH for the Yerkes Center has decreased by 35% to 40% over the past nine years. This has occurred as the result of actual budget cuts during several budget

years and other years of level funding, combined with yearly inflation. This decreasing base grant funding has had significant detrimental effects on core scientific programs at the Center, and has made it extremely difficult for the Center to continue to provide the support services needed (e.g., animal care, clinical medicine, pathology, etc.) to adequately accommodate expanding core and adjunct faculty research programs. This decrease in core support will eventually have severe adverse effects on the quality and number of research programs of core and adjunct scientists, and thereby decrease the acquisition of baseline data, limit pilot studies and new innovative projects, and adversely impact the development of new technology and training of specialized personnel who will be critically needed for future research programs designed to combat the numerous behavioral and disease problems that continue to plague mankind. This eroding base grant funding has reached the critical stage and must be addressed if the NIH wishes to maintain the Regional Primate Research Centers program at its present level of excellence. Failure to address this critical funding problem will have a serious adverse impact on future biomedical and behavioral research which requires the use of nonhuman primates and will, therefore, adversely affect continuing efforts to improve the health and wellbeing of mankind. Significantly increased base grant funding is essential if we are to maintain an acceptable level of scientific excellence, continue the highest possible standards of animal care and use, and adequately provide for the support of core and adjunct faculty research.

A lack of sufficient laboratory and animal housing space to accommodate expanding research programs of both core and adjunct faculty in a timely manner, due in part to decreasing core grant support, is a continuing problem faced by the Yerkes Center. Due to our inability to expand adequately our physical plant and support services, it may soon become necessary to delay important approved projects until space becomes available upon the completion of ongoing projects. This would seriously impede the timely acquisition of needed biomedical and behavioral research data. Another anticipated problem is the potential shortage of domestically produced nonhuman primates that will be needed to accommodate the increased needs for important research programs, especially in the areas of testing AIDS drugs and vaccines, testing other types of vaccines that are needed for improved immunization of humans, cardiovascular, cancer, and aging research. This situation will likely worsen as fewer nonhuman primates are obtained from the wild. It is imperative, therefore, that adequate funding be provided to maintain and expand, as needed, our Center nonhuman primate breeding colonies, in order to provide adequate numbers of animals for our research programs.

Other major problems faced by the Yerkes Center, as well as biomedical research in general, include the continuing efforts of misguided and irrational animal activists to impede or halt

research with laboratory animals, and the increasing number of federal rules and regulations that control and restrict the use of laboratory animals in research. These factors have resulted in the need for increased security, constantly changing cage size requirements, ever expanding volumes of record keeping and changing procedures for the housing, care and use of laboratory animals. All of these factors, and others, have increased substantially the costs associated with research using laboratory animals, especially nonhuman primates, and require the use of limited funds that much more productively could be spent investigating human health problems.

4) Major Equipment Items Purchased

Base Grant*

Quantity	Description	Cost
3	Four Drawer Lateral File Cabinet	$ 1,699
5	Desks	3,094
*1	Ultra Low Cryo-Fridge Freezer	5,103
*1	Sequigen Sequencing System	750
1	Upright Freezer	899
1	Tilt/Swivel Chair	951
1	Cross Linker	1,003
*1	Power Supply	1,408
1	Conference Table	4,100
*1	Shaking Incubator with accessories	5,716
1	VHS Camcorder with accessories	948
1	Caging for infectious disease REPE	65,472
*1	Refrigerated Centrifuge with accessories	4,526
*2	Stackable CO_2 Incubators	5,701
1	Platform Scale	2,150
1	Tabletop Centrifuge	5,725

Base Grant (Cont'd)*

1	Fixed Angle Rotor	1,030
*2	Biological Safety Cabinet	15,939
2	Reznor Unit Heaters	2,043
*1	Large Slab Gel Dryer	925
*1	Digital Pipettor	618
*1	Genie Lift	679
1	Tilt Truck	585
*1	Tissue Embedding System	4,960
1	Ice Maker	1,677
*1	Steam Dishwasher	2,393
*1	-80 Degree Freezer with accessories	7,415
*1	Dual Chamber Waterbath	708
*1	Vacuum Oven	700
*2	Liquid Nitrogen Tanks	3,350
1	Cage Wash Pump	645
*2	Liquid Nitrogen Freezer with Racking System	22,140
*1	Mobile Condenser Discharge Unit	20,400
*1	Curix-60 Processor	4,500
3	Pressure Washers	2,550
2	Differential Amplifiers	2,431
1	Dual Time Base	1,326
1	Storage Oscilloscope Plus	3,154
1	Gusher Motor & Pump	1,252
*1	EM Nitrogen-Burst Photo Developing System	1,105

Base Grant (Cont'd)*

*1	Fume Hood	2,799
1	Scanning Electron Microscope	150,000
**1	Emergency Generator	71,323
**1	Forklift	16,519
**1	Mobile Condenser Discharge Unit	20,500
**1	Processor	4,500
**1	Clinical Medical Relocatable Exterior Primate Enclosures	306,000
*1	Quarantine Relocatable Exterior Primate Enclosure	273,405
**1	"RC" Relocatable Exterior Primate Enclosure	286,216
1	Office Trailer, 60' x 14'	19,960
**25	Rack Units with 100 primate cages	111,500
1	Radio Frequency Security System	48,225
*2	IEC Centra Microcentrifuge	1,208
*23	Rack Units with 92 primate cages	104,693

* AIDS Funds
** Improvement and Modernization Funds

Computer Equipment Purchased

Quantity	Description	Cost
1	Megabyte External Hard Disc	$ 588
1	325 Computer	2,124
5	386 VGA System with accessories	14,275
1	Multiport AUI transceiver unit	750
*1	1 Megabyte of RAM	2,200
*1	Local Repeater	780

Computer Equipment Purchased (Cont'd)

Quantity	Description	Cost
*1	320 Compuadd Computer with accessories	3,209
1	40 CPU Hard Disk	3,982
1	Portrait Display Video Card	1,040
*1	286 Computer with accessories	4,011
*1	SLC Diskless Workstation with 8 meg RAM & Monitor	2,200
1	20 MHZ Portable Computer	4,828
*1	Floppy Disk Drive	550
*1	VGA Monitor	600
1	EXABYTE 8 mm Tape Backup Unit	3,040
1	Upgrade of SUN CPU Board	9,328
1	760 MEG SCSI Hard Drive Unit	2,295
1	IPC Color Workstation with accessories	7,364
2	Netmodems	2,599
1	386/20 Epson	2,110
1	Toshiba Computer	2,795

* AIDS Funds
** Improvement and Modernization Funds

Other Grants

Quantity	Description	Cost
1	Polaron E-3000 Critical Point Dryer with accessories	$ 2,200
1	HP Tradition "L" FO HP	670
1	Sequest Drive	678

Other Grants (Cont'd)

1	Signal Spectrographic Sound Analysis System	7,745
1	Special Linear/Convex/Micro-Convex Console	17,100
1	TFM Linear Transducer	8,550
2	Reverse Osmosis Cartridge	1,210
1	Spectrum Analyzer	12,625
1	Bernoulli Internal Drive	725
1	Gravity Convection Oven	686
1	Laser Jet III Printer	1,215
1	Ultra Sound	32,700
1	386 VGA System	2,695
1	Videomex-V Main Controller with accessories	9,930
1	40 mb Hard Disk with accessories	3,932
2	SLC Diskless Workstations with accessories	4,400
1	40 mb Hard Disc SE	1,674
1	80 mb Hard Disk & 5 mb RAM	2,756
1	RGB Color Monitor	623
1	40 mb Hard Disk & 2 mb RAM	1,107
1	80/4 PROMO Hard Disk	4,329
2	Suzuki V-JA Vehicles	15,800
1	Refrigerated Recirculating Heat Exchanges with condenser	3,195
1	EEJ Unit with RS232 Output	3,900
1	8 mm Camcorder	1,066

Other Grants (Cont'd)

1	VGA 3-D Monitor	629
1	Image Capture Board	931
12	T/C Warmer & Dome	7,500
1	2 Channel Digitizing Unit	3,000
1	Leica Binoculars	990
1	LKB Knifemaker	1,500
1	LK Ultramicrotome	500
1	1.25 Objective	1,027
1	Chest Freezer	4,503
1	Color Video Printer	5,845
1	Sparcstation-1 Computer with accessories	9,338
1	Monochrome Z-159 Computer	1,311
1	1/4" Tape Drive	825
1	8 mybtes DataRAM SIMMS	850
1	686 Computer	600
1	Planachromat 100/1.25 Oil	861
1	486/25 Computer with accessories	7,149
1	ARCH 386 SX 1 MEG RAM	929
2	AST Premium 386/33 ME Computer with accessories	17,759
1	Laptop Computer with accessories	3,001
1	AST Premium 386C Computer	2,645
1	Microwave Oven	1,647

Other Grants (Cont'd)

1	Sequencing Apparatus	898
1	Electroclutor	662
1	Power Supply	2,282
1	Water Bath Shaker	2,515
1	Platform Mixer	940
1	Vacuum Oven	1,530
1	Foto/Prep I UV Trans Illuminator	1,635
1	EVO-9770 HI-8 Editing System	5,657

5) Improvements and Additions to Facilities

*	Renovation of the Cystic Fibrosis Animal Housing Facility at Main Station	$106,948
**	Installation of Clinical Medicine Relocatable Exterior Primate Enclosure at Field Station	306,000
*	Installation of Quarantine Relocatable Exterior Primate Enclosure at Main Station	273,405
**	Completed Rehabilitation of Compounds S-7 and S-8 to prevent soil erosion and damage to the structural integrity of the compound walls	9,200
**	Installation of a Cage Wash Enclosure at Field Station	27,408
**	Installation of Relocatable Exterior Primate Enclosure "RC" at Main Station	286,216
	Installation of 60' x 14' Office Trailer addition to Ophthalmic Research Facility	40,550
**	Renovation of G-2 Compound at Field Station to include caging, flooring, painting and drains	37,777
	The Center's Security System was expanded and updated to add new rooms and facilities to the card access system at Main Station	24,297

Improvements and Additions (Cont'd)

	Electrical upgrade and duct work in the Scanning Electron Microscopy Facility to provide power and cooling for a new Electron Microscope	3,149
	Renovation of room 306 at Main Station for use as a third floor conference room	6,935
	Installation of Trench System at E-Section of the Great Ape Wing at Main Station	2,675
	Renovation of room 351 at Main Station to provide office space for Biomedical Engineer	2,887
	Chain link fence and gate installed at exterior end of E-Section of Great Ape Wing at Main Station	1,485
	Installation of fire alarm equipment and electrical panel replacement and upgrading to serve Ophthalmic Research Facility and Virology Research Wing	3,850
	Installation of 10" Storm Sewer Lines at AIDS Addition and RC Building at Main Station	2,728
	Renovation of room 212 in Eye Building for Contact Lens Lab and office	9,836
	Gravel fill and landscaping to area surrounding SEM, T-14, REPE "RC," RD, Virology Research Wing, RA, RB, and E-Section of the Great Ape Wing at Main Station	26,654
**	Installation of 125 kw Emergency Generator Unit at Main Station	71,323
	Fabrication and Installation of Caging for Infectious Disease REPE at Main Station	65,472
	Replaced roof over the Treatment and Metabolism Rooms of the Great Ape Wing at Main Station	6,025
	Installation of concrete feeding pads at S-5, S-6, S-7, S-8, T-1, T-2, T-3, T-4, D-1, D-2 and G-2, providing clean, dry, easily sanitized areas to feed the primates	8,976
	Construction of wood framed storage shed at Field Station	2,460

Improvements and Additions (Cont'd)

Installed concrete walkway from gate to building G-11 at Field Station	1,670
Installation of 12" Storm Pipe near Compound "A" at Field Station	4,132
All roads inside compound property were re-graded and scraped, including road around perimeter fence line at the Field Station	3,500
Installation of Security System including Smoke Detectors and Temperature Alarms at Field Station	48,225
Grading and installation of crosstie walls for compound BC1A and BC1B at Field Station	9,400
Stonhard applied to slab of Small Primate Wing cage washer and Eye Building cage washer at Main Station	5,601
Crosstie Retaining Walls installed in compound S-5 and S-6 to prevent soil erosion at Field Station	9,400

* AIDS Funds
** Improvement and Modernization Funds

6) Conferences, Workshops and Seminars

"Mechanisms of Learning and Memory," Fifth Annual Spring Symposium of the Atlanta Chapter of the Society for Neuroscience, the Emory Neuroscience Group and the Yerkes Center, April 28, at Emory University.

Dr. Philip Kennedy (Georgia Institute of Technology), "Restoring Muscle Function to Paralyzed Human Limbs," May 9th seminiar for Yerkes faculty, staff and students.

Dr. Sue Savage-Rumbaugh (Yerkes and Georgia State University), "Apes and Us: What Happens When We Begin to Communicate with Each Other," June 15 seminar for Yerkes faculty, staff and students.

Dr. A. A. Ansari (Emory Pathology and Winship Cancer Center and Yerkes), "Can the Virus Responsible for AIDS Infect People Without Making Them Clinically Ill?", August 1 seminar for Yerkes faculty, staff and students.

Dr. Kim Wallen (Emory Psychology Dept. and Yerkes), "Hormones and Sexual Desire," August 22nd seminar for Yerkes faculty, staff and students.

Dr. Leonard Howell (Yerkes), "Respiratory Effects of Caffeine," August 30th seminar for Yerkes faculty, staff and students.

Dr. Michael Iuvone (Emory Pharmacology Dept. and Yerkes), "Eye Drops To Prevent Nearsightedness," Dec. 5th seminar for Yerkes faculty, staff and students.

Dr. Adrian G. Gillin (Emory Dept. of Medicine), "How Pregnant Baboons are Studied to Prevent Hypertension-in-Pregnancy," Dec. 13th seminar for Yerkes faculty, staff and students.

Dr. Kathryn Bayne (NIH), "Psychological Wellbeing/Cage Enrichment," Dec. 11th seminar for Yerkes faculty, staff and students.

7) Yerkes Visiting Speakers Series

Dr. Emile Rissman (University of Virginia), "The Taming of the Shrew: Neuroendocrine Regulation of Sexual Interest in an Insectivore," co-sponsored with Emory Department of Psychology.

Dr. Roger V. Short (Monash University, Australia), "Chimpanzees and HIV Research," May 2nd presentation for Yerkes faculty, staff and students.

Dr. Thomas Zoeller (University of Missouri School of Medicine), "Neuroendocrine Integration: Interaction of Neural and Humoral Factors Regulating TRH Gene Expression," May 15th seminar co-sponsored by Georgia State University's Department of Biology, the Atlanta Chapter of Society for Neuroscience, the Emory Neuroscience Group, and the Yerkes Center.

Dr. Chris Pryce (Anthropology Institute and Museum of the University of Zurich, Switzerland), "The Regulation and Failure of Maternal Behavior in Primates," Oct. 9th seminar for Yerkes faculty, staff and students.

Dr. Patrick T. Mehlman (University of Montreal), "Population Dynamics in Wild Barbary Macaque," with the Emory Department of Psychology, Dec. 6, at Emory.

8) Administrative and Operational Changes

During 1990, the Yerkes Animal Resources Committee (YARC) was disbanded and replaced by two new committees, the Yerkes Resources and Science Review Committee (YRSRC) and an IACUC Primate Subcommittee. The latter committee reviews all proposals, campus-wide, that utilize nonhuman primates and reports directly to the

main University IACUC. This committee reviews research protocols for concerns related to the humane care and use of nonhuman primates, and to insure that each protocol meets all Federal rules and regulations concerning the use of laboratory animals in research. The YRSRC is an advisory committee and reports directly to the Center Director. This committee reviews research protocols for scientific merit as well as their relationship to the scientific mission, goals and programs of the Yerkes Center. This committee also considers the availability of Center resources, animals and support services that will be required by each research proposal.

9) Narrative Progress Report for Non-Research Units

A. Animal Resources: Yerkes Animal Resources is an administrative unit comprising the Division of Veterinary Medicine, Animal Records, and the three units of Animal Care; the Great Ape Unit, Small Primate Unit and Field Station. Animal Resources personnel are responsible for all aspects of laboratory animal care at the Center. This includes routine husbandry, veterinary care, meeting federal regulations and guidelines, and interfacing with scientists undertaking studies with animals.

Yerkes places high priority on the proper training of all personnel working with Center animals to help ensure quality and humane care of the animals under its charge and strict adherence to all policies and regulations. During the 1990 reporting period, significant advances were made in the establishment of training programs for Animal Care personnel and research scientists, technicians and students working with animals. This has included the establishment of formal training courses, the expanded use of audio-visual material, and the receipt of an AALAS grant to develop an interactive computer-based training program. Animal Resources personnel continued to work closely with the Emory University Division of Animal Resources to provide AALAS training classes for animal care and research technicians. This was expanded to the Field Station this year and a total of 18 Yerkes staff members took AALAS accreditation tests.

The Yerkes Primate Subcommittee of the Emory Institutional Animal Care and Use Committee is based in Animal Resources. Subcommittee members carefully review all research protocols involving animal usage to ensure that proposed procedures are fully justified and carried out in a manner to ensure minimal distress to the animals. The subcommittee also evaluates the credentials and practical experience of research team members to ensure they are suitably qualified to undertake the proposed experimental procedures which involve animals.

A major emphasis of Animal Resource personnel over the past

year has been in preparation for the NIH site visit for 5-year base grant renewal in October and the AAALAC site visit for institutional accreditation renewal in November. Both of these site visits went exceptionally well with no major deficits or problems being noted in any of the Animal Resources units and divisions.

In the 1989 Annual Report we reported that we had just introduced the provision of research services by Animal Care personnel to Center scientists as part of the expansion of career structure opportunities for Animal Care personnel. This has worked well and has been expanded during 1990, with key staff members being trained in specialized research techniques. Animal Resources now provides such services for 4 different projects (or scientists) on a charge back basis and there are several new grants submitted for funding which incorporate such services.

All Animal Resources' revenue and expenditures have been carefully monitored over the reporting period and categorized in much more detail than in the past. This information is being used to develop revised cost centers, which will be used to implement a more accurate charge back system for services rendered. It remains the goal of Animal Resources to become more cost effective and to fully integrate all unit responsibilities and functions into standardized operating procedures which maximize personnel efficiency while providing the highest level of professional and humane care to Yerkes' animals.

1. Clinical Medicine

The Division of Veterinary Medicine is a service unit that provides health care for approximately 2660 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 1990 a total of 235 major surgical operations were performed under the supervision of the veterinary unit. Of these, 157 were experimental procedures done by the investigator, 40 were experimental procedures done by the veterinary staff for investigators and 28 were diagnostic or therapeutic procedures done by the veterinary staff.

The radiology service of the Division was utilized to radiograph 792 animals for a total of 1059 films. Of

these, 181 apes and 440 monkeys were radiographed for clinical reasons (illness, injury or health surveillance) and 72 were done for experimental reasons.

During 1990, 1064 new cases of illness or injury were treated. 960 of these were in monkeys and 104 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 in to 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 34 core and affiliate scientists. In addition, a number of biological samples were made available to outside investigators. These are listed elsewhere. Comparable activity is anticipated in 1991.

2. Animal Records

Animal Records is responsible for maintaining the clinical, experimental and historical records of all primates maintained by the Center. The unit comprises one supervisor and two data entry personnel at the Main Station and one data entry coordinator at the Field Station.

All aspects of animal records were fully computerized at the beginning of 1990, and during the year we have created 3,614 incidents with a corresponding 31,789 actions. These actions include items such as weights, TB tests, reproductive cycles, cage moves, physical exams, clinical interventions, laboratory workups, acquisitions, histopathology, radiology, immunizations, immunology, necropsy, pregnancy tests, surgery, and research data.

We are constantly striving to ensure the accuracy of data and to this end we have created 48 separate error reports that run each night to check the consistency of the data.

This has worked exceptionally well and has enabled us to immediately identify and correct data entry errors and other erroneous information.

Animal Records is interfaced with Budgets and Accounts to enable investigators to be sure their accounts are billed accurately and in a timely manner. Per diem calculations are done monthly and financial projections are provided when required.

A large volume of historical records is maintained by Animal Records which is available to Yerkes scientists and outside investigators. Due to the demand for historical and current information, those requests from non-Yerkes affiliated investigators which require considerable amounts of personnel time are accommodated on a recharge basis.

3. Primate Care and Housing --- Main Station

a) Great Ape Wing

Great Ape Care is a service unit which is responsible for the daily care, cleaning and feeding of all great apes at the Yerkes Main Station. This presently comprises 177 chimpanzees, 5 gorillas, 13 orangutans and 16 gibbons. Additionally, primate care technicians assist research and veterinary personnel working with the great apes.

The majority of the Main Station's great apes are housed on the Great Ape Wing which is made up of 59 indoor/outdoor units which allows for social housing of all animals. There are three areas in which great apes can be temporarily housed in metabolism cages for research or clinical access. A fourth area houses chimpanzees involved in long-term acquired immuno-deficiency syndrome studies with large fixed cages similar to the interior units of the Great Ape Wing.

A Great Ape Nursery currently houses 22 chimpanzees ranging in age from infants to 3 year olds. While every attempt is made to have infants remain with their mothers, those which cannot due to maternal rejection are brought into the nursery where they receive specialized attention designed to ensure healthy animals and ameliorate the effects of nonmaternal rearing.

Five experimental solar heated indoor/outdoor units house the Center's gibbons. These environmental units have been designed to approximate an arboreal wooded

habitat that the animals would be exposed to in the wild.

Continuous care is provided for all great apes and monkeys at the Main Station by a night staff. These primate care technicians check each animal and every facility every two hours, provide feeding and care for nursery animals, and administer medication to ill or injured animals.

During the past year the following items were accomplished:

1. New locking devices were installed on the Great Ape Wing guillotine doors which separate the indoor/outdoor areas. The new lock allows one person to lock animals in or out whereas it previously took two people.

2. The interior corridors of the Great Ape Wing and Great Ape Wing treatment room were repainted.

3. Sheets of mirrored plexiglas were installed at intervals on the interior corridor wall of the Great Ape Wing to provide additional environmental enrichment for the animals. Fifty-five gallon plastic drums are also being utilized as play objects for both the great apes and monkeys.

4. A Great Ape Nursery room which serves as a play area for groups of young apes was paneled with 4' x 8' x 1/4" sheets of polypropylene in an effort to find a long lasting durable, maintenance free wall covering.

5. A Relocatable Exterior Primate Enclosure (REPE)was erected and fixed caging was installed for long-term housing of chimps involved in the acquired immunodeficiency syndrome study. The interior cage areas, which are 8' x 10' x 9' allow for social housing of these animals.

b) Small Primate Wing

The Small Primate Care Unit is a service unit which is responsible for the daily care, cleaning and feeding of all monkeys at the Main Station. Sixteen primate care technicians take care of 8 species of monkey, totaling over 900 animals. Technicians also assist in various research projects as well as aiding veterinary personnel in the clinical care of the animals.

Monkeys are housed primarily in single cages in thirty animal rooms in six separate buildings or enclosures. There are sixteen large fixed cages in two additional enclosures which allow for social housing small groups of monkeys.

A number of commercially available products were purchased for environmental enrichment of singly housed monkeys. Dr. Kathryn Bayne of NIH was invited as a consultant to assess the existing enrichment program and advise the Center on further enrichment implementation.

During the past year, the following improvements were made:

1. Thirty stainless steel cages with 3.7 square feet of floor space and five stainless racks were purchased as replacement caging for squirrel monkeys.

2. Forty-three stainless steel double tiered racks and stainless steel caging were purchased to accommodate 43 group four and 43 group five primates (10-15 and 15-25 kg). The cages were designed so that if there were no longer a need to house large primates, partitions could be inserted and the caging used as social or single housing for a number of small primates.

3. Six animal rooms within the AIDS Research Addition (Virology Research) were completed and occupied. This unit can house up to 150 animals. It is designed with air flow under negative pressure, and all exhaust air is HEPA filtered.

4. A relocatable exterior primate enclosure (RC) was erected to replace trailers which had served as animal housing and testing areas. The new facility has four animal housing rooms for a total of 128 monkeys and five smaller rooms which are used as testing and treatment areas.

5. An enclosed compound area (CF Facility) was renovated to provide twelve runs for small social groups of monkeys. Renovations included resloping the floor and installing an epoxy resin floor surface, adding chain link and polypropylene caging, replacing the roof and adding skylights, and supplementing the existing heating and lighting fixtures.

6. Epoxy resin flooring was installed in the interior runs and corridor of the RF facility to provide an impervious surface. Additionally, the entire facility was painted.

7. A sidewalk was installed to connect the new Virology Research Wing and the RC facility to an exterior cagewasher. This sidewalk greatly facilitated movement of cages and racks to and from the wash area.

8. An epoxy resin flooring was installed on the concrete floors in two cage wash areas. The concrete had become pitted and could no longer be sanitized effectively or considered moisture proof.

9. The Ophthalmic Research Facility animal areas were repainted with an epoxy paint. Four of the areas had experimental polypropylene panels installed to protect portions of walls that have had to be repeatedly resealed.

10. The second floor Small Primate Wing room walls were resealed with epoxy paint.

11. Two rooms within the Small Primate Wing were converted from animal housing areas to experimental testing areas.

4. Primate Care and Housing --- Field Station

The Field Station Animal Care unit is a service unit that provides care for approximately 1600 great apes and monkeys which are maintained at the Yerkes Primate Center Field Station in Lawrenceville. The unit is also responsible for providing support to the Division of Veterinary Medicine and research services to core and affiliate investigators. The unit consists of 1 Superintendent, 2 Assistant Superintendents, 1 Administrative Assistant, and 16 Primate Care Technicians.

The unit assists the Division of Veterinary Medicine by monitoring the health of the colony, providing support during diagnostic and therapeutic procedures and the administration of the preventive medicine program. Animal care staff also provide after hours and weekend care for hospitalized animals. The unit closely coordinates its activities with Yerkes' research personnel to provide assistance, equipment and support services for the studies. Primate care technicians are also assigned to research units for the purpose of collecting and

processing behavioral data and biological samples.

During 1990, continued emphasis was placed on improving animal care, methods of animal housing, and the performance of animal care personnel. Items accomplished during the past year are summarized below:

Erosion control concrete channels were constructed at A-1, A-4, BC2A and BC2B compounds. These structures will reduce erosion and provide drainage and a clean area for feeding.

The rehabilitation of the inside compounds of S-5, S-6, S-8, BC1A and BC1B 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, an underground drain pipe and applying a layer of crushed rock to the surface. The inside of compounds BC2A and BC2B were graded and re-graveled.

The inside quarters of A-1 and A-4 compounds were renovated with new paint, perching, caging, light fixtures and Stonhard flooring. A more efficient ventilation system has been installed to improve ventilation.

Animal indoor quarters were painted in the following locations: BC2A&B, BC2C-F, M-3, M-2, G-8 and corn crib pads CC-3 through 6.

New chain link fencing was installed on BC2C through BC2F runs. Portions of the chain link fencing around T-2, T-3, T-4 and A-1 through A-4, BC1A&B and BC2A&B compounds. The new fencing prevents escapes and possible injuries caused by broken pieces of wire. New indoor caging was installed for A-1 through A-4 compounds.

A new roof was installed over the outdoor areas of BC2C-F. This provides shade and shelter for the animals during the summer months and inclement weather.

Outside drinkers were installed in G-2, T-1 and T-2 compounds providing additional water sources for the animals. Drainage basins were installed with these drinkers to eliminate standing water in the compound.

The indoor quarters of G-2 were renovated. One extra den was added along with an extra cage to hold sick

animals. The area was painted, the floors were covered with Stonhard, and new, larger drains were installed.

Stonhard flooring was installed in the G-8 indoor and outdoor animal areas and work space and in M-3 and G-1 indoor animal areas and work space. This is an epoxy flooring that is impervious to cleaning compounds and chemicals and facilitates the routine cleaning and maintenance of these areas. The kitchen floor was coated with Stonclad flooring material. The walls of the indoor animal quarters of S1&2 were Stonglazed.

Playground equipment was installed in D-1 and D-2 providing the animals with structures on which they can climb and swing.

Concrete feeding pads were installed at S-5, S-5, S-7, S-8, T-1, T-2, T-3, T-4, D-1, D-2 and G-2, providing clean, dry, easily sanitized areas on which the animals can be fed.

Construction of a cage wash facility and installation of the cage washer was completed. This facility provides the capability to sanitize all caging equipment.

Construction of a new Clinical Medicine Building (nearing completion). This building will provide radiological, surgical and research support facilities for the Field Station.

B. Physical Plant

1) Main Station

Significant progress accomplished during 1990:

a) Construction was completed on the AIDS Research Addition (Virology Research Wing) to the Ophthalmic Research Facility. The first floor of this 2-story facility provides housing for animals, and the second floor contains laboratories and offices for virological studies.

b) A new office trailer was added to the Ophthalmic Research Facility. An opening was made in the existing building and the trailer attached in order to provide contiguous space. This trailer provides four new offices and a reception area for ophthalmic studies.

c) Standard acoustical ceiling tile in the hallway of the Small Primate Wing and Necropsy suite was replaced with Milar ceiling tile. This type of tile is impervious to water and is more durable than the standard tile.

d) An air filter system was installed in the second floor conference room and in the Neural Ultrastructure Laboratory. This was necessary to prevent emission of dirt particles.

e) The air duct in the Ophthalmic Research Facility was sealed and insulated in order to increase the efficiency of the HVAC system.

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

g) The electricity was upgraded and duct work rerouted in the Scanning Electron Microscopy facility to provide the necessary power and cooling for a new electron microscope obtained by the Center.

h) The chiller serving the main building was added to the temperature alarm system. This will allow immediate notification when the chiller becomes off line.

i) Overhead lines serving the security lights inside the perimeter fence were relocated underground to increase protection.

j) Room 306 of the main building was renovated for use as a third floor conference room. Renovation included removal of casework and utilities, installation of a lay-in ceiling, light fixtures and carpet, painting, and the purchase of furniture. Refurnishing of the second floor conference room occurred in conjunction with this renovation.

k) A grating system was installed on the trench of E-section of the Great Ape Wing. This grate was necessary to ensure the safety of animal care staff and others working in this area.

l) A new generator was purchased and installed to provide electricity during power failures. The 125kw unit allowed relief for other overloaded units and allowed for the redistribution of emergency power to facilities at the Center.

m) Horizontal pipe handrail was installed for safety reasons behind the Great Ape Wing extending the length of B-Section to the treatment room. The railing was installed for safety rather than support.

n) Room 351 of the main building was renovated for the Center's Biomedical Engineer. Renovation included removal of casework, installation of lay-in ceiling, light fixtures and carpet, painting, and purchase of furniture.

o) The fire alarm panel serving the Ophthalmic Research facility was replaced and upgraded. The new panel was upgraded to serve the recently attached Virology Research Wing.

p) A new forklift was purchased to assist with unloading deliveries at the Center and to move heavy items around within the Center.

q) Storm sewer lines were installed at the Virology Research Wing and RC. This will prevent improper water drainage and soil erosion.

r) Gravel fill was applied to the areas surrounding SEM, T-14, RC, and the area between the main building and RF. This will reduce the amount of grounds maintenance and also enhance the appearance of these areas.

s) The Center contracted with BFI Medical Waste Systems for removal of biomedical wastes. Prior to this contract waste was incinerated in the center-owned incinerator.

t) The electrical panel was replaced and the electrical capacity upgraded in the SEM facility. Prior to this, circuit breakers often tripped because of inadequate electrical supply.

u) The roof over the treatment and metabolism rooms of the Great Ape Wing was replaced. The existing roof was framed with wood that had deteriorated. The new roof is made of metal panels which will be more durable and appealing than the wood.

v) A considerable amount of landscaping was required around RD, RC, Virology Research Wing, RA, RB, and the end of E-Section of the Great Ape Wing in order to control erosion and to enhance the appearance of

4) An additional 8 cases of yersiniosis were diagnosed at necropsy during 1990. This naturally occurring enteric bacterial infection continues to be a problem in our Field Station colony. Yersinia species have been isolated from 182 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 animal from which Yersinia were isolated.

5) Seven animals (3.3% of necropsies) were found to have neoplasms in 1990. Tumors encountered in 1990 included three intestinal carcinomas in rhesus monkeys, one hepatic carcinoma in a squirrel monkey, three lymphomas of the gastric wall (one each in a rhesus, stumptail and pig-tailed macaque), one multifocal lymphoma in a mangabey, one adrenal adenoma in a rhesus monkey, one adrenal pheochromocytoma in a rhesus, and one pig-tailed macaque had multifocal fibrosarcomas of the skin/subcutis.

6) Fifteen additional cases of listeriosis were diagnosed in 1990. These included six newborn rhesus (1-4 days old), seven rhesus abortuses or stillbirths, one newborn pig-tailed macaque (1 day old), and one adult rhesus. This brings the total number of cases of listeriosis seen in our colony to 54, since the disease was first diagnosed in 1982.

Significant lesions observed in the 172 surgical pathology specimens examined in 1990 included amyloidosis, chronic colitis, carcinoma of the cecum, carcinoma of the skin, lymphoid hyperplasia of lymph nodes, calcinosis cutis and hepatocystis in the liver.

Histopathology Service: During 1990 the histopathology laboratory processed 542 necropsy cases and/or biopsies. This entailed the production, and subsequent filing of 15,741 paraffin blocks. A total of 15,961 microslides were prepared from these blocks. Following microscopic review, all slides are maintained on file in the light microscopy laboratory.

Clinical Pathology Service: During 1990, the clinical pathology laboratory received 10,639 specimens for evaluation. These determinations can be categorized as follows:

Laboratory Determination	Number of Specimens
Hematology Examinations	2,348
Bone Marrow Examinations	4
Bacterial Cultures	3,392
Mycoplasma Cultures	1
Viral Cultures	75
Fungal Cultures	7
Fecal Parasitology Examinations	616
Serum Chemistries	1,032
Pregnancy Tests	35
Urine Analysis	166
Imprint Smear Preparations	800
Spinal Fluid Examinations	119
Immunologic Examinations	931
Specific Gravity	6
Special Chemistries (Kidney Stone Analysis)	1
FACScan Analyses	874
FACScan and RID analyses	232

When compared with 1989, this number of laboratory specimens represents an increase of 454 submissions (4.3% increase). Increases were noted in the number of hematology examinations, bacterial cultures, spinal fluid examinations and imprint smear preparations.

Selected pathogenic microorganisms isolated during the past year include:

Staphylococcus aureus	Streptococcus pneumoniae
Campylobacter pylori	Crytococcus neoformans
Candida albicans	Listeria monocytogenes
Salmonella typhimurium	Shigella flexneri
Salmonella berta	Yersinia enterocolitica
Salmonella anatum	Yersinia frederickseni
Yersinia pseudotuberculosis	Campylobacter coli
Yersinia kristensenii	Campylobacter fetus
Yersinia intermedia	Klebsiella pneumoniae
Enteropath. E. coli	Pasteurella multocida
Campylobacter jejuni	Vibrio cholerae Non-01
Campylobacter butzleri	

A total of 499 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 1990, strongyloidiasis occurred in 2 animals and 13 cases of giardiasis were diagnosed.

Pathology Electron Microscopy Laboratory: During 1990, the pathology electron microscopy laboratory received 121 specimens for processing for ultrastructural evaluation. Specimens received included 51 cell cultures, 9 lymph nodes, 3 Peyer's patch specimens, 2 spleen specimens, 4 G.I. tract specimens, 33 testicular cell specimens, eight lung specimens, four brain specimens, three tumor specimens, and 1 each of kidney, skin lesion, skin nodule and gingiva.

Specimens Collected for Other Investigators: During 1990, 4612 specimens were collected and shipped to 110 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 (Yersinia species), hair, spines and fecal samples. This includes 32,363 ml of whole blood, 1100 ml of serum and 442 ml of plasma from 14 nonhuman primate species. When compared to 1989, the number of specimens shipped represents a decrease of 23%.

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 from Emory University, and other investigators outside of the Emory community. Determinations are provided on sample charge basis comprised of the cost of technical time, chemical reagents, equipment used, and waste disposal. During calendar year 1990, individuals who utilized the services of the RIA Laboratory are as follows:

Yerkes Core Scientists:

Dr. Ken Gould: Gonadal hormone determinations for studies on fertility in apes and exotic mammals.

Dr. Kim Wallen: gonadal hormone determinations for studies on female sexuality.

Dr Mark E. Wilson: adrenal, gonadal, pituitary, pineal and metabolic hormones were determined for studies on the neuroendocrine regulation of puberty, growth and lactational infertility.

Dr. Ron Nadler: pituitary hormone determinations for studies on sexuality in gibbons.

Professor 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 for studies on male sexuality.

Dr. Larry Byrd: gonadal hormone determinations for studies on the effects of cocaine.

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 for studies on development and osteoporosis.

Dr. David Martin (Georgia State University): gonadal and pituitary hormones for studies on sexuality in quadriplegic men.

Dr. Susan Schwartz (Caribbean Primate Research Center): gonadal, pituitary, and metabolic hormone determinations for studies on puberty in monkeys.

Dr. Debbie Gust: gonadal, pituitary, and adrenal hormone determinations for studies on social stress.

Dr. Kim Bard: adrenal hormone determinations for studies on individual differences in reactivity.

Emory University Scientists

Dr. Jennifer Lovejoy - Department of Medicine
Dr. Susan Gebhart - Department of Medicine
Dr. Larry Phillips - Department of Medicine
Dr. Mario DiGirolamo - Department of Medicine
Dr. Patrick Delafontaine - Department of Medicine
Dr. Floyd Culler - Department of Medicine

Non-Emory University Scientists

Dr. Carol Shively - Bowman Gray University School of Medicine
Dr. Paul Musey - Atlanta University
Dr. Jay Kaplan - Bowman Gray University School of Medicine
Dr. Betsy Welles - Bowman Gray University School of Medicine
Dr. Jan Wagner - Bowman Gray University School of Medicine
Dr. Thomas Clarkson - Bowman Gray University School of Medicine
Dr. Dietrich Schaff - Zoo Atlanta

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

Steroid Hormones

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

Other

osteocalcin
creatinine (spectrophotometric)
glucagon
melatonin
B-endorphin
glucose (spectrophotometric)
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
T_3
T_4 (total)
oxytocin
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
T_4 (free)
T_3 (reverse)
somatostatin

During the calendar year 1990, the RIA Laboratory performed 24,052 determinations as follows:

Hormone	Number
B-endorphin	235
ACTH	1,084
C-peptide	142
cortisol	2,154
creatinine	818

Hormone	Number
dihydrotesterone	12
estradiol (free)	108
estradiol	3,012
estriol glucuronide	390
estrone glucuronide	86
estrone	390
ethinyl estradiol	4
FSH (human, ape)	164
GH	779
GH antibodies	64
glucagon	65
glucose	1,015
IGF-1	767
insulin (free)	83
insulin	2,705
iodination (custom)	14
LH (bioassay)	1,157
LH (human, ape)	323
LH (monkey)	42
melatonin	552
osteocalcin	149
oxytocin	406
pregnanediol	456
progesterone	2,182
prolactin	2,847
SHBG	658
T_3 (total)	93
T_4 (total)	199
testosterone (free)	157
testosterone (total)	647
TSH	93

E) General Office Services

This office is responsible for the following functions:

a) processing and distributing 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 is staffed by two individuals: the Administrative Associate for Special Projects (who also holds the title of Chief, Public Affairs) and the Public Affairs Assistant. The second individual joined the Yerkes Center in 1990, occupying a position until then held by the

Secretary to the Administrative Associate for Special Projects and the Administrative Associate responsible for computer services. Thus, the addition of the Public Affairs Assistant did not result in an expansion of the Yerkes staff.

With the Public Affairs Assistant and "desktop publishing" technology, the Administrative Associate for Special Projects was able to provide Yerkes faculty and staff, Emory officials, and members of the community with publications about the Yerkes Center that previously had been impossible to publish due to the high costs of typesetting. The cost of producing a document through this technology (which enables typesetting and layout-design to be accomplished by using a computer-word processor) is dramatically lower than the fees that are charged by conventional typesetting and layout-design services.

As a result of the availability of desktop publishing and the employment of a Public Affairs Assistant talented in layout and design via this technology, the Yerkes Center was able to produce during 1990 the following publications:

(1) Two issues of Inside Yerkes with a much more professional appearance and readability than previous issues of this publication, which was created in 1979 for distribution to Yerkes faculty and staff and Emory officials. These two issues were distributed to government officials, scientists in related fields, appropriate news media, selected business and civic leaders in Atlanta, as well as Yerkes faculty, staff and students and Emory officials.

(2) Eight copies of Inside Yerkes for Yerkes personnel. These one-page sheets were used to announce an upcoming research briefing for Yerkes faculty and staff. Each issue explained the research so that individuals unable to attend the briefings would be informed about the nature of the studies.

(3) Annual Report, the 60th Year: 1989-1990 of the Yerkes Center. This 44-page report marked the anniversary of the founding of the Yerkes Center by Dr. Robert M. Yerkes in 1930. While the Yerkes Center's rich history was described in the report, its primary emphasis was the achievements of the Center in research, animal care and conservation in the past decade, a period of tremendous growth at the Center. The report earned the Yerkes Center the Silver Flame Award from the International Association for Biomedical Communicators/Atlanta.

(4) Yerkes Field Station: A Unique Research Facility. This four-page booklet, which describes the unique research opportunities of the Yerkes Field Station, is distributed to

scientists, students and members of the public upon request.

In addition to publications, which are highlighted above, the Information Services Office was active in news media relations, tours, special events, and presentations to scientific and civic groups and special projects assigned by the Yerkes Director.

News Media Relations:

The Information Services Office assisted a wide range of international, national and local media in preparation of stories about the Yerkes Center. Examples include British Broadcasting Corporation, National Broadcasting Corporation, Public Broadcasting Corporation, Discover magazine, Newsday newspaper, The Atlanta Journal and Constitution, Gwinnett Daily News and Clayton Sun News.

News releases were prepared about Yerkes research on AIDS, vision studies, vocal communication, and the Center's 60th anniversary report. The news release about the report mentioned that copies were available to the public and resulted in stories in three Emory publications.

Tours and Community Relations:

Many of the tours of the Yerkes Center during 1990 were arranged and/or conducted by the Information Services Office. Groups visiting the Center ranged from Leadership DeKalb to the National Science Teachers Association. Many tours were provided for Emory student groups, particularly those in the Freshman Seminar program of the university.

The Information Services Office also responded to numerous telephone and letter requests from students and other members of the public who wanted information about the Yerkes Center, primates, or the value and treatment of animals in research. Interviews with scientists were arranged for several students as part of their class projects.

Special Events and Projects:

During 1990, the Yerkes Center was site visited by the National Center for Research Resources. The Information Services Office assisted the Yerkes Director in many of the arrangements for the visit.

The Administrative Associate for Special Projects also assisted the Director in evaluating the feasibility of conducting appropriate fundraising for Yerkes programs and facilities. The Administrative Associate for Special Projects compiled a "case statement" as part of this evaluation

process.

The Administrative Associate for Special Projects provided descriptions of Yerkes research studies for inclusion in the publication by the Oregon Primate Research Center, Primate News Special Report, Toward Better Health: the Role of Primates in Biomedical Research at the Regional Primate Research Centers.

The Administrative Associate for Special Projects also wrote an article about the Yerkes Center's 60th anniversary for the membership publication of the American Psychological Society. She also authored an article about the Yerkes gorillas on loan to Zoo Atlanta and the zoo's male gorilla Willie B., for Friends of Zoo Atlanta's Zoom magazine. The article was titled "Gorilla Love."

Presentations:

The Administrative Associate for Special Projects assisted the Yerkes Director in the preparation of presentations to scientific, educational and civic groups. Examples include his poster presentation at the American Physiological Society/Chinese Physiological Society Joint Meeting and his speeches to the Marietta Rotary Club in Atlanta and the Emory Faculty Dinner. She also assisted other Yerkes faculty in the preparation of their speeches for civic and educational groups.

She gave speeches about the Yerkes Center or particular topics of interest to various groups, including the Emory Women's Club, the American Heart Association/Georgia Chapter, and Woodward Academy.

During 1990, seven Yerkes researchers presented their research at informal meetings of Yerkes faculty and staff. Invitations for these sessions were made by the Information Services Office who also handled the arrangements and publicity.

6) 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, administrative coordination of fund raising activities, and liaison with selected government and professional agencies. 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 1990:

Peripheral and processor enhancements were made to the Sun server to help accommodate a growing number of users. The server's central processing unit was upgraded from a Sun 3 to a Sun 4 Sparc processor. A 2.3 gigabyte tape backup unit was added to augment the existing 60 MB cartridge tape. The number of different individuals with login ids is now 105.

Sun diskless workstations were added to the network for use by researchers and by computer services staff. Workstations were also installed that support 800 MB of disk storage and a CD-ROM drive for Sun software distribution. These resources are integrated into the Center's network and are part of overall user support. These upgrades provided the expansion necessary to accommodate the growing Network and serial connection were extended to several buildings on the Main Station grounds using a combination of twisted-pair and optical cabling. Additional serial links were established between the Field Station and the central server via dial-up modems.

Four microcomputers and five terminals were installed to accommodate new users of computer services. Also, emphasis was placed on upgrading existing PC's where feasible. The NeXT system previously located at the Main Station was moved to the Language Research Center for sound recognition studies.

The primary focus of attention for scheduled application development during the year was in the Budgets and Accounts System (BAS). Significant enhancements were made to the BAS system related to indirect cost accounting and budget projection reporting. A new program menu system was implemented to provide a better user interface and improved database access control.

Development and support for the Animal Records System (ARS) was concerned primarily with correcting programming problems and providing timely system changes required by unexpected circumstances. Major modifications were made to maintenance programs based on user recommendations. A prototype facility was established to begin allowing authorized users free-form query access to the database.

Database tuning was performed that resulted in dramatic run-time improvement in several areas.

In addition to consultation, a limited amount of direct support was provided for scientific programming. Several ad hoc reports and SQL queries were developed to extract ARS data for scientific purposes. A FORTRAN program was

modified to allow for larger sets of observation data.

A third-party inventory management system was installed on the PC's of staff responsible for the General Office Supplies; they currently are using this system to maintain the Center's inventory.

Contracts and Agreements with Outside Agencies - The Yerkes Center is currently involved in 38 agreements and contracts for research sponsored by, or carried out for, private industry, universities, and other outside agencies. Additionally there are several other contracts or agreements in various stages of negotiation. 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.

Bone Care International
Boston University
Busch Entertainment Corp.
Dana Farber Cancer Institute
Eagles Max Baer Heart Fund
The Edna McConnell Clark Foundation
Emory - Georgia Tech Biotechnology Research Center
General Electric Company
Genetics Institute
Georgetown University
Georgia State University
Harvard University
Institute of Primate Research and California Primate Research Center
Morehouse University School of Medicine
Optical Sensors for Medicine
University of Alabama

Liaison with Selected Government and Professional Organizations - In 1990 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 memberships. 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 1990 the Administrative Associate's office provided assistance to Director in promoting fund raising for expansion of the Center. The Yerkes Center is working directly with the Emory's Office of Development with whose help fund raising consultants are being evaluated.

H) Bioelectronics and Instrumentation Shops

During 1990 the Instrumentation and Electronics shop repaired and maintained numerous pieces of commercial and custom equipment, including computer and other data processing equipment.

Several specialized pieces of equipment were designed and built for Yerkes Research staff such as:

A general purpose I/O interface circuit for the portable computer that can be controlled by software. This device is currently being used for training rhesus monkeys by Dr. Ronald Boothe and associates.

An adjustable analog delay line for analyzing intercranial recorded data for Dr. J. Wilson.

A two channel variable gain amplifier for Dr. J. Wilson.

The temperature control units for the gibbon cages were modified to handle the high lamp inrush current, and manual override switches were installed in the control panel for Dr. Dahl.

Two pneumatic micro-manipulators for handling ova were designed and built for Dr. Gould.

A tool for gel coating microscope slides was fabricated for Dr. Gould.

A set of animal handling wands was fabricated for Dr. Byrd.

Two head-restraint boards were built for Dr. Fritz.

A new monkey interface was designed for Dr. Boothe's research. It combines animal inter-changeability with optimal optics alignment, and incorporates guide plates to properly direct the monkey's vision.

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 services to the Yerkes Center. Professor Warner's consultation services during the past year included determination of the frequency stability of a telemeter used by the Division of Reproductive Biology, an evaluation and discussion regarding the vibrational and electromagnetic environmental specifications for a scanning electron microscope, determined the electric current density in probe electrodes of an EEJ instrument, and prepared schematics and instructional material for the Yerkes EEJ stimulator.

I) General Shop

During 1990 the General Shop processed and completed over 400 work orders; about 250 of them requiring immediate response.

Routine work consisted of the completion of several laboratory environments for researchers as follows:

Final outfitting of the new AIDS laboratories with shelving, freezer benches and work benches for Dr. McClure's group.

Modified and installed specialized equipment in Dental

Research Laboratory for Dr. Fritz.

Installed special benching and shelving in the Small Primate Wing for Dr. Kennedy's laboratory.

Installed conduit and cable runs in Dr. Byrd's research area in RC.

Fabricated several pieces of labware for Dr. Villinger.

Other routine work was performed for administrative areas, such as the installation of shelving and cabinets.

The majority, by far, of shop time was consumed in the animal care areas as follows:

Repairing/rebuilding cages, cage racks, fencing, and cage washing equipment.

Completing new or refurbished animal quarters with such necessary items as perches, auxillary heating, and door locks.

Designing a new bedboard system for the Great Ape Wing, and generating production drawings for new "communing" doors in the great ape wing.

J) Library

The Yerkes Research Center 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 3,200. 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 in-house 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.

The online databases, DIALOG, and DOBIS, the online catalog of Emory's library holdings, were indispensable for reference use, and for literature and bibliographic searches. VUTEXT was cancelled, as DIALOG duplicated many of their databases.

The library is open around the clock. Additionally, it is utilized for research projects requiring a quiet work space, as video coding and viewing.

K) Business Office

The Business Office provides four main service functions to the Center.

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

2) Budget and Accounts - includes grants and contracts preparation and grant administration. During 1990 this office administered 65 accounts.

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

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

L) Photography

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

During 1990, 723 requests 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. Acquisition of a second SEM, an ISI DS130 with a field emission gun provides a unique capacity for high resolution SEM within the facility. 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 1990, staff of the facility organized a successful short course on high resolution imaging, and provided support for a variety of research projects. Among these, not expanded upon elsewhere in the report, were a study to view and photograph the bacteria and other microbes on soil particles and the root surface of a plant from two granite outcrop plant communities. This study was an approach investigation of bacterial consortia of two plant communities with an aim toward understanding bacterial diversity, community structure, and functional roles. The SEM observations will be coupled with physiological and genetic studies of the soil microbes. In addition, the scanning electron microscope was used to study endothelial seeding on endarterectomized vessels in vivo (acute and chronic) and was also used to evaluate endothelial seeding on dacron pre-clotted grafts. Parameters evaluated included the presence of cells, the evenness of their distribution, their density, extent of spreading and the presence of thrombus and platelets. A related study monitored changes in the blood vessel wall similar to those seen in restenosis using balloon injury and arterial stents. That work sought to define the response of the blood vessel to injury using light microscopy and EM. Specifically, it measured the thickness and composition of the intima, type of cells associated with the stent line and occurrence of thrombus formation.

As part of continuing studies on thrombus formation and vascular wall damage associated with techniques designed to modify blood vessel potency and diameter scanning electron microscopy was used to look at the effects of cilazapril, an angiotensin converting enzyme blocker on vessel wall lesions

and healing. Twenty baboon left carotid and femoral arteries were endarterectomized and ballooned, respectively, 30 days prior to collection.

In addition, the study used scanning electron microscopy (SEM) to evaluate the effects of fish oil diet on baboon vessel wall recovery following acute 3 day and chronic 30 day endarterectomy of carotid arteries.

Studies related to the field of Ophthalmology included the evaluation of a viscous collagen biosynthetic material photo-polymerized directly to the cornea (Bowman's layer). The objective of this work is to provide a new refractive surface to the cornea using synthetic polymers. Scanning electron microscopy was used to ascertain the surface topography of the photo-polymerized collagen specimen. As part of an ongoing study for the development of improved methods for use of computer guided laser ablation of the cornea for correction of visual defects the efficacy of the diaphragm delivery versus the mask delivery system was compared. Two cornea were laser ablated using each system. The ablated corneas were evaluated using Scanning Electron Microscopy for the smoothness of the corneal surface at 0.05 micron resolution and for evidence of the presence/absence of residual cellular debris which could affect subsequent healing and visual correction.

The following investigators conducted research using Scanning Electron Microscopy at the Center during 1990:

Name:	Affiliation:
Sandra Bowden	Agnes Scott College
Kamala Dutt	Morehouse College Medical School
Laurence Harker	Department of Medicine, Emory University
Steven Karos	Cardiology/Radiology Dept., Emory University
Ken Gould	Yerkes Research Center, Emory University
Takaharu Tsuno	Chemistry Department, Emory University
Keith Thompson	Ophthalmology Department, Emory University
Robert Maloney	Ophthalmology Department, Emory University
Ray Gailitis	Ophthalmology Department, Emory University
Patricia White	Agnes Scott College

Visiting Scientists at the SEM Facility in 1990 included:

O. J. Castejon	Insituto De Investigaciones Biologicas, Universidad del Zulia, Maracaibo, Venezuela

D. Joy	EM Facility, University of Tennessee, Knoxville, Tennessee
G. Pasquinelli	Division of Hematology, University of Bologna, Italy
R. Reichelt	Division of Biophysics at Westfalische Wilhems-Universitat, Munster, Germany
K. Robinson	Department of Exercise and Physiology, Western Carolina University, Cullowhee

B. HIGHLIGHTS

1) Research Completed

a) Thrombus Formation and Dissolution In Vivo

Thrombosis is a major life-threatening, naturally occurring pathologic process in humans and may also be a complication of cardiovascular surgery. In a search for improved therapies for this disease process, investigators at the Yerkes Center have evaluated numerous peptides and procedures in a nonhuman primate model. Tyr-sulfated dodecapeptide from residues 53-64 of hirudin (H-peptide) was tested, and the findings suggested that fibrin-rich venous-type thrombus formation may be selectively prevented and, thus, be a therapeutically attractive regimen for preserving normal platelet function when conventional anticoagulant therapy is contraindicated. Hirudin, a highly potent and specific antithrombin, was compared to heparin, an antithrombin III-dependent inhibitor of thrombin. These studies indicated that platelet-dependent, thrombotic and hemostatic processes are thrombin-mediated and that hirudin produced a potent, dose-dependent inhibition of arterial thrombus formation which greatly exceeded the minimal antithrombotic effects produced by heparin. Studies with D-phe-pro-arg chloro-methylketone (D-FPR CH_2 Cl) during carotid endarterectomy indicated that short-term therapy with this agent produced long-term antithrombotic benefits without risk of abnormal bleeding when administered immediately after surgical hemostasis has been achieved. Applaggin was also found to be a potent reversible inhibitor of platelet recruitment into forming thrombus which may be therapeutically useful in humans. Hirulog was assessed and exhibited greater antithrombotic efficacy than D -FPR CH_2 Cl and hirudin and approached the potency of D-FPR CH_2 Cl without its potential toxicity. Locally treated small caliber Dacron vascular grafts were implanted end-to-end with D-FPR CH_2 Cl and found to prevent subsequent thrombus formation without risk of hemorrhage. Local versus systemic effects of hirudin, D-FPR

CH_2 Cl and heparin were compared for blocking platelet deposition onto segments of thrombogenic Dacron vascular grafts, and showed that short-term treatment of forming thrombi with D-FPR CH_2 Cl markedly reduced or prevented (for > 21 hours) subsequent thrombus growth. These observations may have important implications regarding the treatment or prevention of thrombosis in humans.

b) Perinatal Transmission of SIVsmm

Due to the increasingly important problem of HIV infection and AIDS in the human pediatric population, studies were done to evaluate the perinatal/postnatal transmission of SIVsmm in experimentally infected rhesus macaques and to determine the feasibility of using experimentally infected rhesus macaques as a model system for the study of perinatal HIV infection. In these studies, 15 timed pregnant rhesus monkeys were infected with SIVsmm during various stages of gestation, and their offspring were monitored for evidence of virus infection. Three groups of five animals were infected with SIVsmm during early (day 28-35), mid (day 71-78) and late (day 146-150) gestation. Offspring delivered by these experimentally infected macaques included two stillbirths and 13 livebirths; one liveborn infant died at 3 days of age. There was no evidence of virus infection in the stillbirths or neonatal death. The remaining infants and their mothers were evaluated within a week of parturition and at quarterly intervals thereafter by serology and virus culture of PBMC; milk samples were also collected from the mothers at each examination for virus culture. All infants were virus negative at birth; all infants in the early and mid-gestation groups and one infant in the late gestation group had low levels of maternal antibodies to SIVsmm. These maternal antibodies disappeared prior to three months of age in 4 of 9 infants, and between 3 and 6 months in the other 5 infants. Three infants subsequently seroconverted and became virus positive at 9-15 months of age. Milk samples from all mothers were virus negative at parturition, but milk samples from 4 animals were virus positive at 9 and 12 months post-partum. Two of the three infected infants have died (7 and 9 months from time infection was documented), and the other infant is showing lymphadenopathy and progressive immunosuppression. This represents the first documentation of maternal-infant transmission of SIV and also represents the first isolation of SIV from milk of infected macaques. These observations suggest that maternal-infant transmission occurred by breast-feeding, and indicate that breast-feeding may be a more important mechanism for transmission of lentiviruses (e.g., HIV and SIV) than is presently believed.

2) Research in Progress

a) Social and Endocrine Effects on Immune Function

Considerable information is available that provides compelling evidence that factors associated with social life and changes in social environment may lead directly to alternations in immune function and, thereby, to increased susceptibility to pathogens. Moreover, steroid hormones are known to affect immune function by acting as immunoregulators. Overall, the immune system may be viewed as a major integrative network involved in biological adaptation. A large number of experimental and clinical studies have shown that psychosocial variables produce an endocrine response, including changes in adrenal, pituitary and gonadal secretion, and also directly affect both humoral and cell-mediated immune responses. Studies were, therefore, initiated to examine the social and endocrine modulation of immune function in rhesus and mangabey monkeys. In these studies, removal of juvenile rhesus monkeys from their natal, social group to indoor, individual housing resulted in increased basal cortisol secretion and significant decrements in immune parameters. Baseline immune and cortisol measurements were obtained before seven subjects were removed from the group and placed in individual cages. The remaining seven subjects, which served as controls, remained in the social group throughout the study. Test subjects showed a significant decrease in $CD4^+$ and $CD8^+$ T cells and a significant increase in basal cortisol levels following removal to individual caging; some effects lasted through seven weeks. During the second phase of the study, the test subjects were returned to their natal group 18 weeks after removal from the group. Based on behavioral data recorded immediately after the return, one could predict which animals would show the greatest decline in immune parameters 24 hours after returning to the group. Similar results were obtained from six yearling mangabey monkeys removed to indoor, group-type housing. Work is continuing to examine the parameters of this model including species differences, endocrine modulation and the role of social variables in modulating the effects.

b) Pre-chemotherapy Marrow Priming with Recombinant CSF's

Methodology has been developed for in vitro clonogenic assays and FACS analysis to be used in experiments in which rHuIL-3, rHuGM-CSF, or rHuIL-6 are administered to rhesus monkeys; the normal range and variance of the assays has also been established in untreated rhesus monkeys. Experiments involving the animals were conducted in which marrow and peripheral blood samples were obtained before, during and after administration of 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 and rHuIL-6 administration. rHuIL-6 also lead to significant increases in circulating platelets. In addition, it has been 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. 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. Such use could involve priming the marrow donor prior to collection of marrow or blood stem cells with HGF's to augment the numbers of primitive hematopoietic cells collected, or administering HGF's post chemotherapy or marrow transplant to accelerate regeneration.

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

Executive Committee (Cont'd)

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.
B. Swenson	D.V.M.	Associate Research Professor and Chief of Veterinary Medicine	Animal Resources	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.

Executive Committee (Cont'd)

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 Language Research Center Coordinator	Behavioral Biology	Yerkes
		Professor and Chairman	Psychology	Georgia State Univ.

2) Yerkes Resources and Science Review Committee

The Yerkes Resources and Science 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, and appropriateness of the primate species selected; (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. The composition of the Yerkes Resources and Science Review Committee is as follows:

Yerkes Resources and Science Review 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.

Yerkes Resources and Science Review Committee (Cont'd)

T. Gordon (Co-Chair)	M.S.	Associate Research Professor and Field Station Coordinator	Behavioral Biology	Yerkes
		Adjunct Professor	Psychology	Emory Univ.
R. Boothe	Ph.D.	Research Professor	Neurobiology	Yerkes
		Associate Professor	Psychology	Emory Univ.
		Assistant Professor	Ophthalmology	Emory Univ.
J. Else	D.V.M.	Associate Director for Animal Resources, Associate Research Professor	Animal Resources	Yerkes
J. Herndon	Ph.D.	Associate Research Professor	Neurobiology	Yerkes
		Adjunct Assistant Professor	Biology	Emory Univ.
		Adjunct Assistant Professor	Psychology	Emory Univ.
R. Nadler	Ph.D.	Research Professor	Reproductive Biology	Yerkes
		Adjunct Associate Professor	Psychology	Emory Univ.
M. Tigges	Ph.D.	Research Professor	Neurobiology	Yerkes
		Associate Professor	Anatomy and Cell Biology	Emory Univ.
		Associate Professor	Ophthalmology	Emory Univ.
M. Wilson	Ph.D.	Associate Research Professor	Reproductive Biology	Yerkes
		Associate Professor	Medicine	Emory Univ.
		Associate Professor	Psychology	Emory Univ.

3) IACUC Primate Subcommittee

This committee was formally established in January, 1990, and was charged with the responsibility for review of research proposals for humane treatment of laboratory animals and other elements mandated by USDA/PHS regulations. This committee is a subcommittee of the University IACUC and has the responsibility for review of all University proposals that involve the use of nonhuman primates. Actions taken by the IACUC Primate Subcommittee are forwarded directly to the University IACUC for final disposition. The composition of this committee is as follows:

IACUC Primate Subcommittee

Name	Degree	Academic Titles	Department or Division	Institution
J. Else (Chair)	D.V.M.	Associate Director for Animal Resources, Associate Research Professor	Animal Resources	Yerkes
D. Anderson	D.V.M.	Associate Research Professor	Pathobiology and Immunobiology	Yerkes
T. Gordon	M.S.	Associate Research Professor and Field Station Coordinator	Behavioral Biology	Yerkes
		Adjunct Professor	Psychology	Emory Univ.
K. Gould	D.V.M. Ph.D.	Research Professor and Chief, Division of Reproductive Biology	Reproductive Biology	Yerkes
		Adjunct Professor	Biology	Emory Univ.
J. Magnotta	B.S.	Associate Director for Administration	Administration	Yerkes
B. Swenson	D.V.M.	Associate Research Professor and Chief of Veterinary Medicine	Animal Resources	Yerkes

4) 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 of Veterinary Medicine	Animal Resources	Yerkes
J. Roberts		Chief Superintendent	Main Station	Yerkes
D. Chikazawa		Superintendent	Field Station	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.	Associate Director for Animal Resources and Associate Research Professor	Animal Resources	Yerkes
K. Pralinsky	B.A.	Superintendent	Main Station	Yerkes

5) Computer Committee

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

Computer Committee

Name	Degree	Academic Titles	Department or Division	Institution
R. Boothe (Chair)	Ph.D.	Research Professor Professor	Neurobiology	Yerkes
		Associate Professor	Psychology	Emory Univ.
		Assistant Professor	Ophthalmology	Emory Univ.
R.Buddington	Ph.D.	Administrative Associate	Administration	Yerkes
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.
C. Lin	B.S.	Computer Services Coordinator	Computer Services	Yerkes
J. Magnotta	B.A.	Associate Director for Administration	Administration	Yerkes

Computer Committee (Cont'd)

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.

6) Library Committee

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

Library Committee

Name	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.
M. Johns		Librarian	Administration	Yerkes
J. Magnotta	B.A.	Associate Director for Administration	Administration	Yerkes

Library Committee (Cont'd)

B. Swenson	D.V.M.	Associate Research Professor and Chief of Veterinary Medicine	Animal Resources	Yerkes
N. Wilson	Ph.D.	Associate Research Professor	Reproductive Biology	Yerkes
		Associate Professor	Medicine	Emory Univ.
		Associate Professor	Psychology	Emory Univ.

7) Affirmative Action Committee

The three main areas of responsibility of this committee include: (1) to serve as a vehicle for the proper disposition of complaints 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.	Superintendent	Main Station	Yerkes
F. Jewell		Receptionist	Administration	Yerkes
J. Magnotta (ex officio)	B.A.	Associate Director for Administration	Administration	Yerkes

8) Task Force on 1990 Budget

Due to projected changes for FY 1990-91 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:

1990 Budget Task Force

Name	Degree	Academic Titles	Department or Division	Institution
J. Magnotta (Chair)	B.A.	Associate Director for Administration	Administration	Yerkes
J. Else	D.V.M.	Associate Director for Animal Resources and 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.

9) 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. 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)

R. Boothe	Ph.D.	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. Setzekorn	---	Supervisor Animal Records	Animal Resources	Yerkes
B. Swenson	D.V.M.	Associate Research Professor and Chief of Veterinary Medicine	Animal Resources	Yerkes
D. Vinson	---	Secretary I	Field Station	Yerkes

10) 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.	Associate Research Professor	Reproductive Biology	Yerkes
		Associate Professor	Medicine	Emory Univ.
		Associate Professor	Psychology	Emory Univ.
D. Anderson	D.V.M.	Associate Research Professor	Pathobiology and Immunobiology	Yerkes
K. Pralinsky	B.A.	Superintendent	Main Station	Yerkes

Biohazard Safety Committee (Cont'd)

J. Magnotta B.A.	Associate Director for Administration	Administration	Yerkes

11) 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.

12) 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 maki 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.

13) Primate Enrichment Committee

This committee was established in 1990 with a mandate to provide improvements in housing and other types of enrichment for Yerkes nonhuman primates. The committee will evaluate enrichments such as manipulanda; food varieties; food distribution devices; "toys"; climbing devices; opportunity of choice of visual, auditory, and other sensory stimulations; opportunities for increased socialization; and other related changes that may enhance normal behaviors. The committee is expected to not only conceptualize enrichment opportunities, but to implement them through discussions and arrangements with the appropriate units of the Center, and evaluate them objectively as to their effectiveness.

Primate Enrichment Committee

Name	Degree	Academic Titles	Department or Division	Institution
J. Else (Chair)	D.V.M.	Associate Director for Animal Resources and Associate Research Professor	Animal Resources	Yerkes

Primate Enrichment Committee (Cont'd)

J. Ellis	Ph.D.	Research Associate	Behavioral Biology	Yerkes
T. Gordon	M.S.	Associate Research Professor and Field Station Coordinator	Behavioral Biology	Yerkes
		Adjunct Professor	Psychology	Emory Univ.
D. Gust	Ph.D.	Research Associate	Behavioral Biology	Yerkes
K. Paul	D.V.M.	Research Associate	Pathobiology and Immunobiology, and Veterinary Medicine	Yerkes
K. Pralinsky	B.A.	Superintendent	Main Station	Yerkes
E. Strobert	D.V.M.	Associate Veterinarian	Veterinary Medicine	Yerkes

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 ininitiating 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.

DIVISION OF BEHAVIORAL BIOLOGY

Larry D. Byrd, Ph.D., Chief

Core Faculty: L.D. Byrd
I.S. Bernstein
T.P. Gordon
E.S. Savage-Rumbaugh
E.O. Smith
K. Wallen

Associate, Affiliate and Collaborative Faculty:

G.G. Berntson	Departments of Psychology and Pediatrics, Ohio State University
S.T. Boysen	Department of Psychology, Ohio State University
F.B.M. de Waal	Wisconsin Regional Primate Research Center, University of Wisconsin-Madison
C.L. Ehardt	Department of Anthropology and Linguistics, University of Georgia
J.E. Ellis	Yerkes Regional Primate Research Center, Emory University
D.M. Fragaszy	Department of Psychology, Washington State University
H.T. Gouzoules	Department of Psychology, Emory University
S.M. Gouzoules	Yerkes Regional Primate Research Center, Emory University
D.A. Gust	Yerkes Regional Primate Research Center, Emory University
S.G. Holtzman	Department of Pharmacology, Emory University
W.D. Hopkins	Department of Psychology, Georgia State University
L.L. Howell	Yerkes Regional Primate Research Center, Emory University
T.L. Maple	School of Psychology, Georgia Institute of Technology, and Zoo Atlanta
E.W. Menzel	Department of Psychology, State University of New York at Stony Brook
D.L. Molfese	Departments of Psychology, Physiology, and Behavioral and Social Sciences, Southern Illinois University at Carbondale
R.D. Morris	Department of Psychology, Georgia State University
M.A. Romski	Department of Communication, Georgia State University
D.M. Rumbaugh	Department of Psychology, Georgia State University
R.A. Sevcik	Department of Psychology, Georgia State University
W.M. Tomasello	Department of Psychology, Emory University
E. Visalberghi	Primate Laboratory Unit, Institute of Psychology (CNR), Rome, Italy
I.J. Wundram	Division of Social Sciences, Oxford College of Emory University

Visiting Scientists:

A.P. Kaiser	Departments of Special Education and Psychology, and Human Development, George Peabody College, Vanderbi University
J. Fagot	Laboratoire de Neurosciences Fonctionnelles, Centre National de la Recherche Scientifique, Marseilles, France

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TITLE: Modification of Aggressive Expression in Abnormal Males

AXIS I: 1a

AXIS II: 36, 41, 60, 72

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: The primary objective of this project is to determine whether the patterns of agonistic behavior exhibited by young males raised in the absence of adult males will approximate normal male agonistic behavior following resocialization. During the sixth and final year of this study, subject males which had been raised in the absence of adult males were housed in normally-constituted, intact social groups. Half of the subjects remained in their natal groups, and half were transferred to a new group. Group transfer is typical for male rhesus macaques of this age. Data recorded during this period are being analyzed, and the results will be compared with each subject's previous agonistic and social behavioral scores, and with age-peer control males living in groups in the absence of adult males.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Development of Numerical Competence in the Chimpanzee (Pan troglodytes)

AXIS I: 1a

AXIS II: 36, 41

PRC UNIT: Behavioral Biology

INVES1: Boysen, Sarah T.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: O

INVES2: Berntson, Gary G.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: O

SPECIES1: Pan troglodytes
NUM1: 5

NON-HOST INST: The Ohio State University

ABSTRACT: The chimpanzee is particularly appropriate as an animal model for the exploration of numerical competence. Studies to characterize and further investigate potential numerical skills in the chimpanzee (Pan troglodytes) have been completed. During the study period, training of counting and rudimentary addition were elaborated further, and testing was completed using larger counting repertoires. These tests included counting and summation using zero to eight items, with the chimpanzee using the Arabic symbols 0-8. A study of subtraction using arrays of 0-6 items was also completed with the same animal. Motor tagging by the chimpanzees during counting was evaluated, and an adult chimpanzee with previous language-like training was introduced to counting skills. Prerequisite cognitive training, including matching-to-sample of colors, shapes and relative size, was introduced to an infant chimpanzee prior to the introduction of one-to-one correspondence. These tasks served as preparatory procedures that were prerequisite to the introduction of numerical symbols to the infant chimpanzee. In addition, a computer-modulated, touch-screen training apparatus was developed and introduced to the subjects in order to provide automated training and testing with minimum opportunities for social cuing. Studies of transitive inference using both color and numerical stimuli were also completed, and the results suggest that an emergent concept of number may be necessary for a nonhuman primate to be able to infer the ordinal features of the number sequence. In summary, current efforts to evaluate numerical competence in the chimpanzee indicate a rich capability for number manipulation and symbolic representation relative to quantity. These studies promise to contribute unique insights into the possible evolution of cognition in nonhuman primates as well as humans.

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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 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.

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TITLE: Chronic Cocaine Exposure during Gestation

AXIS I: 1a, 2, 15, 21, 23

AXIS II: 36, 50b, 60, 63h, 71, 87

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

INVES3: Howell, Leonard L.
DEGREE3: Ph.D.
DEPT3: Behavioral Biology
STAFF3: O

INVES4: Patterson-Barnett, C. Anne
DEGREE4: M.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: O

SPECIES1: Macaca mulatta
NUM1: 32

ABSTRACT: Cocaine use has increased dramatically among Americans, and users now include young adults of child-bearing age and pregnant women. Clinical reports have indicated that a pregnant woman and her fetus are subjected to a host of potential problems due to cocaine use. However, few studies have examined under controlled laboratory conditions the consequences of cocaine use during pregnancy and, therefore, cocaine's effects on maternal, fetal and neonatal behavior and development are poorly understood. This project is studying in rhesus monkeys the effects of cocaine administration during gestation to characterize effects on the pregnant female, the developing fetus and the resulting offspring. Several doses of the drug are being administered in order to determine differences in effects as a function of dose and to determine the most appropriate dose to use in a subsequent experiment. The drug is being infused via chronically-implanted osmotic pumps, and drug levels in maternal blood and in amniotic fluid are being monitored. In control monkeys, saline is substituted for cocaine solution and infused. *In utero* growth and activity of the fetus are being measured using diagnostic ultrasound. Neonates will be tested and studied until 24 months of age using selected visual, psychomotor and developmental tasks to characterize differences in behavioral development and physical growth. Adult and infant

monkeys will also be monitored for evidence of tolerance or sensitization to the presence of cocaine, and both will be studied for evidence of withdrawal following birth of the infant and subsequent removal of the infusion pump from the adult. The research will characterize a nonhuman primate model of *in utero* cocaine exposure in order to understand better the risks of cocaine use during pregnancy in humans.

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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: The objective of this research is to characterize the effects selected drugs can have on the central nervous system of nonhuman primates by studying the effects of these drugs on operant 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 schedule-controlled behavior as an index of central nervous system activity. Through the use of various 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), this laboratory has demonstrated the involvement of the dopamine system in the behavioral and reinforcing effects of selected drugs. In addition to developing appropriate animal models for studying the effects of drugs, the project also uses 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.

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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 central nervous system is the source of control of behavior. The central nervous system is also 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. The long-range objective of this research is to characterize relations between changes in cardiovascular activity and ongoing behavioral processes. 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. These procedures can modulate cardiovascular activity in the squirrel monkey in an attempt to identify factors determining control 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.

TITLE: Development of a Scale to Assess Rhesus Physical and Neuromotor Development

AXIS I: 1a, 21

AXIS II: 36, 50b, 60

PRC UNIT: Behavioral Biology

INVES1: Ellis, Jane E.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: O

INVES2: Patterson-Barnett, C. Anne
DEGREE2: M.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: O

INVES3: Platzman, Kathleen A.
DEGREE3: M.D.
DEPT3: Reproductive Biology
STAFF3: O

SPECIES1: Macaca mulatta
NUM1: 22

ABSTRACT: Although the rhesus monkey frequently has served as a model for human growth and development, surprisingly few descriptive data have been published on its early neuromotor development. The primary objective of this study was to develop a scale based upon items modified from the Brazelton Neuromotor Behavioral Assessment Scale and the Bayley Scales of Infant Development, used to describe infant development in humans, which would be useful and valid for describing neuromotor functioning in infant rhesus monkeys. A second aim was to describe the physical and neuromotor development of newborn and infant rhesus monkeys in terms of the onset and offset of behaviors contained in the scale. Using this scale, 22 infant rhesus monkeys (Macaca mulatta) were assessed daily for a period of at least three months. Measures of physical growth, including body weight and crown-rump length, were recorded once per week. Five of these monkeys were infants of mothers that had served as subjects in a previous study designed to simulate asphyxia by reducing oxygen levels during labor and delivery, which can lead to a cerebral palsy-like syndrome in the infant. Two monkeys were infants of mothers that were exposed to cocaine for brief intervals during pregnancy. Data were compiled to provide the mean age in days, range and standard deviation for which onset and offset of the behaviors occurred. Growth measures were also compiled to show averages at successive weeks of age. These data are in close agreement with the few data published on growth and development, suggesting that the proposed scale may be a valid and useful scale for describing physical and neuromotor development in the rhesus monkey.

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TITLE: Postural and Other Lateral Asymmetries in Infant Chimpanzees

AXIS I: 1a

AXIS II: 36, 60

PRC UNIT: Behavioral Biology

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

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

SPECIES1: Pan troglodytes
NUM1: 15

NON-HOST INST: Laboratoire de Neurosciences Fonctionnelles, Centre National de la Recherche Scientific, Marseille, France (JF)

ABSTRACT: Several behavioral asymmetries in humans have been reported before infants are capable of reaching for objects, including asymmetrical postures, motility, grasping and stepping reflexes. The presence of such asymmetries shortly after birth is potentially important for understanding the development of lateral differences and hemispheric differentiation. However, very little attention has been paid to the development of hand preference in nonhuman primates. This study examined behavioral and hemispherical asymmetries in neonatal chimpanzees (Pan troglodytes). Primary attention was given to the lateralization of grasping and the tonic neck reflexes. A gripometer was used to determine asymmetries in the duration and strength of grasps by the hand or foot. Tonic neck reflexes were recorded via a VCR system. Data have now been collected and are being analyzed. It is anticipated that the data derived from this study on the existence of population-level asymmetries during infancy in a nonlinguistic species will help evaluate the phylogenetic relationship between the emergence of lateralized function and language competency.

TITLE: Manual Lateralization in Macaca mulatta

AXIS I: 1a

AXIS II: 36

PRC UNIT: Behavioral Biology

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

INVES2: Wallen, Kim
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: C

SPECIES1: Macaca mulatta
NUM1: 50

NON-HOST INST: Laboratoire de Neurosciences Fonctionnelles, Centre National de la Recherche Scientific, Marseille, France (JF)

ABSTRACT: The primary objective of this study was to investigate manual preferences in socially-living rhesus monkeys (Macaca mulatta) using a series of tactually- and visually-guided tasks. First, the hand preferences of 29 subjects were monitored while the animals were solving a haptic-discrimination task that required a hanging posture. Results revealed a significant left-hand bias (21 monkeys showed a significant left-hand bias, four showed a significant right-hand bias, and four failed to reveal a significant bias toward either hand). A second experiment varied critical components of the first experiment, i.e. posture (hanging, sitting or tripedal) and sensory requirement (tactile or visual). There was a significant left-hand bias for both sensory modalities, although the bias was stronger for 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.

TITLE: Behavioral Enrichment for Captive Gorillas and Orangutans

AXIS I: 1a, 11

AXIS II: 36, 38, 41, 54b, 78

PRC UNIT: Behavioral Biology

INVES1: Forthman, Debra L.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: 0

SPECIES1: Gorilla gorilla gorilla
NUM1: 17

SPECIES2: Pongo pygmaeus abelii
NUM2: 10

NON-HOST INST: Atlanta/Fulton County Zoo, Inc.

ABSTRACT: The three main objectives of this study are: (1) to develop safe and cost-effective methods for promoting activity patterns consistent with those observed in wild gorillas and orangutans; (2) to provide alternative activities for animals when it is necessary to keep them indoors; and (3) to quantify the effects of enrichment techniques on the frequency of feeding, foraging and social interactions in the naturalistic outdoor exhibits and in the indoor quarters used at night. During the past year, five phases of gorilla data collection were completed: baseline outdoors and indoors; two phases of baseline outdoors/enrichment indoors; and two phases of enrichment outdoors/baseline indoors. During each phase, data were collected for four consecutive weeks. The four enrichment phases consisted of providing: (1) "holzrugels", or small logs drilled and filled with raisins (indoors); (2) banana leaves, corn-on-the-cob and celery (outdoors); (3) drilled "boomer balls" containing puffed rice (indoors); and (4) cucumber and kiwi or cucumber and cantaloupe (outdoors). Data collected during these phases are currently being analyzed. Following alterations in the composition of the existing gorilla groups, additional phases of enrichment data collection will be conducted.

TITLE: Social and Endocrine Effects on Immune Function

AXIS I: 1a, 15, 17

AXIS II: 31, 36, 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

INVES5: Ansari, Aftab A.
DEGREE5: Ph.D.
DEPT5: Pathobiology and Immunobiology
STAFF5: C

SPECIES1: Cercocebus atys
NUM1: 16

SPECIES2: Macaca mulatta
NUM2: 26

ABSTRACT: A growing literature has provided compelling evidence that factors associated with social life, and changes in social environment, may lead directly to alterations in immune function and, thereby, to increased susceptibility to pathogens. Moreover, steroid hormones are known to affect immune function by acting as immunoregulators. The immune system may be viewed as a major integrative network involved in biological adaptation. A large number of experimental and clinical studies have shown that psychosocial variables produce an endocrine response, including changes in adrenal, pituitary and gonadal secretion, and also directly affect both humoral and cell-mediated immune responses. This is an ongoing project to examine social and endocrine modulation of immune function in rhesus and mangabey monkeys.

Removal of juvenile rhesus monkeys from their natal, social group to indoor, individual housing resulted in increased basal cortisol secretion and significant decrements in immune parameters. Baseline immune and cortisol measurements were obtained before seven subjects were removed from the group and placed in individual cages. The remaining seven subjects, which served as controls, remained in the social group throughout the study. Test subjects showed a significant decrease in CD4+ and CD8+ T cells and a significant increase in basal cortisol levels following removal to individual caging; some effects lasted through seven weeks. During the second phase of the study, the test subjects were returned to their natal group 18 weeks after removal from the group. Based on behavioral data recorded immediately after the return, one could predict which animals would show the greatest decline in immune parameters 24 hours after returning to the group. Similar results were obtained from six yearling mangabey monkeys removed to indoor, group-type housing. Work is continuing to examine the parameters of this model including species differences, endocrine modulation and the role of social variables in modulating the effects.

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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: O

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

SPECIES1: Macaca nemestrina
NUM1: 45

ABSTRACT: Vocalizations produced by pigtail macaques (Macaca nemestrina) during agonistic encounters are important in the recruitment of support from allies against opponents. These calls were studied using spectrographic and multivariate analyses. Direct discriminant analysis was used to classify screams recorded from 45 monkeys living in a stable, captive group at the Yerkes Center Field Station. Pigtail macaques employed 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 aggressive encounter. 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. There were significantly more classification errors for calls emitted by monkeys under three years of age than for those of older monkeys in each of the four agonistic contexts. Calls correctly classified into the four agonistic contexts were assigned a significantly higher probability for older monkeys, suggesting that the calls emitted by older monkeys were closer to the "prototype" for a particular context than were the calls of younger monkeys. Appropriate contextual usage and scream production appear to undergo developmental modification. Among juveniles, females were found to be more proficient than males both in proper contextual usage and in production of recruitment screams. Analyses also indicate the existence of matrilineal vocal signatures that may serve to identify kin-related groups and to promote efficient communication. The results suggest that learning plays a major role in the development of vocal communication among pigtail macaques in the context of agonistic aiding.

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: It is known that many Old World monkeys, especially females, behave preferentially ("recognize") maternally-related kin. However, there is less evidence that these species are able to "recognize" paternally-related kin. This ongoing study was designed to determine whether young rhesus monkeys can recognize their paternally-related siblings and how gender might influence such kin recognition. Twenty-three group-living, immature rhesus macaques (Macaca mulatta), housed in a large outdoor enclosure, served as subjects. Paternity was determined with the use of blood-typing reagents and a serum protein polymorphism developed to designate paternity in rhesus macaques. Focal data on the frequency and duration of occurrence of behaviors were recorded blind for all interactions between subjects. Results indicated that paternally-related, female sibling dyads engaged in grooming behaviors and were in proximity significantly longer and more often than were non-sibling dyads. Furthermore, there were consistent trends toward behaviors such as contact, approach and play. Paternally-related, female sibling dyads engaged in these behaviors more often than did non-sibling dyads, while male-female dyads showed the opposite pattern. Results for the small number of male-male dyads did not reveal a clear preference for either paternally-related siblings or non-siblings. This study suggests that female rhesus monkeys possess some ability to recognize paternally-related siblings, and this recognition appears to extend to patterns of agonistic aiding. Moreover, high-ranking males provided a significant amount of agonistic aiding toward offspring, and in particular, offspring whose mothers were no longer living.

TITLE: Aspects of Reproduction in the Sooty Mangabey

AXIS 1: 1a, 15, 23

AXIS 2: 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 atys
NUM1: 18

ABSTRACT: The overall goal of this project is to increase our understanding of reproduction and sexual behavior in the sooty mangabey. The most recent studies conducted during the past year involved investigation of the seasonal aspects of reproduction and comparison of sexual behavior during conceptual and post-conceptual swellings. Female sooty mangabeys are known to exhibit a seasonal decrease in conceptions during the summer months. Since perineal swellings have been shown to be indicative of ovulatory cycles, plans are underway to document hormonal changes which occur (a) with the seasonal decrease in conceptions during the late spring and (b) with the seasonal increase in conceptions during the fall. To preclude pregnancy, six adult females initially were housed in a small compound with no male. Blood samples were collected from the females three times per week to document the pattern of estradiol (E2) and progesterone (P4) secretion over the year. Data revealed that perineal swellings are not completely absent during the summer months. Additionally, because females exhibit a post-conception maximum tumescence that is virtually identical to the maximum tumescence associated with ovulation, a study was conducted to compare E2 and P4 levels and to compare rates of male mountings of females during these two stages. Results to date suggest that alpha males directed mounts to females significantly more often during the maximum tumescence associated with ovulation than during the post-conception maximum tumescence. This finding has implications for theories which postulate that post-conceptional, female sexual behavior serves to promote male investment. It is believed that studies of the behavioral and hormonal correlates of reproduction will enhance the breeding success of this AIDS-related animal model species.

TITLE: Group Formation of Unfamiliar Rhesus Affects Immune/Pituitary Adrenocortical Systems

AXIS I: 1a, 15

AXIS II: 36, 64

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

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

INVES5: McClure, Harold M.
DEGREE5: D.V.M.
DEPT5: Pathobiology and Immunobiology
STAFF5: C

SPECIES1: Macaca mulatta
NUM1: 8

ABSTRACT: Social stress associated with the formation of a new group of rhesus monkeys resulted in increased basal cortisol secretion and significant decreases in immunological parameters. Eight adult, female rhesus monkeys, all raised in social groups but with no common social history, were simultaneously introduced into an outdoor enclosure along with an adult male. Behavioral data were collected during the introduction and over 9 weeks thereafter, and blood samples were collected prior to group formation and at intervals for nine weeks thereafter. Establishment of a dominance hierarchy, apparent within 48 hours, was accomplished with no serious fighting and an absence of wounds or trauma. Overall, the group showed a significant increase in cortisol and a significant decrease in CD4+ and CD8+ T cells at 24 hours post-formation, but not thereafter. However, when partitioned into high and low dominance rank, differences in some immune measures persisted for more than 24 hours, with low-ranking subjects showing significantly lower values where differences

existed. Housing conditions (indoors in individual cages or outdoors in social groups) of the subjects immediately prior to introduction may have mediated these results. Data derived from this project demonstrate that social group formation can be a potent psychosocial stressor in nonhuman primates since stress-sensitive changes were observed in the absence of contact aggression.

TITLE: Seasonal Immune Comparison of a Stable and a Newly-Formed Group of Rhesus Monkeys

AXIS I: 1a, 15

AXIS II: 36, 64

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

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

INVES5: McClure, Harold M.
DEGREE5: D.V.M.
DEPT5: Pathobiology and Immunobiology
STAFF5: C

SPECIES1: Macaca mulatta
NUM1: 16

ABSTRACT: The overall objective of this project was to assess between-group differences in behavioral and immunological measures recorded in a recently-formed group of rhesus monkeys and a stable group of the same species. Eight females in each group served as subjects. Preliminary data revealed that there were no significant differences between groups in CD4+ or CD8+ T cell subsets during the first quarter; however, the recently-formed group showed significantly lower numbers of T cell subsets during the second quarter. The lower number of T cells in the recently-formed group correlated with the occurrence of social reorganizations. There was no difference in immune parameters over the first two quarters for the stable group. These very preliminary results suggest that season has no dramatic effect on the immune system in the stable group. The data also suggest that the social structure of the recently-formed group was dynamic and the stress resulting from this fact was reflected in a decrease in immune parameters.

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: Methylxanthines are chemical agents, related to caffeine, that are used in the medical treatment of several breathing disorders, including respiratory depression, breathing difficulties in newborn infants, and bronchial asthma. Studies continue to investigate the role of endogenous adenosine and phosphodiesterase (PDE) activity as possible biochemical mechanisms that mediate the respiratory-stimulant and behavioral effects of methylxanthines. 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 increased concentrations of CO_2 (hypercapnia) or decreased concentrations of O_2 (hypoxia) in inspired air. Caffeine and a selective PDE inhibitor lacking adenosine antagonist effects (rolipram) had similar pharmacological profiles under all conditions. In contrast, a potent adenosine antagonist lacking PDE inhibitory effects (CGS 15943) was considerably less efficacious than caffeine or rolipram. The adenosine agonists, CPA, NECA and CGS 21680, did not alter sensitivity to CO_2 in a manner similar to that of caffeine and rolipram. It appears that the increases in respiratory frequency produced by the adenosine agonists were mediated through activation of the A_2-receptor subtype and likely involved peripheral O_2-sensitive mechanisms. Behavioral experiments provide direct comparisons between the respiratory and behavioral effects of selected xanthines and adenosine agonists. Behaviorally-inactive doses of caffeine and rolipram were shown previously to have respiratory-stimulant effects. In contrast, only behaviorally-active doses of the adenosine agonists, CPA, NECA and CGS 21680, were shown to have respiratory effects. In subsequent experiments, CGS 15943 was approximately 30-fold more potent than caffeine as an antagonist of NECA's behavioral effects. The latter results demonstrate that CGS 15943 is a potent antagonist of adenosine and, in conjunction with the modest respiratory effects of CGS 15943, provide additional evidence that caffeine's respiratory-stimulant effects are not mediated through adenosine antagonism.

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TITLE: Post-occupancy Evaluation of Gorilla Exhibits

AXIS I: 1a, 11

AXIS II: 36, 41, 54b

PRC UNIT: Behavioral Biology

INVES1: Maple, Terry L.
DEGREE1: Ph.D.
DEPT1: Behavioral Biology
STAFF1: 0

INVES2: Ogden, Jacqueline J.
DEGREE2: M.S.
DEPT2: Behavioral Biology
STAFF2: 0

SPECIES1: Gorilla gorilla gorilla
NUM1: 15

NON-HOST INST: Atlanta/Fulton County Zoo, Inc (TLM, JJO);
Georgia Institute of Technology (TLM, JJO)

ABSTRACT: A post-occupancy evaluation of recently-completed naturalistic gorilla habitats was conducted. The three primary objectives of this study were: (1) to quantify the adaptation of eleven lowland gorillas to their new habitats; 2) to provide a longitudinal assessment of enclosure utilization in order to isolate relevant environmental variables of naturalistic exhibits; and 3) to document the socialization of a previously solitary male gorilla owned by Zoo Atlanta with two females on loan from the Yerkes Regional Primate Research Center of Emory University. Data collection on the adaptation aspect of the study was concluded prior to this reporting period; results showed that the gorillas exhibited low and attenuated exploration of their new habitats. During the past year, a longitudinal assessment of utilization was concluded. These data are being analyzed to investigate the environmental variables which are most predictive of enclosure use. The study of the previously solitary male is now ongoing, but on a reduced schedule, in order to document this male's continuing socialization including the development of reproductive behavior.

P51RR00165-30 1/1/1990 - 12/31/1990 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 (MAR, RAS)

ABSTRACT: During calendar year 1990, this project continued to analyze data derived from the longitudinal study of augmented symbol acquisition in 13 school-aged subjects (mean CA = 12:8) with mental retardation. First, an analysis of the effectiveness of symbols for communication at home and in school was completed. Results suggest that the subjects continued to gain the attention of their partners via vocalization. However, symbols influenced how the partners responded to the subjects' communications. In general, the symbols permitted the subjects to convey specific information to which their partners could respond, thus promoting the initiation, as well as the continuation, of conversations and the addition of new information. Second, the role of social symbols, such as please and thank you, in conversation was assessed. Results indicated that social symbols were used in well over half of the subjects' conversational turns with a social focus as soon as such symbols were available. Moreover, the availability of these symbols immediately and persistently shifted the focus of the subjects' conversational turns. The finding that social symbols are acquired rapidly and integrated quickly into conversations has important implications for theory and practice. Finally, the emergence of intelligible speech in previously non-speaking subjects was examined via analysis of intelligibility and phonetic changes in word production. Four of the subjects showed an increase in the percentage of their vocal productions that were reliably identified as words. Changes over time in each of the four improved subjects' individual word forms are being characterized to identify commonalities within each subjects repertoire. Two new studies focusing on observational symbol learning and peer interaction have begun.

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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: 0

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

SPECIES1: Pan troglodytes
NUM1: 3

SPECIES2: Pan paniscus
NUM2: 1

NON-HOST INST: Georgia State University (DMR)

ABSTRACT: A tool-making task was introduced to the oldest bonobo subject, Kanzi. Through observation, Kanzi learned to make and use stone tools for the purpose of cutting a string to open a box containing a prized item. The primary goal of this study was to determine how Kanzi's skills contrasted with those of early hominids. Kanzi's capacity was of particular interest in this regard since many current theories of hominid evolution assume that language appeared much later than did tool construction.

A comparative study of imitative skills was conducted with members of all three species (Pan troglodytes, P. paniscus and Homo sapiens) in cooperation with Dr. Michael Tomasello. A variety of novel tasks demonstrated whether they could imitate and, if so, the complexity of the task imitated. Of particular interest was whether language-using subjects were more facile imitators than were nonlanguage-using subjects.

A comparative study of tool use was also undertaken in collaboration with Dr. Elisabetta Visalberghi. The aim of this study was to compare the problem-solving capacities of language-using apes with those of nonlanguage-using apes and to contrast the problem-solving skills of all apes with capuchin monkeys.

Continuation of counting studies resulted in the P. troglodytes subjects learning to count to 7 in a task which required the constant manifestation of the concepts of 1-1 correspondence and ordination during counting. Visual reinforcement using slides was introduced to two subjects and proved to be a viable means of motivating task-related behaviors. These subjects distributed their reinforcement choices equally between food and slide-viewing, and they also showed strong preferences for certain types of slides.

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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 program of research embraces four projects of comparative inquiry into the processes and parameters that are requisites to symbol learning, language and complex cognition. Project 1 is "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 through 5 via the use of a new test apparatus (LRC-CTS) described elsewhere. Project 3, "GSU Mental Retardation Project", focuses upon language acquisition processes of mentally retarded children in our public schools. Project 4, "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.

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: O

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

SPECIES1: Pan paniscus
NUM1: 3

SPECIES2: Pan troglodytes
NUM2: 4

SPECIES3: Homo sapiens
NUM3: 3

NON-HOST INST: Georgia State University (DMR, RAS, SLW)

ABSTRACT: The primary objective of this project is to understand more fully 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 Pan paniscus and Pan troglodytes subjects were introduced to a keyboard presented via a video monitor. Instead of touching symbols, the subjects were required to use a joystick in order to locate a cursor over a symbol for 3 seconds. Successful completion of the task caused that symbol to appear at the top of the screen and a speech-board to pronounce the word. All of the subjects easily transferred their previous keyboard knowledge to this new media, indicating that their knowledge of the symbolic nature of the symbols was independent of the media or manner of symbol selection.

A test of semantic word boundaries imposed by an ape was undertaken with the bonobo, Kanzi. These tests revealed that this animal was able both to over-extend and to under-extend the same word, depending upon the test context.

The co-rearing study of the Pan paniscus and the P. troglodytes was terminated, and data are now being analyzed. The daily language-environmental rearing study is proceeding with the bonobo and her younger, full sister, Tamuli. Tamuli was reared by her mother, Matata, for the first 3-1/2 years of her life, so research is underway to determine whether, at this age, she is still able to acquire language skills.

P51RR00165-30 1/1/1990 - 12/31/1990 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 is an ongoing project designed primarily to collect basic demographic data on free-ranging, savanna-dwelling yellow baboons (Papio cynocephalus cynocephalus) in the Tana River Primate National Reserve, southeastern Kenya. During the past year, census data continued to be collected, and records were maintained on female cycle state, 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. In addition, detailed observations of the social interactions of all adult males have begun. The objective of this protocol is to elucidate mechanism(s) by which males maintain long-term coalitions with females, and tactics used by males when they emigrate from, or immigrate into, social groups. It is hypothesized that variations in tactics covary with age, dominance rank and previous experience. In order to test hypothesis about differing behavioral tactics and their effects on reproductive success, the study group has been trapped and a variety of biomedical samples have been obtained, including blood and hair samples. These samples will be used in DNA fingerprinting analysis to determine precisely the paternity of all known mother-infant pairs.

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TITLE: Noninvasive Monitoring of Reproductive Status in Free-Ranging Female Baboons

AXIS I: 1a, 16c, 23

AXIS II: 74e, 78

PRC UNIT: Behavioral Biology

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

INVES2: Whitten, Patricia L.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: O

INVES3: Stavisky, Ronda C.
DEGREE3: B.S.
DEPT3: Behavioral Biology
STAFF3: O

SPECIES1: Papio cynocephalus cynocephalus
NUM1: 70

ABSTRACT: The availability of estrous females is thought to be an important proximate factor influencing migration of male baboons. Although the swellings of female baboons are obvious external signs of ovulation, they do not permit accurate assessment of other important aspects of reproductive function, such as luteal phase competency and conception. A pilot project was conducted in the Tana River Primate Reserve to determine the feasibility of using fecal steroids for the noninvasive monitoring of reproductive status in free-ranging female baboons, and of females in primate species that lack external signs of ovulation. This project attempted to determine: (1) the ease with which fecal samples could be identified and collected from individual females; (2) the feasibility of extracting steroids from fecal samples in the field using solid phase extraction techniques developed in this laboratory; 3) the stability of steroid extracts; and 4) the extent to which these excreted steroids reflect reproductive stage and cycle swelling state. Although the actual collection of samples proved to be more difficult than anticipated, it was apparent that it was possible to collect and identify reliably fresh fecal samples from individual females. Samples (N=70) were collected by R. Stavisky from pregnant, lactating and cycling females, then extracted and loaded onto solid phase extraction cartridges. An unlabelled steroid tracer was added to assess recovery. Perineal swellings were recorded using a 10-point scale. Upon return to Emory, samples were eluted and analyzed for tracer, estradiol and progesterone by radioimmunoassay in P. Whitten's laboratory. The fecal estradiol profile was characterized by a mid-cycle peak that corresponded to peak swelling and

was followed by a luteal-phase rise in fecal progesterone. These analyses demonstrated that extraction and preservation of fecal steroids is possible under field conditions and can permit relatively fine-grained analyses of the ovarian state of free-ranging nonhuman primates.

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TITLE: Imitative Abilities of Young Chimpanzees

AXIS I: 1a

AXIS II: 36

PRC UNIT: Behavioral Biology

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

SPECIES1: Pan troglodytes
NUM1: 20

ABSTRACT: Fifteen captive chimpanzees (Pan troglodytes) served as subjects in a tool-use task consisting of an out-of-reach food item and a rake tool. The tool worked efficiently only when manipulated in a specific way. Each subject was tested under one of three observation conditions: (1) no observation; (2) observation of a partial model; or (3) observation of the entire model. Subjects which were tested under the latter two conditions performed better than did subjects which observed no model (condition 1). Performance of these two groups (conditions 2 and 3) did not differ from each other, however. It was concluded that chimpanzees learn from one another only about the results of actions (emulation learning), and not about the actions themselves (imitative learning).

TITLE: Influence of Social Factors on the Acquisition of Learning Set Formation

AXIS I: 1a

AXIS II: 36, 41

PRC UNIT: Behavioral Biology

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

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

SPECIES1: Macaca mulatta
NUM1: 55

ABSTRACT: A previous study revealed that social dominance influenced the successful acquisition of color discrimination, and provided evidence of learning-set formation but only in high-ranking animals. Why learning-set formation occurred only in high-ranking animals remained unclear, so the present project was designed to address this problem. An innovative technique was developed to investigate learning in subsets of a large social group. Social-interaction data were used to describe the social dominance hierarchy of a 55-member study group. The group, consisting of six matrilines with comparable numbers of subjects in the three high-ranking and three low-ranking matrilines, was trained to split upon command into two halves between the third- and fourth-ranking matrilines. This procedure enabled the complete social group, the high-ranking matrilines and the low-ranking matrilines to be studied separately. Using this technique, subjects were trained on two color-discrimination problems either solely in their matrilineal groups (high- or low-ranking) or in the entire group. Subjects trained under one social condition were later tested on a given color discrimination in a second social condition (for example, low-ranking animals in the complete social group were tested on a color discrimination which they learned in the presence only of other low-ranking subjects). This enabled the determination of how social rank influences acquisition of color discrimination. This study promises to increase our understanding of how social dominance can interact with learning history to influence social skills and competency, and raises the possibility that socially-dominant animals may learn more readily from their environment due to a history of increased opportunity. Similarly, learning strategies utilized by monkeys are expected to vary as a function of social rank, with high-ranking animals learning discriminations first-hand and low-ranking animals relying upon observation of others.

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TITLE: Hormonal and Environmental Influences on Sexual Behavior

AXIS I: 1a, 15, 23

AXIS II: 36, 62

PRC UNIT: Behavioral Biology

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

INVES2: Mann, David R.
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF2: O

SPECIES1: Macaca mulatta
NUM1: 12

ABSTRACT: This project investigated the ability of a GnRH antagonist (Antide) to suppress pituitary-testicular function and sexual behavior in group-living male rhesus macaques. Consideration of GnRH antagonists as human contraceptive agents makes it crucial to understand the biological and behavioral effects of these agents. Seven vasectomized male rhesus macaques, living as members of a large social group, were observed three times per week, two hours per session, for four weeks before receiving a single injection of Antide (15.0 mg/kg, propylene glycol:H_2O, v:v). Males were separated from the group for 30 minutes prior to behavioral observations to terminate any ongoing sexual interactions. After reintroduction and observation, males were again separated from the social group to obtain blood samples. Prior to Antide treatment and at 2, 4 and 8 weeks following Antide, males received 50.0 ng/kg of native GnRH to test pituitary responsiveness. For all males, Antide reduced testosterone to near-castration levels within 48 hours post-treatment. Luteinizing hormone levels declined over a longer period, reaching near assay sensitivity within one week. Antide levels remained elevated for three weeks in all males, and were detectable eight weeks post-injection. Testosterone returned to pretreatment levels within 4-6 weeks for all males. Male sexual behavior decreased significantly within one week following Antide treatment, and mating behavior ceased completely within four weeks after Antide in six males. Male sexual behavior returned to pretreatment levels within seven weeks post-Antide. Pituitary responsiveness decreased significantly throughout the 8-week, post-Antide period, whereas testosterone secretion following GnRH treatment returned to normal within the 8-week period. These results demonstrate that Antide suppresses pituitary-testicular function and male sexual behavior for 3-4 weeks following a single injection, and suggest that the use of GnRH antagonists as male contraceptives may require androgen supplementation to prevent unwanted effects on male libido.

TITLE: Steroid Binding, Estrogen Availability, and Female Sexuality

AXIS I: 1a, 15, 23

AXIS II: 36, 62

PRC UNIT: Behavioral Biology

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

INVES2: Wilson, Mark E.
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF2: C

INVES3: Drea, Christine
DEGREE3: M.A.
DEPT3: Behavioral Biology
STAFF3: O

SPECIES1: Macaca mulatta
NUM1: 9

ABSTRACT: The role of androgens in female primate sexual behavior is unclear. Evidence from both humans and rhesus macaques suggests that adrenal androgens are important for female sexual interest. Recent work in this laboratory has demonstrated that adrenal function is not required for normal sexual behavior in group-living female rhesus macaques; however, the role of ovarian androgens in female sexual behavior cannot be ruled out. Studies of steroid replacement therapies in ovariectomized human females strongly suggest that androgens are needed to reinstate female sexual desire. This laboratory is testing the hypothesis that levels of bioavailable estradiol are dynamically modulated by levels of sex hormone binding globulin (SHBG) and the androgens testosterone and dihydrotestosterone (DHT). Levels of SHBG and SHBG-binding of estradiol in relation to female sexual behavior were measured during the breeding season in a group of seven ovariectomized rhesus macaques that received 100.0 pg/ml estradiol via Silastic capsules for three weeks. During the fourth week, females received either 500.0 pg/ml estradiol, 600.0 pg/ml testosterone or 800.0 pg/ml DHT concurrently with the basal estradiol. Sexual behavior was observed four days per week with each of two males for 50 minutes per male. During the course of this ongoing study, each female receives all hormonal treatments in a counter-balanced manner. These studies will provide a complete description of the interaction among SHBG, androgens, estradiol and modulation of sexual behavior in female rhesus macaques. If results support the hypothesis being tested, this research will provide an integrated explanation of how estradiol and androgens interact with serum steroid binding to modulate female behavior.

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TITLE: CNS Grafting for Parkinsonism

AXIS I: 1a, 1d, 6, 9, 19, 21

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

PRC UNIT: Neurobiology

INVES1: Bakay, Roy A.E.
DEGREE1: M.D.
DEPT1: Neurobiology
STAFF: 0

INVES2: Byrd, Larry D.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF: C

INVES3: Watts, Ray L.
DEGREE3: M.D.
DEPT3: Neurobiology
STAFF: 0

INVES4: Iuvone, P. Michael
DEGREE4: Ph.D.
DEPT4: Neurobiology
STAFF: 0

SPECIES1: Macaca mulatta
NUM1: 18

ABSTRACT: The objective of this research project is to use a primate model to determine whether adrenal medullary tissue can be successfully transplanted into the CNS and improve fixed neurological deficits. The model uses the administration of MPTP to selectively destroy dopaminergic cells in the nigro-striatal pathway, and results in a movement disorder which is quite analogous to parkinsonism. The MPTP-induced Parkinson-like syndrome is an excellent model for testing CNS transplantation in nonhuman primates in order to identify factors which can produce behavioral improvement. Preliminary studies have demonstrated the potential for correcting the Parkinson-like movement abnormalities using either adrenal medullary tissue or fetal mesencephalic tissue in the rhesus monkey (Macaca mulatta). However, it is clear from these studies that direct application of rodent techniques is inadequate and modification of the grafting technique is required when dealing with primates. The problem is not simply of scaling up to a larger subject. Specifically, we are evaluating a new cografting technique which uses adrenal medullary and peripheral nerve tissue together. We and others have found that additional peripheral nerve tissue intermingled with the adrenal medullary tissue greatly enhances cell survival. Apparently, the Schwann cells provide the neurotrophic factors required by the chromaffin cells. For the first time, sufficiently detailed testing combined with adequate numbers of monkeys should permit a statistical determination of differences between adrenal-nerve cografted monkeys and either surgical or nonsurgical controls.

P51RR00165-30 1/1/1990 - 12/31/1990 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

ABSTRACT: We are conducting behavioral tests of 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.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Seasonal Control of Reproduction in the Male Rhesus Monkey

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: Neurobiology
STAFF2: O

SPECIES1: Macaca mulatta
NUM1: 16

NON-HOST INSTITUTION: VA Medical Center (DCC)

ABSTRACT: In this project we will determine factors which produce seasonal changes in reproductive physiology and behavior in the rhesus monkey. One hypothesis is that annual changes in day length influence seasonal fluctuations in sexual activity in male rhesus monkeys and that this influence is mediated by changing melatonin levels. In one study, 4 male rhesus monkeys were adapted to primate chairs and bled at predetermined times over a 24 hour period. The lighting in the test chamber was set to match the lighting in use in the animal quarters. Animals were tested under long and short photoperiods and blood samples were assayed for melatonin to assure that photoperiodic conditions in place in our laboratory can control the duration of secretion of this indolamine. Our studies demonstrate a nocturnal increase in melatonin under the 16L:8D photoperiod. Melatonin began to rise almost immediately after lights out and remained elevated until about 1 hour after lights on. Melatonin levels from the 8L:16D photoperiod have not yet been analyzed. Photoperiodic control of pineal activity is essential to the hypothesis that photoperiod controls reproduction. In a second experiment, 8 male monkeys were maintained under a constant photoperiod of 16L:8D for a period of 18 months. To test whether the effects of reproductively inhibitory patterns of melatonin can be overridden by providing continuous melatonin stimulation, we implanted males with melatonin capsules. Melatonin treatment was alternated with a control implant. During the middle of the non-breeding season, melatonin administration resulted in a statistically significant increase in rate of mounting in treated males as compared to untreated males. These experiments and others conducted as part of this project contribute to an understanding of seasonal mechanisms of hormonal function and endocrine and behavioral regulation in general. Humans are not commonly thought of as having a reproductive season. Recent research, however, has led some authors to conclude that seasonal trends in human reproduction do exist and that these are based upon biological factors. In light of these new findings in the human, it is of particular importance to understand seasonal mechanisms in other primates.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Apomorphine and Myopia

AXIS I: 1a, 21, 25b

AXIS II: 60, 62

PRC UNIT: Neurobiology

INVES1: Iuvone, P. Michael
DEGREE1: Ph.D.
DEPT1: Neurobiology
STAFF1: 0

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

INVES3: Stone, Richard A.
DEGREE3: M.D.
DEPT3: Neurobiology
STAFF3: 0

INVES4: Lambert, Scott
DEGREE4: M.D.
DEPT4: Neurobiology
STAFF4: 0

INVES5: Laties, Alan M.
DEGREE5: M.D.
DEPT5: Neurobiology
STAFF5: 0

SPECIES1: Macaca mulatta
NUM1: 8

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

ABSTRACT: Myopia is an impairment in visual function that affects a large percentage of the population of the USA. In myopics, distant images focus in front of the retina, at least in part due to an excessive elongation of the eye. The causes underlying myopia are not understood. Recent evidence supports the notion that retinal image quality may be involved in the regulation of eye growth and, thus, may be involved in the development of myopia. Recent results from our laboratories provide new evidence that neonatal eye growth and refraction can be influenced by visual experience. Occlusion of one eye in newborn monkeys with an opaque occluder lens resulted in excessive postnatal eye elongation. Furthermore, the dopamine system in the retina behind the occluder was reduced. To test whether levels of retinal dopamine could be relevant to eye development, we studied the effect of local administration of the dopamine receptor agonist apomorphine on the growth of occluded eyes. Eight rhesus monkeys were monocularly deprived of vision from

birth with opaque contact lenses. Four of the monkeys received drops of 1% apomorphine HCl 2-3 times/day in the occluded eye; the 4 control monkeys received vehicle only. Axial lengths were determined by A-scan ultrasonography at birth and at 5 to 7 months of age. Axial elongation was assessed by comparing the postnatal growth in the axial dimension of the occluded and non-occluded eyes. In 3 of the 4 control monkeys, occlusion increased axial growth by an average of 1.3 mm. 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 and was anomalously small. At 6.5 to 9.5 months of age, 3 of 4 controls had myopic refractive errors (-3 to -7 diopters) in the occluded eyes; 3 of 4 of the apomorphine-treated monkeys had hyperopic refractive errors (+1 to +3 diopters) in their occluded eyes, the 4th monkey's occluded eye was only -0.5 diopters myopic. The results suggest that apomorphine administration retards excessive axial elongation and the concomitant development of myopia associated with visual deprivation in primates.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Long-term Recording of Neural Signals from Monkeys

AXIS I: 1

AXIS II: 21

PRC UNIT: Neurobiology

INVES1: Kennedy, Philip R.
DEGREE1: Ph.D.
DEPT1: Neurobiology
STAFF1: 0

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

INVES3: Bakay, Roy A. E.
DEGREE3: M.D.
DEPT3: Neurobiology
STAFF3: 0

INVES4: Mirra, Sue
DEGREE4: M.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: 0

SPECIES1: Macaca mulatta
NUM1: 4

NON-HOST INSTITUTION: Georgia Institute of Technology (PRK); Veterans Administration Medical Center (SM)

ABSTRACT: Objectives: Determine [1] how long would the cone electrode continue to monitor neural signals in monkeys, [2] what can be revealed at the electron microscopic level regarding the tissue inside the cone, [3] if neurotrophic substances can be used in the monkey to produce neural signals from the electrode, [4] if single units can be controlled by the monkey.

The significance of this research in primates is 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] Recordings have continued until 15 months in one monkey who damaged the implant at that time. Waveshapes have been separated and their waveshape parameters applied to all recording sessions over the 15 months. This has revealed similar waveshapes for two units consistently, and for three other units during most sessions. [2] EM studies in monkey and rat show some myelinated neuronal processes inside the cone, as well as astrocytic cells, collagen and other material. To study this more closely, rats are being used that have cone electrodes filled with neurotropic substances that result in recording of neural signals. At the EM level, myelinated fibers

have been seen throughout the cone tissue. These studies are continuing in rats whose cone electrodes are being harvested at intervals after implantation. [3] Five electrode implants were made with neurotropic substances (Matrigel or Laminin) inside the cone. Disappointingly, no signals were recorded from these implants. This may well be due to the possibility that the neurotrophic substances were inadequate and no neurites grew into the cone. The implant preparation is still intact and histological examination will be made in due course. [4] Experiments are getting underway to study the possibility that monkeys can control the firing of their own separated single units. These behavioral experiments require major equipment that has been installed and modified over the past few months.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Correction of Monocular Aphakia in Monkeys with IOLs

AXIS I: 1a, 25b

AXIS II: 44, 48, 60, 86

PRC UNIT: Neurobiology

INVES1: Lambert, Scott R.
DEGREE1: M.D.
DEPT1: Neurobiology
STAFF1: O

INVES2: Boothe, Ronald G.
DEGREE2: Ph.D.
DEPT2: Neuropsychophysics/Neurobiology
STAFF2: C

INVES3: Tigges, Margarete
DEGREE3: Ph.D.
DEPT3: Neural Ultrastructure/Neurobiology
STAFF3: C

SPECIES1: Macaca mulatta
NUM1: 16

ABSTRACT: The major objectives of this study are: (1) to evaluate the safety and efficacy of intraocular lens implantation in infants; (2) to compare the utility of bifocal with monofocal pseudophakic correction; and (3) to determine whether occlusion therapy is required in monocularly pseudophakic infants in order to achieve good vision in both eyes. The effects of these interventions will be followed regularly in terms of visual acuity, ocular alignment, stereopsis, refractive error, corneal curvature, axial alignment and histopathologically.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Axon Terminals on Betz Cell Somata in Macaques throughout Adulthood

AXIS I: 1a, 21

AXIS II: 30

PRC UNIT: Neurobiology

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

INVES2: Herndon, James G.
DEGREE2: Ph.D.
DEPT2: Neuropsychology/Neurobiology
STAFF2: C

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

SPECIES1: Macaca mulatta
NUM1: 7

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

ABSTRACT: Axon terminals on Betz cell somata of area 4 of 7 adult rhesus monkeys (aged 5 to 35 y) were studied to reveal age-associated changes. Since we had previously demonstrated a decline with age in the perimeter of such cells, we hypothesized that terminals might also change in number or in morphological characteristics. In a sample of 140 Betz cells, we confirmed the gradual decline in Betz cell perimeter. The 1,540 axon terminals upon these cells, however, remained unchanged in number, size, length of membrane apposition, and number of mitochondria throughout the lifespan of the monkey. We then used our material to calculate parametric characteristics of Betz cells and associated terminals. We estimated Betz cell somata to have an average membrane surface area of 5,700 μm^2 with terminals covering about 15% of this area. The contact area of each axon terminal is about 3.33 μm^2, suggesting that each Betz cell receives approximately 260 terminals. Interestingly, the Betz cells of the rhesus monkey appear to be somewhat smaller and less heavily populated with terminals than those of cats, the only other species in which studies similar to ours have been carried out.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Apomorphine and Normal Postnatal Eye Growth

AXIS I: 1a, 21, 25b

AXIS II: 60, 62

PRC UNIT: Neurobiology

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

INVES2: Iuvone, P. Michael
DEGREE2: Ph.D.
DEPT2: Neurobiology
STAFF2: O

SPECIES1: Macaca mulatta
NUM1: 2

ABSTRACT: This project is based on our observation (see abstract "Effects of Apomorphine, a Dopamine Receptor Agonist, on Ocular Refraction and Axial Elongation in a Primate Model of Myopia") that apomorphine administration prevents excessive postnatal axial elongation of the eyes of monkeys fitted with opaque occluder lenses at birth. The follow-up experiment was designed to provide complementary data to the previous study and to further test our hypothesis that a deficiency of retinal dopamine may be involved in the development of myopia. Furthermore, these results might merit investigation of apomorphine or similar dopaminergic agonists as a therapeutic strategy in modifying the development of certain human myopias. However, before clinical trials can be initiated, additional studies in experimental animals on the effect of apomorphine on normal eye growth and development are necessary. A pilot study was began to assess the effect of apomorphine, administered as eye drops, on the postnatal growth of the otherwise unmanipulated eyes of 2 newborn rhesus monkeys. The monkeys were selected based on equal axial lengths of both eyes at birth. Beginning at 1 week of age, the right eye received drops of 1% apomorphine HCl 3X/day and the left eye received drug vehicle (2.2% glycerol in H_2O). Postnatal axial elongation of both eyes was measured at birth and thereafter at 1 month intervals by A-scan ultrasonography. As in our previous study, no indications of systemic toxicity or local discomfort resulting from this treatment protocol was found. Also, up to date (i.e., after 6 months of treatment) the 2 eyes of both monkeys elongated in a similar fashion. Their elongation process is also in the range of eye growth of age-matched control monkeys. The study will continue until the monkeys are at least 9 months old, because we found that it is in this period that monkey eyes experience their fastest growth. If apomorphine does influence eye growth in normal eyes, the effect should be observed at the end of this period.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Signal Changes in the Monkey's Lateral Geniculate Nucleus

AXIS I: 1a, 21, 25b

AXIS II: 92, Neuroscience

PRC UNIT: Neurobiology

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

SPECIES1: Macaca mulatta
NUM1: 2

ABSTRACT: The lateral geniculate nucleus carries visual signals from retina to cortex and is the most well-studied thalamic nucleus in mammals. Much of its anatomy and physiology have been determined, but its function remains elusive. The purpose of this study is to record retinal terminal potentials (S-potentials) simultaneously with the action potentials from individual LGN neurons in order to determine input/output changes which might occur at the level of the LGN. In particular, differences between parvocellular and magnocellular neurons, the two main types of relay neurons in the LGN, will be sought with the intention of correlating any such changes with the synaptic differences already known for individual neurons of the monkey's LGN; i.e., magnocellular neurons have many triadic retinal synaptic arrangements with GABAergic presynaptic dendrites whereas parvocellular neurons have few such arrangements. If a difference in the input/output relationships exist between parvocellular and magnocellular neurons and correlates with the expected signal/noise increase for the magnocellular neurons, it would indicate that a major function of the synaptic arrangements in the LGN is to provide better signals to the cortex.

DIVISION OF PATHOBIOLOGY AND IMMUNOBIOLOGY

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P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Naturally Occurring SIV Infection in a Colony of Macaca Arctoides

AXIS I: 1a, 7b

AXIS II: 31, 64, 66

PRC UNIT: Pathobiology & Immun

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

INVES2: Fultz, Patricia N.
DEGREE2: Ph.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

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

INVES4: Klumpp, Sherry A.
DEGREE4: D.V.M.
DEPT4: Pathobiology and Immunobiology
STAFF4: O

INVES5: Ribas, Jorge L.
DEGREE5: D.V.M.
DEPT5: Pathobiology and Immunobiology
STAFF5: O

INVES6: McClure, Harold M.
DEGREE6: D.V.M.
DEPT6: Pathobiology and Immunobiology
STAFF6: C

SPECIES1: Macaca arctoides
NUM1: 21

NON-HOST INSTITUTION: Henry M. Jackson Foundation and Armed Forces Institute of Pathology, Washington, D.C. (JLR)

ABSTRACT: A colony of Macaca arctoides at the Yerkes Center was established in 1964 and was maintained as a closed colony until 1981 when four animals obtained from another colony were introduced into the group. One animal died shortly after introduction due to fight wounds. The three other animals remained in the colony until the death of two of the animals at seven and eight years after introduction. In 1986, we learned that the animals

introduced into the colony in 1981 were from an SIV infected colony. Sixteen of 31 animals in the colony at the time were tested for SIV antibodies. Two of the three animals introduced into the colony in 1981 were SIV-seropositive. The other 13 animals were seronegative. Virus isolation attempts from the seropositive animals at that time were unsuccessful. The colony remained healthy until mid-1988 when increased clinical disease problems and an increased mortality rate became apparent. In August 1989, all remaining animals in the group (21) were tested for SIV antibodies with all but one infant, born in 1988, being seropositive. Of 17 deaths that occurred from mid-1988 through 1989, 12 were seropositive to SIV and the serologic status of four was unknown. The only known seronegative animal was a 10-month-old infant. The major finding at necropsy was severe weight loss with a significant number of animals having oro-esophageal candidiasis and intestinal mycobacteriosis. Of the two animals that were introduced into the colony in 1981, one had lymphoma involving the lung and hilar lymph nodes and the other had syncytial cells in the lung that were positive for SIV antigen. A lentivirus, designated SIVstm was subsequently isolated from animals in the colony and immunologic evaluation revealed lymphopenia with decreases in $CD4^+$ cells in a number of animals. This study demonstrates widespread natural transmission of SIV infection within a colony of stumptailed macaques with devastating consequences.

P51RR0165-30 1/1/1990 - 12/31/1990 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: 128

SPECIES2: Macaca nemestrina
NUM2: 21

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

NON-HOST INSTITUTION:

ABSTRACT: The occurrence of a high incidence of spontaneous amyloidosis (159 cases in 16 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 (128 rhesus, 21 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. Animal s 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.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Regulation of SIV Replication *in vitro* by $CD8^+$ T Cells from Clinically Asymptomatic Sooty Mangabeys

AXIS I: 1a, 1d, 2, 7b, 9, 19

AXIS II: 31, 64, 66, 83

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

INVES4: Villinger, Francois V.
DEGREE4: D.V.M.
DEPT4: Pathobiology & Immunobiology
STAFF4: O

INVES5: McClure, Harold M.
DEGREE5: D.V.M.
DEPT5: Pathobiology & Immunobiology
STAFF5: C

INVES6: Sell, Kenneth W.
DEGREE6: M.D., Ph.D.
DEPT6: Pathology
STAFF6: O

SPECIES1: Cercocebus atys
NUM1: 10

SPECIES2: Macaca mulatta
NUM2: 10

NON-HOST INSTITUTION:

ABSTRACT: Several investigators have previously shown that $CD8^+$ T cells from the peripheral blood of HIV-1-infected humans and rhesus macaques experimentally infected with SIV strains markedly inhibit the replication of HIV-1 and SIV in $CD4^+$ autologous cells *in vitro*. This function of $CD8^+$ T cells to inhibit replication of lentiviruses was not seen in $CD8^+$ T cells from

uninfected humans or macaques; thus, the presence of such $CD8^+$ T cells was reasoned to be a potent form of cellular immunity that is induced by lentivirus infection. Since both humans and macaques are highly susceptible to the respective lentivirus infections, invariably resulting in disease and death, it was of interest to determine whether similar $CD8^+$ T cells were also present in naturally infected sooty mangabeys, a species which is generally resistant to disease and is clinically asymptomatic. Studies demonstrated the presence of such $CD8^+$ T cells in not only seropositive sooty mangabeys but also seronegative sooty mangabeys. Data indicate that such $CD8^+$ T cells exert their regulation of virus replication most likely by regulating the activation pathway of T cells but not by direct cytolytic mechanisms. Preliminary data show the absence of such regulatory $CD8^+$ T cells in the PBMC of macaques experimentally infected with SIVsmm during the late stages of the disease. This lack of function was not secondary to the absence of $CD8^+$ T cells but due to an intrinsic defect in the functional activity of these cells. These data provide a unique tool to examine the presence and/or absence of a form of cellular immunity that may play a major role in the pathogenesis of AIDS.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Measurement of Cell-Mediated Immunity to SIV in Infected Nonhuman Primate Species

AXIS I: 1a, 1d, 2, 7b, 9, 19

AXIS II: 31, 64, 66, 83

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: Jensen, Peter E.
DEGREE3: M.D.
DEPT3: Pathobiology & Immunobiology
STAFF3: O

INVES4: Jehuda-Cohen, Tamar
DEGREE4: Ph.D.
DEPT4: Pathobiology & Immunobiology
STAFF4: O

INVES5: McClure, Harold M.
DEGREE5: D.V.M.
DEPT5: Pathobiology & Immunobiology
STAFF5: C

INVES6: Anderson, Daniel C.
DEGREE6: D.V.M.
DEPT6: Pathobiology & Immunobiology
STAFF6: C

INVES7: Fultz, Patricia N.
DEGREE7: Ph.D.
DEPT7: Pathobiology & Immunobiology
STAFF7: C

INVES8: Sell, Kenneth W.
DEGREE8: M.D., Ph.D.
DEPT8: Pathology
STAFF8: O

SPECIES1: Cercocebus atys
NUM1: 10

SPECIES2: Macaca mulatta
NUM2: 10

NON-HOST INSTITUTION:

ABSTRACT: The measurement of cell-mediated immunity against the etiologic agent of human AIDS (HIV) in the nonhuman primate model of AIDS (simian immunodeficiency virus, SIV) has been difficult. In general, culture of peripheral blood mononuclear cells from HIV-1- and SIV-infected humans and monkeys, respectively, with purified inactivated HIV and SIV virus preparations has given inconsistent or negative proliferative responses; however, we describe herein an assay which consists of co-culturing monocytes that have been pulsed with inactivated SIVsmm with nylon-wool-purified autologous T cells, leading to antigen-specific T cell proliferation. The proliferative response which predominantly occurs in $CD4^+$ T cells is major histocompatibility complex (MHC) class II-restricted and requires antigen processing. This assay will greatly facilitate the identification of the immunodominant epitopes recognized by T cells in sooty mangabeys, which are naturally infected but remain clinically asymptomatic, and in rhesus macaques, in which experimental infection leads to clinical symptomatology similar to human AIDS, eventually resulting in death.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Spatial Orientations of the Muscles of Mastication in Macaca Mulatta

AXIS I: 1a, 3, 7, 22

AXIS II: 42, 52, 63, 70, 80, 86

INVES1: Bidez, Martha
DEGREE1: B.S., B.S.M.E., M.S.BME, Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: 0

INVES2: Chen, Yifang
DEGREE2: M.S.M.E.
DEPT2: Pathobiology and Immunobiology
STAFF1: 0

NON-HOST INSTITUTION: University of Alabama at Birmingham (MB, YC).

ABSTRACT: Previous studies have reported histochemical and electromyographic analyses of the craniomandibular muscles in the rhesus monkey. The mandible simulating in vivo loading conditions requires a complete description of both muscle magnitude and direction in 3-dimensions. To evaluate these features, the mandibular region was dissected in rhesus monkeys ranging in age from 13 y to 19 y 10 m. Following dissection, the origin and insertion local coordinates of the superficial and deep masseter, medial and lateral pterygoid and temporalis muscles were identified and measured. Previous dissection of the digastric m. necessitated approximation of the origin. Bony landmarks utilized for establishment of local coordinate frame were the angle of the mandible, coronoid process, and the superior aspect of the midsymphseal plane. Bone dimensions were recorded in global coordinates following complete soft tissue dissection. Results indicated right/left symmetry within specimens and generally small variance between specimens. Three dimensional spatial orientations of the muscles of mastication in Macaca mulatta have been identified in both local and global coordinate frames.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Clinical Changes Following Dental Prophylaxis in the Rhesus Monkey

AXIS I: 1a, 3, 7, 22

AXIS II: 42,52,63,70,80,86

PRC UNIT: Pathobiology & Immun

INVES1: Braswell, Laura D.
DEGREE1: D.D.S.
DEPT1: Pathobiology and Immunobiology
STAFF1: 0

INVES2: Eke, Paul I.
DEGREE2: Ph.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: 0

INVES3: Arnold, Roland R.
DEGREE3: Ph.D.
DEPT3: Pathobiology and Immunobiology
STAFF3: 0

INVES4: Fritz, Michael E.
DEGREE4: D.D.S., M.S., Ph.D.
DEPT4: Pathobiology & Immunobiology
STAFF4: 0

SPECIES1: Macaca mulatta
NUM1: 9

NON-HOST INSTITUTION:

ABSTRACT: Nine adult male rhesus monkeys were anesthetized and examined prior to entry into a periodontal research project to study the biology of root form fixtures and blade vent dental implants. Selected teeth on the animals were evaluated for plaque, tissue redness, edema, suppuration, mobility, probing depths and bleeding on probing. The position of the cemento-enamel junction relative to the free gingival margin was recorded for later use in determining attachment loss. Microbiological samples were collected on an anterior and posterior tooth in each animal and placed in anaerobic media. One week later the animals were re-examined and recultured under anesthesia. None of the animals presented with clinically evident suppuration or mobility at either examination date. As expected, there was a statistically significant decrease in plaque and a subsequent decrease in clinical tissue redness. There was no significant change in edema, probing depths and bleeding on probing. A slight change in the attachment level was noted reflecting a gain of attachment. The results of this study further describe the characteristics of periodontal disease in the rhesus monkey and further establish it as an experimental model.

P51RR0165-30 1/1/1990 - 12/31/1990 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 & Immun

INVES1: Collins, William E.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: 0

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

SPECIES1: Pan troglodytes
NUM1: 7

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

ABSTRACT: Animals were infected with malaria 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 - CHUCK (C-359); Plasmodium vivax - OSSABAW (C-421), CHUCK (C-359), HEXAMETHONIUM (C-OC-6), BERTHA (C-530); Plasmodium malariae - OSSABAW (C-421). We will continue these studies in support of the development of vaccines for human malarias.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Primates as Hosts 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: This study is being conducted to determine the dose of infective larvae necessary to establish patent infections in chimpanzees with O. volvulus. The second objective is to more fully evaluate mangabey monkeys as potential hosts for the parasite, with the hope of providing a small primate model for study of this infection. Chimpanzees may continue to play crucial roles in vaccine trials, but more information is needed about the general host response to the parasite before vaccine tests could be conducted. Of primary concern is appropriate inocula size which will result in consistent parasitological infection and what immunological responses this inocula will elicit from the animal. Groups of chimpanzees were inoculated with graded doses of larvae ranging from 200 to 400 each, and they have been monitored monthly for immunological response as well as for parasitological signs of infection. Microfilariae have been detected in several of these animals and immunoblots of sera have shown significant bands. It is premature to begin drawing conclusions, as the majority of animals are still in the prepatent phase. Mangabey monkeys continue to be of special interest because their responses are similar those documented in infected humans. As with the current chimpanzee studies, the mangabey studies are only about midway toward completion and it is too early to fully understand and interpret the results obtained to date.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Growth and Development of Onchocerca in Diffusion Chambers

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: 0

INVES2: Abraham, David A.
DEGREE2: Ph.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: 0

SPECIES1: Pan troglodytes
NUM1: 6

SPECIES2: Cercocebus atys
NUM2: 4

NON-HOST INSTITUTION: Centers for Disease Control (MLE) and Thomas Jefferson University (DAA)

ABSTRACT: The purpose of this project is to develop implantable diffusion chambers as a means of studying the early development of O. volvulus in primate hosts, and as a potential screening method to assay drug trials or potential vaccine candidates. The ability to inoculate larvae into chambers, implant them into animals, and then recover the chambers with contained larvae, has allowed us to answer certain crucial questions which would have been difficult previously. Because larvae are confined to the chambers, yet host cells are permitted to enter, it is possible to monitor the host's response to larvae at predetermined time intervals. Evaluation of drug or vaccine trials would have necessitated either sacrifice of the animal to monitor outcome or undertaken inconclusive parasitological follow-up for at least two years. Now, in a noninvasive manner, these studies can be performed with much better results. Chamber construction, number of larvae per chamber, times of removal, expected growth and development of larvae, etc. have all been standardized. It is anticipated that within the next 12-15 months limited trials with candidate vaccine compounds will be undertaken.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Microbial Flora in Periodontal Sites of the Rhesus Monkey

AXIS I: 1a, 3, 7, 22

AXIS II: 42, 52, 63, 70, 80, 86

PRC UNIT: Pathobiology & Immunobiology

INVES1: Eke, Paul I.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: O

INVES2: Braswell, Laura D.
DEGREE2: D.D.S.
DEPT2: Pathobiology & Immunobiology
STAFF2: O

INVES3: Arnold, Roland R.
DEGREE3: Ph.D.
DEPT3: Pathobiology and Immunobiology
STAFF3: O

INVES4: Fritz, Michael E.
DEGREE4: D.D.S., M.S., Ph.D.
DEPT4: Pathobiology & Immunobiology
STAFF4: O

SPECIES1: Macaca mulatta
NUM1: 9

ABSTRACT: Rhesus monkeys (Macaca mulatta) are being used increasingly as a model for studying various concepts of periodontal disease. This model is being used by our group to study the biology of root form fixtures and blade vent dental implants. In this report we present the natural periodontal flora in nine monkeys among a population selected for dental implant studies. Subgingival plaque was obtained from three clinically healthy sites (8 db, 18 mb, 31 mb) in their natural state and seven days after scaling. Anaerobes were the predominant flora pre-scaling, and the major groups identified include the black pigmented Bacteroides (BPB) (85% of site positive representing a range of relative proportion to total anaerobic count (TAC) of 0-0.54), Hemophilus spp (100%, 0.04-0.6), Wolinella spp (64%, 0-0.18), F. nucleatum (93%, 0-1.4) A. actinomycetemcomitans (76%, 0-0.32) and P. micros (95%, 0.03). Rarely cultivated were Capnocytophaga spp (30%), E. corrodens (3.5%, 0-0.01) and coliforms (0%). Post scaling TAC declined in 60% of sites and a declining trend was observed for total BPB counts represented by a decrease at 75% of sites. Interestingly coliforms were now cultured in 25% of site although in low proportions (0.001-0.006). Other bacterial groups did not change consistently either way after scaling. A tremendous variability was observed in microbial flora composition in sites within and between monkeys. Our data begin to establish a baseline for distinguishing important bacterial groups associated with artificially induced periodontal disease around natural teeth and implants.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Implant, Prosthetic, and Periodontal Studies in Monkeys

AXIS I: 1a, 3, 7, 22

AXIS II: 42, 52, 63, 70, 80, 86

PRC UNIT: Pathobiology & Immunobiology

INVES1: Fritz, Michael E.
DEGREE1: D.D.S., M.S., Ph.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: 0

INVES2: Turner, Kenneth A.
DEGREE2: D.D.S.
DEPT2: Pathobiology and Immunobiology
STAFF2: 0

INVES3: Braswell, Laura D.
DEGREE3: D.D.S
DEPT3: Pathobiology and Immunobiology
STAFF3: 0

INVES4: Arnold, Roland R.
DEGREE4: Ph.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: 0

INVES5: Hall, E.C.
DEGREE5: Ph.D.
DEPT5: Pathobiology and Immunobiology
STAFF5: 0

SPECIES1: Macaca mulatta
NUM1: 40

NON-HOST INSTITUTION:

ABSTRACT: The present study integrates the disciplines of biomaterials, clinical dentistry, digital radiology, and biomechanics to study the behavior of dental implants. Root-form fixtures and blade-vent dental implants will be produced under stringent conditions in a Department of Biomaterials, and biology of these will be assessed in a partially edentulous monkey model system, utilizing 40 rhesus monkeys housed at Yerkes Regional Primate Research Center. After implant (fixture) and bridge placement, clinical and microbiological monitoring, radiological assessment, and computer models of loading characteristics will be analyzed on a regular basis and implant (fixture) abutments will be compared to natural teeth abutments. Routine scalings will be performed in the monkeys on a once monthly basis to prevent periodontitis for a period of 24 months. After 24 months, periodontitis and peri-implant disease will be created by the use of silk ligatures being tied around teeth

or implants (fixtures) for 6 months. Clinical, microbiological, and radiological measurements, and computer modeling will again be performed. The data produced will provide the comparison of 2 types of implants and/or fixtures, and the natural teeth in both non-diseased and diseased environment in a monkey model. These data are not in existence, and will be important as they provide immediate application to patient care. Implant dentistry will become more prevalent in our society as technology is improving rapidly and our population ages, and this population has a high percentage of partially or fully edentulous individuals.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Effects of Prostaglandin E_2 on Replication of HIV-1

AXIS I: 2, 4, 7b

AXIS II: 31, 64, 66

PRC UNIT: Pathobiology & Immun

INVES1: Fultz, Patricia N.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVES2: Emau, Peter
DEGREE2: Ph.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: O

SPECIES1: None
NUM1: None

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

ABSTRACT: The ability of the human immunodeficiency virus type 1 (HIV-1) to replicate in $CD4^+$ T lymphocytes is dependent on activation and proliferation of the infected cells. HIV-1 infection is known to stimulate production of cytokines, lymphocyte membrane metabolism and production of arachidonic acid metabolites, including prostaglandin (PG) E_2, from monocytes. Because PGE_2 suppresses lymphocyte activation and proliferation and inhibits synthesis of some lymphokines, we tested the effect of exogenous PGE_2 on HIV-1 replication in interleukin 2 (IL-2)-stimulated and unstimulated normal human peripheral blood mononuclear cells (PBMC). The results showed that PGE_2 resulted in 90% suppression of productive infection by the LAV-1_{BRU} strain of HIV-1 in both IL-2-stimulated and unstimulated PBMC. PGE_1, but not PGF_2-alpha, also inhibited replication of LAV-1_{BRU} by 60%. PGE_2 and PGE_1 suppress activation and proliferation of PBMC by a common pathway involving increased cAMP and feed-back inhibition of IL-2 synthesis; this is the most likely mechanism for down-regulation of HIV-1 replication. These results may be important in vivo because significant amounts of PGE_2 may be produced in a local cellular environment by monocytes in response to a variety of inflammatory and immunologic stimuli. This suggests a complex interplay between cytokines and PGE_2 at the cellular level may regulate the level of HIV expression during infection.

TITLE: Prolonged $CD4^+$ Lymphocytopenia and Thrombocytopenia in a Chimpanzee Infected with HIV-1

AXIS I: 1a, 7b

AXIS II: 31, 64, 66, 77

PRC UNIT: Pathobiology & Immun

INVES1: Fultz, Patricia N.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: C

INVES2: Swenson, R. Brent
DEGREE2: D.V.M.
DEPT2: Animal Resources
STAFF2: C

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

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

SPECIES1: Pan troglodytes
NUM1: 1

ABSTRACT: The immunologic and virologic status of a chimpanzee inoculated with multiple isolates of the human immunodeficiency virus type 1 (HIV-1) were assessed over 57 months to determine whether prolonged thrombocytopenia and $CD4^+$ lymphocytopenia observed in the animal might be associated with long-term HIV infection. Although the chimpanzee showed no signs of disease, it lost both $CD4^+$ (as low as 134 cells/ul) and $CD8^+$ lymphocytes ~30 months after initial infection, followed by thrombocytopenia that has persisted for >2 years. Lymphopenia and thrombocytopenia were preceded by or coincided with the appearance of antibodies cross-reactive with histone H2B and decreased levels of complement component C4; an eightfold decrease in HIV-specific antibody titers; the inability of $CD8^+$ lymphocytes to suppress virus replication; impaired proliferative responses to T cell mitogens; and the isolation of cell-free HIV from plasma. These data suggest that, given sufficient time, HIV-infected chimpanzees may develop disease.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Characterization and Molecular Cloning of Antigens of O.volvulus

AXIS I: 1a, 1d, 7c

AXIS II: 64, 91

PRC UNIT: Pathobiology & Immun

INVES1: Greene, Bruce M.
DEGREE1: M.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: O

INVES2: Chakravarti, Deb N.
DEGREE2: Ph.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: O

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

SPECIES1: Pan troglodytes
NUM1: 2

NON-HOST INSTITUTION: University of Alabama at Birmingham (BMG, DNC)

ABSTRACT: Parasite antigen specific T cells are believed to be important in both pathogenic and protective immune responses in filarial infections, but precise definition of antigens that elicit these responses is limited. We are examining O. volvulus antigens that elicit blastogenic response in peripheral T-lymphocytes from chimpanzees (permissive host) immunized with live non-attenuated (L) or radiation-attenuated (L*) O. volvulus infective larvae. Initial fractionation of the 35,000 x g supernatant of the O. volvulus adult worm homogenate into three distinct pools was carried out by gel filtration using Bio-Gel A-5m with lymphocyte blastogenic activity predominantly in Pool-II. Further purification of Pool-II by ion-exchange H.P.L.C. using Mono Q yielded several fractions which differed in their ability to induct T-cell proliferative response in the above chimpanzees. Two distinct regions, Pool-A (eluted unbound at 10 mM NaCl) and Pool-B (eluted with 0.26 M to 0.42 M NaCl) induced significant lymphocyte blastogenic activity in PBMC's from chimpanzees immunized with L* and skin microfilariae negative. In contrast, only one of these (Pool-B) reproducibly caused significant lymphocyte blastogenesis of PBMC's from the chimpanzee which was immunized with L and skin microfilariae positive. SDS-PAGE analysis (7.5%, acrylamide, w/v) showed that Pool-A contained nine major proteins of Mr from approx. 24 to 130 K whereas Pool-B contained about nineteen major proteins of Mr from approx. 21 to 200K. These antigens will be explored as possible candidates for future design of a vaccine against onchocerciasis.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Evaluation of Small Vessel Prostheses

AXIS I: 1a, 2, 3, 13, 17

AXIS II: 48, 50b, 63f

PRC UNIT: Pathobiology & Immun

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

INVES2: Kelly, Andrew B.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

SPECIES1: Papio cynocephalus
NUM1: 20

NON-HOST INST:

ABSTRACT: The objective of this study is to define mechanisms and pharmacologic interventions for preventing the failure of small caliber arteries (< 5 mm internal diameter) or synthetic arterial grafts due to thrombosis which occurs acutely following arterial injury, or which may occur at later times secondary to stenotic tissue ingrowth (neointimal hyperplasia). Based on promising studies reported in rats, we evaluated the capacity of an oral angiotensin enzyme converting enzyme (ACE) inhibitor (cilazapril) to block arterial smooth muscle cell (SMC) proliferation in 14 baboons (papio cynocephalus) 3 months following procedures for carotid artery endarterectomy, iliac artery vascular grafting, and femoral artery balloon catheter deendothelialization. Despite effective inhibition of plasma ACE activity (> 98%), SMC proliferation was equivalent to that in untreated control animals, suggesting important differences between primates and lower species for regulation of vascular wall cellular responses. We are presently evaluating the effects on vascular healing of potent inhibitors of platelets and coagulation enzymes, and are comparing the healing of clinical vascular grafts with grafts coated with ultrathin layers of blood compatible polymers or acutely harvested endothelial cells. Thus, several strategies are being developed in baboons to prevent short-term and long-term vessel occlusion which is commonly observed in man following procedures for arterial reconstruction.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Thrombus Formation and Dissolution in vivo

AXIS I: 1a, 2, 3, 13, 17

AXIS II: 48, 50b, 63f

PRC UNIT: Pathobiology & Immun

INVES1: Hanson, Stephen R.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: O

INVES2: Kelly, Andrew B.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

SPECIES1: Papio cynocephalus
NUM1: 13

NON-HOST INST:

ABSTRACT: Thrombosis and hemostasis centrally involve the reactions of blood platelets. While in vitro studies have suggested that platelet adhesion and aggregation are mediated by the selective binding to platelet receptors of adhesive plasma glycoproteins (such as fibrinogen and von Willebrand Factor), the physiologic relevance of many of these observations is unknown. Using a baboon (Papio cynocephalus) model of arteriovenous shunt thrombus formation, we have identified specific monoclonal antibody and synthetic peptide inhibitors of the platelet glycoprotein IIb/IIIa receptor which profoundly inhibit thrombus formation but produce some tendency for increased bleeding. We are currently characterizing the relative antithrombotic vs antihemostatic effects of these agents and their relationships to antagonist affinity, specificity, and platelet binding kinetics. Amino acid sequencing of baboon platelet receptor proteins has been initiated and will allow preparation of sequence-specific antibodies and definition of platelet receptor functional domains. These studies will allow further optimization of the safety, potency, and specificity for inhibitors of platelet-dependent thrombosis.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Thrombus Formation and Dissolution in vivo

AXIS I: 1a, 2, 3, 9, 13, 17

AXIS II: 48, 50b, 63f, 86

PRC UNIT: Pathobiology and Immuno

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

INVES2: Hanson, Stephen R.
DEGREE2: Ph.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: O

INVES3: Kelly, Andrew B.
DEGREE3: D.V.M.
DEPT3: Pathobiology and Immunobiology
STAFF3: C

SPECIES1: Papio cynocephalus
NUM1: 19

ABSTRACT: We evaluated numerous peptides and procedures in non-human primates. Tyr-sulfated dodecapeptide from residues 53-64 of hirudin (H-peptide) was tested, and the findings suggested that fibrin-rich venous-type thrombus formation may be selectively prevented and therapeutically attractive for preserving normal platelet function when conventional anticoagulant therapy was contraindicated. Hirudin, a highly potent and specific antithrombin, was compared to heparin, an antithrombin III-dependent inhibitor of thrombin. We concluded that platelet-dependent, thrombotic and hemostatic processes are thrombin-mediated and that hirudin produced a potent, dose-dependent inhibition of arterial thrombus formation which greatly exceeded the minimal antithrombotic effects produced by heparin. We also studied D-Phe-Pro-Arg chloro-methylketone (D-FPRCH_2Cl) during carotid endarterectomy and concluded that short-term therapy with this agent produced long-term antithrombotic benefits without risk of abnormal bleeding when administered immediately after surgical hemostasis had been achieved. Applaggin was found to be a potent reversible inhibitor of platelet recruitment into forming thrombus which may be therapeutically useful in humans. Hirulog was assessed and exhibited greater antithrombotic efficacy than D-FPRCH_2Cl and hirudin and approached the potency of D-FPRCH_2Cl without its potential toxicity. Locally treated small caliber Dacron vascular grafts were implanted end-to-end with D-FPRCH_2Cl and found to prevent subsequent thrombus formation without risk of hemorrhage. Local vs systemic effects of hirudin, D-FPRCH_2Cl and heparin were compared for blocking platelet deposition onto segments of thrombogenic Dacron vascular grafts, and it was concluded that short-term treatment of forming thrombi with D-FPRCH_2Cl markedly reduced or prevented (for $\geq$ 21 hours) subsequent thrombus growth.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Endarterectomy: Prevention of Thrombosis and Restenosis

AXIS I: 1a, 2, 3, 9, 13, 17

AXIS II: 48, 50b, 63f, 86

PRC UNIT: Pathobiology & Immun

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

INVES2: Hanson, Stephen R.
DEGREE2: Ph.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: 0

INVES3: Kelly, Andrew B.
DEGREE3: D.V.M.
DEPT3: Pathobiology and Immunobiology
STAFF3: C

INVES4: Lumsden, Alan
DEGREE4: M.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: 0

SPECIES1: Papio cynocephalus
NUM1: 11

SPECIES2: Pan troglodytes
NUM2: 4

NON-HOST INST:

ABSTRACT: We examined the potential antithrombotic usefulness of locally treating small caliber (1 cm long, 4mm ID) Dacron vascular grafts implanted end-to-end in baboon carotid arteries with the potent irreversible antithrombin, D-Phe-Pro-Arg chloromethyl ketone (D-FPRCH$_2$Cl), and concluded that brief local treatment of implanted vascular grafts with high-dose D-FPRCH$_2$Cl immediately after establishing surgical hemostasis prevents subsequent thrombus formation without risk of hemorrhage. In addition, we compared the local vs. systemic effects of hirudin, D-FPRCH$_2$Cl and heparin for blocking platelet deposition onto segments of thrombogenic Dacron vascular graft (0.5 cm^2) incorporated into exteriorized AV shunts in baboons and concluded that short-term ($\leq$ 15 min) treatment of forming thrombi with D-FPRCH$_2$Cl markedly reduces or prevents (for $\geq$ 21 hrs) subsequent thrombus growth. We also synthesized a 20-mer peptide (Hirulog), combining the antithrombin activities of D-Phe-Pro-Arg (D-FPR) and the carboxy terminal dodecapeptide of hirudin and assessed it in baboons for its relative antithrombotic and antihemostatic effects in comparison with the parent

molecules, and concluded that this hybrid antithrombin peptide exhibits greater antithrombotic efficacy than the parent molecules, approaching the potency of D-FPRCH$_2$Cl without its potential toxicity. We also evaluated the relative antithrombotic and antihemostatic effects of applaggin, an 18 kDa disulfide-linked Arg-Gly-Asp-containing dimeric polypeptide isolated from Agkistrodon piscivorus piscivorus, in 4 chimpanzees because infusions of applaggin into baboons produced reversible thrombocytopenia in a dose-dependent manner due to transient reciprocal sequestration in the liver and concluded that applaggin is a potent reversible inhibitor of platelet recruitment into forming thrombus in chimpanzees and may be therapeutically useful in humans. Finally, we determined the relative antithrombotic and antihemostatic effects during carotid endarterectomy of D-FPRCH$_2$Cl infused (100 nmol/kg per min) for 1 hour in baboons and concluded that short-term D-FPRCH$_2$Cl therapy produces long-term antithrombotic benefits without risk of abnormal bleeding when administered immediately after surgical hemostasis has been achieved.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Dietary Omega-3 Fatty Acids: Thrombosis and Vascular Healing

AXIS I: 1a, 2, 3, 9, 13, 17

AXIS II: 48, 50b, 63f, 86

PRC UNIT: Pathobiology & Immun

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

INVES2: Hanson, Stephen R.
DEGREE2: Ph.D.
DEPT2: Pathobiology and Immunology
STAFF2: 0

INVES3: Kelly, Andrew B.
DEGREE3: D.V.M.
DEPT3: Pathobiology and Immunobiology
STAFF3: C

SPECIES1: Papio cynocephalus
NUM1: 8

NON-HOST INST:

ABSTRACT: Despite the biochemical effects on platelet hemostatic function, there is little direct information regarding effects of w3 fatty acids on platelet-dependent arterial thrombosis. We found that within weeks chronic dietary omega 3 fatty acids reciprocally displace other fatty acids and that these changes are associated with minimal impairment in platelet hemostatic function but a marked reduction in the expression of tissue factor activity by monocytes ex vivo. While the thrombotic response of blood to prosthetic vascular grafts was significantly reduced, thrombus formation induced by experimental vascular injury of w3 treated arteries was strikingly decreased due to the effects of omega 3 fatty acids on arterial wall thrombogenicity. We therefore concluded that the documented effects of omega 3 fatty acid dietary supplementation on eicosanoid production fails to fully explain the profound interruption of thrombus formation observed after damage to w3 fatty acid treated vessels, and we postulate that vascular cellular membranes are altered, thereby preventing thrombus formation mediated by tissue factor expression in a manner similar to that shown for blood monocytes.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Effect of Simian Immunodeficiency Virus (SIV) Infection on Hematopoietic Stem Cell Populations in Rhesus Macaques and Sooty Mangabeys

AXIS I: 1d, 2, 17, 19

AXIS II: 31, 39, 64, 66

PRC UNIT: Pathobiology and Immun

INVES1: Hillyer, Christopher D.
DEGREE1: M.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: O

INVES2: Ansari, Aftab A.
DEGREE2: Ph.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: C

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

SPECIES1: Macaca mulatta
NUM1: 5

NON-HOST INSTITUTION:

ABSTRACT: The objective of this study is to 1) examine the frequency of $CD34^+$ pluripotential stem cells and the specific lineage precursors (BFU-E, CFU-GM, CFU-GEMM and T-CFC) in the bone marrow of disease-susceptible SIV^+ rhesus macaques compared to age and sex-matched SIV^- rhesus monkeys, 2) to correlate these data with clinical parameters, blood and lymphocyte counts and antiglobulin tests for peripheral destruction and to determine the temporal, kinetic and prognostic significance of the hematopoietic suppression and/or peripheral blood destruction that is observed in SIV-infected animals further elucidating the hematologic aspects of the rhesus model for AIDS and 3) to investigate the role of cellular components (monocytes/macrophages or T-cell subpopulations), cytokine deficiencies (GM-CSF, IL-3, IL-6) and/or secreted inhibitors in an attempt to determine the mechanism of the abnormalities defined in 1) and 2) above. This study commenced in December 1990. The preliminary data suggest that 1) there is a 54%, 72% and 73% reduction in BFU-3, CFU-GEMM and CFU-GM in SIV infected animals, respectively and 2) that SIV^+ sera (n=2), is able to decrease the CFU capabilities of normal bone marrow by approximately 70% when cultured with 1ng/ml GM-CSF and with 5 ng/ml GM-CSF. It is our hope that this study will help elucidate the pathogenesis of the cytopenias seen in the SIV infected macaques and thus lead to new treatment strategies.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Effect of Simian Immunodeficiency Virus (SIV) Infection on Circulating Erythrocytes: Autoimmune Hemolytic Anemia in Infected Rhesus Macaques

AXIS I: 1d, 17

AXIS II: 31, 64, 66

PRC UNIT: Pathobiology and Immun

INVES1: Hillyer, Christopher D.
DEGREE1: M.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: 0

INVES2: Brodie, Anne R.
DEGREE2: MT (ASCP)
DEPT2: Pathobiology and Immunobiology
STAFF2: 0

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

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

INVES5: McClure, Harold M.
DEGREE5: D.V.M.
DEPT5: Pathobiology and Immunobiology
STAFF5: C

SPECIES1: Macaca mulatta
NUM1: 13

NON-HOST INSTITUTION:

ABSTRACT: The objective of this study is to describe the autoimmune hemolysis seen in Macaca mulatta infected with simian immunodeficiency virus (SIV) and its relationship to the anemia observed in these animals. Using animals inoculated in 1989 with SIVsmm9, complete blood counts, Coomb's and serum compatibility tests, and serum iron, total iron binding capacity and lactate dehydrogenase (LDH) are obtained. Two animals have exhibited severe autoimmune hemolysis with the presence of both cold (IgM) and warm (IgG) agglutinins and elevated LDH values. Four of the 13 animals had positive antiglobulin (Coombs') tests and IgG could be demonstrated at the erythrocyte membrane. Weakly positive antiglobulin tests do not appear to correlate with disease state or anemia, while strongly positive tests appear in animals with significant anemia. Autoimmune hemolysis has been shown in rare cases of

human immunodeficiency virus infection but has not been described in SIV infection. Moreover, the pathogenesis of the anemia seen in SIV infected animals is unclear. It is our hope that this study will help elucidate autoimmune hemolytic anemia as a cause of anemia in this animal model and thus lead to treatment strategies.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Molecular Analysis of SIV from Sykes Monkeys (SIVsyk)

AXIS I: 1a, 1d, 7b

AXIS II: 31, 66

PRC UNIT: Pathobiology & Immun

INVES1: Hirsch, Vanessa M.
DEGREE1: D.V.M.
DEPT1: Pathobiology and Immunobiology
STAFF1: 0

INVES2: Johnson, Philip R.
DEGREE2: M.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: 0

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

SPECIES1: Cercopithecus mitis
NUM1: 9

NON-HOST INSTITUTION: Georgetown University (VMH and PRJ)

ABSTRACT: SIV was originally isolated from Sykes monkeys (Cercopithecus mitis) at the Yerkes Primate Center. Cryopreserved, cell-free culture supernatant stored at the time of initial isolation was used to infect peripheral blood mononuclear cells (PBMC) from a seronegative Sykes monkey, and the human CD4$^+$ cell line CEM x 174. Genomic DNA from the productively infected CEM x 174 cell line was used as the template for "low stringency" polymerase chain reaction amplification (PCR) of the gag region. Primers were derived using regions highly conserved among SIV isolates (SIVagm, SIVmac and SIVsmm) as previously described for highly divergent SIVagm isolates. The gag region was amplified, purified and cloned into the plasmid pGEM 7ZF. Sequence analysis revealed that the SIVsyk gag region was distantly related to the other reported SIV sequences. Thus, 50% amino acid identity was observed between SIVsyk and either SIVsmm, or two divergent SIVagm isolates. This identify is lower than that observed between SIVsmm and SIVagm (60%) due to a 25 amino acid insertion near the amino terminus of the gag protein of SIVsyk. In addition, by nucleotide comparisons, SIVsyk is only distantly related to SIV from mandrills (SIVmnd) and HIV-1. Thus, SIVsyk is a novel member of the SIV family of viruses, distinct from all other strains previously described.

Further studies are aimed at obtaining a full-length, biologically-active molecular clone. Our strategy includes: (1) Southern blot analysis (using the gag probe) to identify restriction enzymes that do not cut within the SIVsyk genome, and (ii) PCR to obtain the 5′ and 3′ portions of the genome.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Quantitative Digital Subtraction Radiography for Assessment of Peri-Implant Bone Change

AXIS I: 1a, 3, 7, 22

AXIS II: 42, 52, 63, 70, 80, 86

PRC UNIT: Pathobiology & Immun

INVES1: Jeffcoat, Marjorie K.
DEGREE1: D.M.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: 0

INVES2: Reddy, Michael
DEGREE2: D.D.S., Ph.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: 0

NON-HOST INSTITUTION: University of Alabama at Birmingham (MKJ, MR)

ABSTRACT: The purpose of this study was to develop a digital subtraction technique to assess peri-implant bone loss in terms of area and mass in blade and root form implants. 10 phantoms were fabricated with simulated osseous defects of known size. Each phantom was radiographed in duplicate and pairs of radiographs subtracted after contrast correction. Specialized software was written to isolate the area and mass of peri-implant bone change. In brief, the subtraction image was thresholded to create a binary image and a morphological OPEN operation was performed. The software calculated the size of the isolated lesion utilizing a reference wedge. The repeatability of the method was taken as the standard deviation of five measurements was taken from each subtraction image. The validity of the method was determined by correlating calculated with actual lesion mass. There was no significant difference in repeatability in area measurement between root form and blade implants (.63±22, .61±.29mm2, respectively). Overall, there was excellent correlation between the calculated lesion size (in milligrams) and actual lesion size ($r=.94, p<.001$). These data indicate that quantitative digital subtraction radiography may be of value in measuring peri-implant bone loss in both blade and root form implants.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Implant, Prosthetic, and Periodontal Studies in Monkeys

AXIS I: 1a, 3, 7, 22

AXIS II: 42, 52, 63, 70, 80, 86

PRC UNIT: Pathobiology & Immun

INVES1: Jeffcoat, Marjorie
DEGREE1: D.M.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: O

INVES2: Webber, Richard
DEGREE2: D.D.S., Ph.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: O

SPECIES1:
NUM1:

NON-HOST INSTITUTION: University of Alabama at Birmingham (MJ, RW)

ABSTRACT: The major objective of the radiographic section of the proposed program project is to non-invasively enhance our understanding of the implant success and failure in the primate model. Digital radiography and digital subtraction radiography will be used to allow quantitative assessment of the osseous changes over time surrounding the implants and abutment teeth. Quantitative assessment of bony change is fundamental to analyzing the effect of root form, and periodontal disease in implant success or failure. Digital subtraction radiography has been successfully applied to longitudinal studies of periodontal disease and has been shown to have greatly increased sensitivity in detecting bony changes over conventional radiographic scoring techniques. The non-destructive nature of digital radiography permits longitudinal study of the same implant over time in a single animal without sacrifice. The study design will allow analysis of the time course of bony changes under any or all of the study conditions. Standardized radiographs will be taken every three months in order to determine over time the effect of root form, and periodontal status on the success or failure of the implant. Outcome measures will include the tightness of adaptation of the bone to the implant, the bony support of the implant, and the bony support of the abutment teeth.

A second aim is to develop methods which will allow quantitative assessment of the amount of bone loss or gain in hydroxyapatite equivalents. These methods will take into account beam hardening errors and permit comparisons between animals.

As part of the program project these data will be used in the core and modeling programs. In addition, radiographic data will be correlated with histologic data at the time of animal sacrifice.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Comparison of SIV Replication in $CD4^+$ T Cells and Monocytes from Mangabeys and Macaques.

AXIS I: 1a, 1d, 2, 7b, 9, 19

AXIS II: 31, 64, 66, 83

PRC UNIT: Pathobiology & Immun

INVES1: Jehuda-Cohen, Tamar
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: 0

INVES2: Powell, Jonathan D.
DEGREE2: B.S.
DEPT2: Pathobiology and Immunobiology
STAFF2: 0

INVES3: Villinger, Francois V.
DEGREE3: D.V.M.
DEPT3: Pathobiology & Immunobiology
STAFF3: 0

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

INVES5: Sell, Kenneth W.
DEGREE5: M.D., Ph.D.
DEPT5: Pathology
STAFF5: 0

INVES6: Ansari, Aftab A.
DEGREE6: Ph.D.
DEPT6: Pathobiology & Immunobiology
STAFF6: C

SPECIES1: Cercocebus atys
NUM1: 10

SPECIES2: Macaca mulatta
NUM2: 10

NON-HOST INSTITUTION:

ABSTRACT: The fact that sooty mangabeys are naturally infected with SIV but remain clinically asymptomatic and that virus isolated from this species, when experimentally injected into macaques, induces an AIDS-like disease which invariably results in death prompted us to determine whether this difference was secondary to differential susceptibility of $CD4^+$ T cells as compared to

monocytes from these two species to SIV replication. Toward this goal, highly enriched population of monocytes and $CD4^+$ T cells from these two species were cultured *in vitro* with a fixed dose of live SIVsmm. The relative replication of SIV in these cultures was monitored by assaying the supernatant fluid for levels of reverse transcriptase (RT) activity. Results demonstrate that there is a significantly ($p < .001$) higher level of virus replication (high mean RT activity) in monocytes from sooty mangabeys than in those from rhesus macaques; however, no difference was seen in the relative amounts of virus replication in enriched populations of $CD4^+$ T cells from these two species. Of interest was the observation that addition of $CD8^+$ T cells to autologous cultures of monocytes or $CD4^+$ T cells from these two species resulted in a marked suppression of virus replication. The degree of suppression induced by $CD8^+$ T cells was more marked in monocytes from mangabeys than in those from macaques. In addition, $CD8^+$ T cells from not only seropositive mangabeys but also seronegative mangabeys appear to exert this regulatory function. In contrast, $CD8^+$ T cells from rhesus macaques experimentally infected with SIVsmm-9 but not from uninfected rhesus macaques showed this regulatory function. These data demonstrate two findings: (1) The monocytes from mangabeys appear to be relatively more susceptible to SIV replication than do monocytes from macaques. (2) $CD8^+$ T cells from mangabeys very effectively regulate the extent of virus replication in these monocytes. This differential susceptibility of monocytes and the selective increased regulation of virus replication in monocytes by $CD4^+$ T cells from mangabeys may play a role in the asymptomatic state of SIV-infected mangabeys and in the disease susceptibility of rhesus macaques.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Detection of Occult HIV-1 Infection in HIV-1 Seronegative Humans at High Risk for AIDS

AXIS I: 2, 4, 5a, 5b, 7b, 9

AXIS II: 31, 56, 66, 83

PRC UNIT: Pathobiology & Immun

INVES1: Jehuda-Cohen, Tamar
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: O

INVES2: Slade, Barbara A.
DEGREE2: M.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: O

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

INVES4: Villinger, Francois
DEGREE4: D.V.M.
DEPT4: Pathobiology & Immunobiology
STAFF4: O

INVES5: De, Barun
DEGREE5: Ph.D.
DEPT5: Pathobiology and Immunobiology
STAFF5: O

INVES6: Folks, Thomas M.
DEGREE6: Ph.D.
DEPT6: Pathobiology and Immunobiology
STAFF6: O

INVES7: McClure, Harold M.
DEGREE7: D.V.M.
DEPT7: Pathobiology & Immunobiology
STAFF7: C

INVES8: Sell, Kenneth W.
DEGREE8: M.D., Ph.D.
DEPT8: Pathobiology and Immunobiology
STAFF8: O

INVES9: Ansari, Aftab A.
DEGREE9: Ph.D.
DEPT9: Pathobiology & Immunobiology
STAFF9: C

SPECIES1: Homo sapiens
NUM1: 165

NON-HOST INSTITUTION: Grady Memorial Hospital (B.S.)
Centers for Disease Control (B.D., T.F.)

ABSTRACT: Identification of human immunodeficiency virus type 1 (HIV-1)-infected individuals is of paramount importance for the control of the spread of AIDS worldwide. Currently, the vast majority of screening centers throughout the world rely on serological techniques. As such, clinically asymptomatic but HIV-infected, seronegative individuals are rarely identified. In this report we show that 18% (30/165) of seronegative individuals who were considered to be a unique cohort of patients at high risk for HIV infection had circulating B cells that, upon in vitro polyclonal activation with pokeweed mitogen, produced antibodies reactive with HIV. Furthermore, polymerase chain reaction analysis of DNA obtained from aliquots of the peripheral blood mononuclear cells from these seronegative but pokeweed mitogen assay-positive individuals tested revealed the presence of HIV-specific sequences in a significant number of samples. In addition, depletion of $CD8^+$ T cells from peripheral blood mononuclear cells of HIV-1-seronegative individuals prior to in vitro culture with pokeweed mitogen resulted in increased sensitivity for detecting HIV-reactive antibodies. This assay has obvious epidemiological implications, especially in the case of high-risk groups, and also provides a simple technique to enhance detection of HIV-infected individuals. Of further interest is the determination of the mechanisms related to the lack of HIV-specific antibodies in the serum of these infected individuals.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Transmission of SIV Infection from Seronegative Mangabeys to Offspring

AXIS I: 1a, 1d, 2, 7b, 9, 19

AXIS II: 31, 66, 83

PRC UNIT: Pathobiology & Immun

INVES1: Jehuda-Cohen, Tamar
DEGREE1: Ph.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: O

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

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

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

INVES5: Sell, Kenneth W.
DEGREE5: M.D., Ph.D.
DEPT5: Pathobiology & Immunobiology
STAFF5: O

INVES6: Ansari, Aftab A.
DEGREE6: Ph.D.
DEPT6: Pathobiology & Immunobiology
STAFF6: C

SPECIES1: Cercocebus atys
NUM1: 10

SPECIES2: Macaca mulatta
NUM2: 10

NON-HOST INSTITUTION:

ABSTRACT: A large number of sooty mangabeys in our colony at the Yerkes Regional Primate Research Center are naturally infected with a simian immunodeficiency virus (SIVsmm). The route of transmission was reasoned to be most likely via sexual means since the rate of seroconversion was coincident with the onset of sexual maturity; however, serum samples from three infant

mangabeys (ages, 26, 19, and 9 months) were found to contain readily detectable antibodies against SIVsmm as determined by ELISA. These antibodies specifically reacted with *env*, *gag*, and *pol* proteins of the SIV by Western blot analysis. Of significance was the finding that all three infants were born to mangabeys which were seronegative for SIV. These data prompted us to examine in more detail the natural history of these mothers and the possible route of transmission in the infants. Sera samples from the three mothers, as far back as 3 years and up to the time of birth and after delivery, did not show any detectable levels of antibody against SIV; however, serial sera from all three infants contained high levels of SIV-reactive antibodies. Peripheral blood mononuclear (PBMC) from two of the mothers and their respective infants were subjected to more detailed *in vitro* analysis. The data obtained showed that the PBMC from all mothers and infants (a) secreted readily detectable levels of SIV-reactive antibodies upon polyclonal activation *in vitro*, (b) showed significant levels of RT activity, and (c) contained SIV-specific sequences as determined by PCR.

These data demonstrate that SIV infection must be transmitted from mother to offspring either *in utero* or perinatally and further caution the use of serology as a sole criterion for the detection of lentivirus infection, at least in individuals (humans) or nonhuman primates, such as mangabeys, that are at an exceptionally high risk of lentivirus infections.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Comparison of Isolation of Typical and Atypical Campylobacter Species from Nonhuman Primates Using Campy-CVA and Campy-BAP.

AXIS I: 17a, 16c

AXIS II: 66

PRC UNIT: Pathobiology & Immun

INVES1: Kielbauch, J.A.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: O

INVES2: Richardson, Karen J.
DEGREE2: B.S.
DEPT2: Pathobiology and Immunobiology
STAFF2: O

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

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

INVES5: Wachsmuth, I.K.
DEGREE5: Ph.D.
DEPT5: Pathobiology and Immunobiology
STAFF5: O

SPECIES1: Saimiri sciureus
NUM1: 27

SPECIES2: Cercocebus atys
NUM2: 25

SPECIES3: Cercopithecus aethiops
NUM3: 2

SPECIES4: Macaca arctoides
NUM4: 22

SPECIES5: Macaca fascicularis
NUM5: 15

SPECIES6: Macaca mulatta
NUM6: 363

SPECIES7: Macaca nemestrina
NUM7: 62

SPECIES8: Papio cynocephalus
NUM8: 10

SPECIES9: Hylobates lar
NUM9: 3

SPECIES10: Gorilla gorilla
NUM10: 2

SPECIES11: Pan paniscus
NUM11: 1

SPECIES12: Pan troglodytes
NUM12: 43

SPECIES13: Pongo pygmaeus
NUM13: 7

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

ABSTRACT: Recently, Campylobacter species have been described which will not grow on standard selective media (Campy-BAP) or at 42°C. As Campylobacter species are commonly isolated from nonhuman primates, we compared their isolation from 661 routine enteric specimens using Campy-CVA plates incubated at 35°C (CC35) in parallel with Campy-BAP plates incubated at 42°C (CB42). All isolates were identified using standard phenotypic techniques and non C. jejuni/coli isolates were examined by rDNA hybridization. Of 58 C. jejuni isolates, 26 were isolated on both media. Of 234 C. coli isolates, 86 were only isolated on CB42, 12 were only isolated on CC35, and 136 were isolated on both media. In addition, 15 aerotolerant Campylobacter strains and 9 strains phenotypically consistent with C. fetus subsp. fetus were isolated on CC35 only. Of the 9 strains, 5 had typical C. fetus subsp. fetus rDNA patterns and 4 strains had atypical patterns. All aerotolerant Campylobacter rDNA patterns were similar to those of a newly-recognized DNA hybridization group (Group 2). Although we did not investigate primary isolation by filtration, it appears that isolation of Campylobacter species from nonhuman primates should include a minimum of both Campy-CVA at 35°C, and Campy-BAP at 42°C.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Disease in Mangabey Monkeys Associated with Simian Immunodeficiency Virus and Simian T-Lymphotropic Virus Type 1.

AXIS I: 1a, 7a, 16c, 16d, 16f, 17, 18, 19, 22, 24, 26, 27

AXIS II: 31, 66, 76b

PRC UNIT: Pathobiology & Immun

INVES1: Klumpp, Sherry A.
DEGREE1: D.V.M., M.S.
DEPT1: Pathobiology & Immunobiology
STAFF1: 0

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

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

INVES4: Ribas, Jorge L.
DEGREE4: D.V.M.
DEPT4: Pathobiology and Immunobiology
STAFF4: 0

INVES5: Ansari, Aftab A.
DEGREE5: Ph.D.
DEPT5: Pathobiology & Immunobiology
STAFF5: C

INVES6: McClure, Harold M.
DEGREE6: D.V.M.
DEPT6: Pathobiology & Immunobiology
STAFF6: C

SPECIES1: Cercocebus atys
NUM1: 7

NON-HOST INSTITUTION: Armed Forces Institute of Pathology and Henry M. Jackson Foundation (JLR).

ABSTRACT: Following the isolation of simian immunodeficiency virus (SIVsmm) from 14 of 15 healthy mangabey monkeys (Cercocebus atys) in a colony at the Yerkes Primate Center, we reviewed necropsy records for all mangabey deaths between 1968 and 1986 for opportunistic infections or other evidence of immunosuppressive disease. Potential immunosuppressive diseases were rarely encountered. These included two 3-month-old neonates of unknown status for SIVsmm, which died of CMV glomerulitis following prolonged treatment for head

trauma. Additional cases included a 5-month-old female mangabey with severe necrotizing gingivitis and an 11-year-old female mangabey with gastric and colonic amebiasis; both monkeys were positive for SIV and the latter was positive also for simian T-lymphotropic virus type 1 (STLV-1). Mangabey monkeys are typically asymptomatic despite the high rate of natural infection with SIVsmm and/or STLV-1. Of the 148 mangabey monkeys presently in the colony, 57% (84 of 148) were seropositive for SIVsmm, and SIVsmm has been cultured from 56% (79 of 140). Thirty-one percent (46 of 148) of the mangabey colony were seropositive for STLV-1. Since 1987 three female mangabey monkeys, who were concurrently infected with both SIVsmm and STLV-1, died with diseases likely related to infection by either or both of these viruses. A 23-year-old, wild-born mangabey had a clinical history of lymphocytosis of 7 years duration; a diffuse lymphoid interstitial pneumonia with syncytial giant cells was present at death. A 16-year-old mangabey with a clinical history of T cell leukemia and dermal lymphoreticular infiltrates died with myelosclerosis, widespread myeloid metaplasia, syncytial giant cells within the liver and lymphadenopathy. A 10-year-old mangabey had multicentric lymphoma and syncytial giant cells in the lungs, liver, lymph nodes and bone marrow at necropsy. The presence of SIV antigen within pulmonary syncytial giant cells has been demonstrated by immunocytochemistry in one of these three monkeys and testing for SIV antigen in syncytial giant cells in a second mangabey is currently underway. These findings indicate that SIV and/or STLV-1 infection may, on occasion, produce disease in mangabey monkeys.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Descriptive Analysis of Bone Marrow Abnormalities in Simian Immunodeficiency Virus (SIV) Seropositive Rhesus Macaques

AXIS I: 1a, 7b, 17

AXIS II: 31, 66

PRC UNIT: Pathobiology and Immunobiology

INVES1: Klumpp, Sherry A.
DEGREE1: D.V.M., M.S.
DEPT1: Pathobiology and Immunobiology
STAFF1: 0

INVES2: Hillyer, Chris D.
DEGREE2: M.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: 0

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

SPECIES1: Macaca mulatta
NUM1: 20

NON-HOST INSTITUTION:

ABSTRACT: The objectives of this study are: 1) to describe the bone marrow morphology of chronically infected SIV positive macaques and 2) to correlate the abnormalities in bone marrow morphology found in objective 1) with the previously described peripheral blood abnormalities (anemia, lymphopenia). Preliminary findings indicate that hypercellularity of the bone marrow, an absolute lymphocytosis in the marrow and iron depletion in the marrow are the most common findings in clinically ill and chronically infected SIV macaques. SIV infected, but clinically normal, rhesus macaques do not demonstrate any abnormalities in bone marrow morphology. The more frequently encountered peripheral blood abnormalities of clinically ill and chronically infected SIV macaques include anemia and lymphocytopenia. The anemia, in some cases, is related to iron deficiency. Since data collection is in the early stages, it is not yet possible to meaningfully correlate bone marrow and peripheral blood abnormalities. It is intended that the results of this study will provide a framework from which the pathogenesis of these peripheral blood and bone marrow derangements in SIV infection may be understood.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Determination of the Pathogenicity of Campylobacter

AXIS I: 1a, 7a, 16c, 17

AXIS II: 66, 77

PRC UNIT: Pathobiology & Immun

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

INVES2: Richardson, Karen F.
DEGREE2: B.S.
DEPT2: Pathobiology & Immunobiology
STAFF2: O

INVES3: Paul, Katherine
DEGREE3: D.V.M.
DEPT3: Veterinary Medicine
STAFF3: O

INVES4: Orkin, Jack
DEGREE4: D.V.M.
DEPT4: Veterinary Medicine
STAFF4: C

INVES5: McClure, Harold M.
DEGREE5: D.V.M.
DEPT5: Pathobiology and Immunobiology
STAFF5: C

INVES6: Wachsmuth, I. Kay
DEGREE6: Ph.D.
DEPT6: Pathobiology and Immunobiology
STAFF6: O

INVES7: Kiehlbauch, Julie A.
DEGREE7: Ph.D.
DEPT7: Pathobiology and Immunobiology
STAFF7: O

SPECIES1: Macaca mulatta
NUM1: 4

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

ABSTRACT: The objective of this study was to determine if Campylobacter butzleri (formally designated Group 2 aerotolerent Campylobacter) causes chronic diarrhea in rhesus monkeys. Four adult rhesus monkeys were inoculated with 10^8 organisms of Campylobacter butzleri via a nasogastric tube. Post-

inoculation, the monkeys were monitored for signs of illness and feces were cultured for bacteria. Campylobacter butzleri was isolated from a fecal culture of one monkey 24 hours after challenge. However Campylobacter jejuni was isolated from fecal cultures of 3 animals 48 and 72 hours following challenge with Campylobacter butzleri. These three monkeys had temperatures up to 104 F from 1 to 4 days post-inoculation. Changes in fecal consistency did not occur and colonic biopsies showed no pathologic changes. Approximately 50% of our primate colony is infected with Campylobacter jejuni or Campylobacter coli. The high prevalence of infection with these latter species of Campylobacter may induce cross-immunity for Campylobacter butzleri. To avoid prior exposure to all Campylobacter species, an additional study has been proposed in which infant rhesus monkeys rather than adults will be challenged with Campylobacter butzleri to determine the pathogenicity of this organism for rhesus macaques.

P51RR0165-30 1/1/1990 - 12/31/1990 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 & 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: Pathobiology and Immunobiology
STAFF5: 0

SPECIES1: Macaca mulatta
NUM1: 5

SPECIES2: Macaca nemestrina
NUM2: 5

NON-HOST INSTITUTION:

ABSTRACT: Intravesical/subureteric injection of Polytef paste has been used to treat vesicoureteral reflux in over 2,000 children world wide. This treatment has been used in children in the United States 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 injected 0.4 cc (1/2 of the human dosage) of Polytef paste transurethrally into the intravesical/subureteric space of ten monkeys. Five monkeys were

sacrificed at six months, two monkeys at 24 months, and two monkeys at 32 months. The injection sites, pelvic and para-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 can be clearly imaged radiologically. CT scanning and magnetic resonance imaging at intervals up to four years have shown over a six fold increase in the average volume of the intravesical granulomas. It does appear however that their growth stabilizes 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, as stated above, at three years post-injection neovascularity has been identified within intravesical granulomas.

In order to observe the granulomatous reaction as well as the possible carcinogenic effects, one healthy monkey is being followed radiologically by both CT scanning and magnetic resonance imaging (planned follow up is 15 years). Although it is only one monkey, it will allow documentation of change in size over time as well as long term pathologic analysis.

We believe 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. To our knowledge we have the only long term living animal model for continued study.

ADDENDUM: 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 a 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 post-operative urinary continence following radical prostate surgery by increasing functional urethral length, maintaining the normal configuration of the bladder neck, and by leaving undisturbed most of the external striated urethral sphincter. It is our hope that we ill continue to study and advance this technique in primates.

ADDENDUM II: In an effort to find an alternative substance for Polytef paste, Drs. Malizia and Haber have invented and patented a genitourinary spheroidal membrane which is called the Genisphere. The Genispheres are inflatable silicone pellets which are implanted cutaneously to help increase urethral resistance. Human clinical trials are currently underway (at four major university centers) and the initial phase 1 results seem promising. The device has been submitted to the FDA for approval and the system is manufactured by Bard Corporation.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Study of Refractive Keratoplasty

AXIS I: 1a, 25b

AXIS II: 62, 86

PRC UNIT: Pathobiology and Immun

INVES1: McCarey, Bernard E.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: 0

SPECIES1: Macaca mulatta
NUM1: 11

NON-HOST INSTITUTION:

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.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

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

AXIS I: 1a, 28 (All systems)

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

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

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 34 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, 75 of the initial group of animals died. Thirty-six of the 75 (48.0%) animals which died had one or more neoplasms at the time of death. Tumors occurred in 31 of 55 (57.4%) irradiation-exposed animals which died, and in 5 of 20 (25.0%) non-exposed controls which died. Consequently, 31 of 36 (86.1%) tumor cases occurred in irradiation-exposed animals.

Tumors were diagnosed in 17 of 26 (65%) bomb-exposed animals which died; 8 of 17 (47%) 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 (13 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.

P51RR0165-30 1/1/1990 - 12/31/1990 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 & 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: Gordon, Thomas P.
DEGREE4: M.S.
DEPT4: Behavioral Neuroendocrinology
STAFF4: 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 contact or perinatally). These observations suggest the use of this colony of naturally infected mangabeys as

a model system for study of the epidemiology and pathogenesis of an HIV-like retrovirus, 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. Studies are ongoing to determine the age and circumstances surrounding seroconversion in all seronegative mangabeys in the colony. A small number of seronegative mangabeys have been placed in a social group in an attempt to develop a seronegative mangabey breeding colony.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Serological Survey of Nonhuman Primates in Kenya

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: Pathobiology and Immunobiology
STAFF3: C

INVES4: Isahakia, Mohamed
DEGREE4: Ph.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: O

SPECIES1: Cercopithecus mitis
NUM1: 120

SPECIES2: Cercopithecus aethiops
NUM2: 542

SPECIES3: Papio cynocephalus
NUM3: 373

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 (59% seropositive) and African green monkeys (51% seropositive). A somewhat lower prevalence of antibodies to STLV-1 has been observed (30% of Sykes monkeys and 43% 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. The incidence of antibodies to SIV and STLV-1 is considerably lower in baboons; 0.2% of baboons were found to have antibodies to SIV and 5% had antibodies to STLV-1.

P51RR0165-30 1/1/1990 - 12/31/1990 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 & 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: Klumpp, Sherry A.
DEGREE4: D.V.M.
DEPT4: Pathobiology and Immunobiology
STAFF4: 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 12 chronically infected macaques (61.5%) died from an AIDS-like disease between 14 and 43 months post-infection. One addition animal continues to show immunosuppression, periodic episodes of diarrhea and poor weight gain. 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. These extended observations also suggest that SIVsmm infection in macaques may not always result in fatal disease as was initially believed. Animals which survive such infections should be extensively evaluated to attempt to determine the reasons for their ability to resist fatal infection.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

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

SPECIES1: Macaca mulatta
NUM1: 30

ABSTRACT: Due to the increasing importance and magnitude of HIV infection and AIDS in the human pediatric population, these studies were initiated to evaluate the perinatal/postnatal transmission of SIVsmm in experimentally infected rhesus macaques and to determine the feasibility of using experimentally infected rhesus macaques as a model system for the study of perinatal HIV infection. In these studies, 15 timed pregnant rhesus monkeys were infected with SIVsmm during various stages of gestation, and their offspring were monitored for evidence of virus infection. Three groups of 5 animals were infected with SIVsmm during early (day 28-35), mid (day 71-78) and late (day 146-150) gestation. Offspring delivered by these experimentally infected macaques included 2 stillbirths and 13 livebirths; one liveborn infant died at 3 days of age. There was no evidence of virus infection in the stillbirths or neonatal death. The remaining infants and their mothers were evaluated within a week of parturition and at quarterly intervals thereafter by serology and virus culture of PBMC; milk samples were also collected from the mothers at each examination for virus culture. All infants were virus negative at birth; all infants in the early and mid-gestation groups and one

infant in the late gestation group had low levels of maternal antibodies to SIVsmm. These maternal antibodies disappeared prior to 3 months of age in 4 of 9 infants, and between 3 and 6 months in the other 5 infants. Three infants subsequently seroconverted and became virus positive at 9-15 months of age. Milk samples from all mothers were virus negative at parturition, but milk samples from 4 animals were virus positive at 9 and 12 months postpartum. One of the 3 infected infants has died (7 months from time infection was documented), and the other infants are showing lymphadenopathy and progressive immunosuppression. These studies have demonstrated maternal-infant transmission of SIVsmm in the experimentally infected macaque model and suggest that transmission occurred by breast-feeding.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Immunological and Molecular Studies of Primate Antigens

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

AXIS II: 1be; 39, 60, 64, 74ah, 76ab, 91

PRC UNIT: Pathobiology and Immun

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

SPECIES1: Pan troglodytes
NUM1: 3

NON-HOST INSTITUTION: Duke University Medical Center

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 non-primate 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 and prokaryotic expressed recombinant apomucin proteins. Recombinant proteins and peptides selected from the rodent studies, which have stimulated good antibodies to various regions of this large apomucin (greater than 200,000 M.W.), and which show restricted specificity for normal or malignant mucin producing cells are being evaluated for immunogenicity and specificity in chimpanzees. Other 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.

These immunological studies of human tumor antigens in higher apes are unique and important preclinical 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 counterparts so that antibodies to either carbohydrate or peptide determinant could detect the post-translational modifications of these tumor antigen molecules.

Two chimpanzees have been immunized and are currently being utilized for these studies. One animal received the recombinant human apomucin protein and the other was injected with a synthetic peptide representing the cytoplasmic tail portion of the membrane glycoprotein. The polyclonal antibody response of these animals has been characterized and the response is suitable for monoclonal antibody studies. A collaborative agreement has been reached with

Stratacyte Corporation to evaluate their new method for creating human monoclonal antibody expression libraries in their patented bacteriophage lambda expression vector. Since chimpanzee and human immunoglobulin primers should work well in PCR amplification of immunoglobulin mRNA.

In the past, we have been unable to stable IgG hybridomas that secrete the desired chimpanzee monoclonal antibodies to human tumor antigens. The new technology described above to produce combinatorial libraries expressing monoclonal antibodies should solve the problem of an appropriate fusion partner and other shortcomings of primate hybridoma technology. The results of these studies will be of paramount importance in the design of future protocols utilizing higher apes in human tumor diagnostic and therapeutic strategies.

P51RR016-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Neuropathological Study of SIV-infected Macaques

AXIS I: 1a, 7b, 21

AXIS II: 66

PRC UNIT: Pathobiology and Immunobiology

INVES1: Mirra, Suzanne S.
DEGREE1: M.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: O

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

SPECIES1: Macaca mulatta
NUM1: 7

SPECIES2: Macaca nemestrina
NUM2: 38

NON-HOST INSTITUTION: VA Medical Center (SSM)

ABSTRACT: Simian immunodeficiency virus (SIV) infection in macaque monkeys produces central nervous system (CNS) lesions sharing some histopathological features with human immunodeficiency virus (HIV) infection of the CNS in man. Retrospective autopsy studies of SIV-infected macaques have shown meningoencephalitis with multinucleated giant cells and macrophages within meninges and parenchyma of the brain. Yet little is known about the early changes in the nervous system with SIV infection. In order to investigate such changes, we examined autopsy brains and spinal cords from macaque monkeys at various intervals post-SIV inoculation. We used a mangabey-derived SIV isolate (PBj-14) passaged through a pig-tailed macaque (PBj) which usually produced a fulminant acute illness and death within one to two weeks post-intravenous inoculation. Thus far, we have examined brains from 17 pig-tailed macaques dying 8-18 days post inoculation with PBJ-14; two additional animals died at 7 and 9 months respectively. Three of the brains were obtained from macaques inoculated with blood collected at death from PBj. We are also examining brains from chronically ill animals infected with other SIV isolates. Preliminary neuropathological study reveals lesions in the brain as early as eight days post inoculation. Two main changes have been identified in animals dying soon after infection: (1) Choroid plexitis characterized by mononuclear cell inflammation, along with degeneration and necrosis of the choroid plexus epithelial cells and (2) Meningitis with mononuclear and rare syncytial cell inflammation. Parenchymal lesions within the brain were rare. In contrast, the chronically infected animals displayed a less striking choroid plexitis but a more frequently prominent parenchymal multinucleated giant cell infiltrate. Similar giant cell inflammation was also seen in animals with acute infection, however, it generally was far less apparent. We are nearing completion of our neuropathological examinations in parallel with virological, immunocytochemical, and electron microscopic studies in these

macaques. These studies may provide important information related to the pathogenesis of CNS involvement in acquired immunodeficiency syndrome (AIDS).

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Molecular Diversity of SIVsmmPBj and a Cognate Variant (SIVsmmPGg)

AXIS I: 1a, 1d, 7b

AXIS II: 31, 66

PRC UNIT: Pathobiology & Immun

INVES1: Novembre, Francis J.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: 0

INVES2: Hirsch, Vanessa M.
DEGREE2: D.V.M.
DEPT2: Pathobiology and Immunobiology
STAFF2: 0

INVES3: Johnson, Philip R.
DEGREE3: M.D.
DEPT3: Pathobiology and Immunobiology
STAFF3: 0

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

SPECIES1: Macaca nemestrina
NUM1: 11

NON-HOST INSTITUTION: Georgetown University and NIAID, NIH (FJN), Georgetown University (VMH and PRJ)

ABSTRACT: Experimental inoculation of SIVsmmPBj (PBj) into pig-tailed macaques induces an acute syndrome characterized by fulminant diarrhea, acid-base imbalance, and death. This outcome is in distinct contrast to the more protracted immunodeficiency syndrome (AIDS) caused by other SIVsmm isolates, including the PBj parental strain, SIVsmm9. Thus, by defining the viral properties responsible for the acute syndrome phenotype, we may further our understanding of viral determinants important for AIDS.

The starting materials for our studies were tissues taken from a pig-tailed macaque (PGg) that died after inoculation with PBj. Subgenomic molecular clones were derived (by PCR) from three sources of genomic DNA: (i) splenic tissue; (ii) ileum (Peyer's patch); and (iii) CEMx174 cells infected by cocultivation with a filtrate from a Peyer's patch homogenate. Analyses of nucleotide sequences from clones of LTR, envelope, and the entire 3' half of the genome revealed the following findings. By comparison with clones from SIVsmm9 and SIVsmH-4 (a molecular clone of SIVsmm that does not induce acute disease), two areas of primary structural divergence were observed: an envelope region analogous to the "peptide T" domain in HIV-1, and the U3 region in the LTR. The peptide T region in gp120 in most PGg clones contained an insertion of 6 to 9 amino acids relative to smm9 or smH-4. For the LTR, an

insertion of 22 nucleotides representing a duplication of the NF-kB enhancer element was present in 5 of 22 clones sequenced. Overall, clones derived from CEMx174 cells were generally reflective of sequences present in tissues. Comparative analyses of clones of the 5′ half of the PGg genome (gag/pol) did not reveal any distinctive findings (except the duplicated core enhancer).

To define regions of the PGg genome important for induction of acute disease, chimeric molecular clones have been constructed using the 5′ half of smH-4 and various 3′ halves of PGg. Several biologically active proviral clones have been generated, some of which contain the distinctive primary structural features described above. Virus stocks of these clones were prepared by transfection of these clones into CEMx174 cells. Four of these viruses were used for animal inoculation to test for induction of the acute death syndrome. None of the clones tested induced the rapidly fatal disease in inoculated pig-tailed macaques. Virus has been recovered from all macaques and they are being monitored for development of disease.

We have now gone back and are trying to isolate new 5′ and 3′ halves from the biological clone of PBj (bcl 3). Using PCR, we have again generated 5′ and 3′ halves for cloning. Upon sequence analysis of selected regions, it has been determined that they are closely related to the sequence of the molecular clone of PBj that induces the rapidly fatal disease. We will continue on this course to try and determine the viral sequences responsible for the acute phenotype.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Molecular Cloning and Analysis of SIV from Stumptailed Macaques

AXIS I: 1a, 1d, 7b

AXIS II: 31, 66

PRC UNIT: Pathobiology & Immun

INVES1: Novembre, Francis J.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: 0

INVES2: Johnson, Philip R.
DEGREE2: M.D.
DEPT2: Pathobiology and Immunobiology
STAFF2: 0

INVES3: Hirsch, Vanessa M.
DEGREE3: D.V.M.
DEPT3: Pathobiology and Immunobiology
STAFF3: 0

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

SPECIES1: Macaca arctoides
NUM1: I

SPECIES2: Macaca mulatta
NUM2: 10

SPECIES3: Macaca nemestrina
NUM3: 10

NON-HOST INSTITUTION: Georgetown University and NIAID, NIH (FJN), Georgetown University (VMH and PRJ)

ABSTRACT: The stumptail lentivirus (SIVstm), isolated at the Yerkes Regional Primate Research Center, was passaged in CEMx174 cells to produce virus stocks (SIVstm/174). Genomic DNA prepared from these infected cells was used in PCR amplification of SIVstm-specific sequences. Both 5' and 3' halves (centered around the conserved Bcl I restriction site) were cloned by PCR. The 5' and 3' halves were joined at the Bcl I site to construct full-length viral clones. One of these clones (5'37-3'16) was sequenced in its entirety. Biological activity of the full-length clones was tested by transfection into CEMx174 cells. A total of 9 full-length clones were prepared this way. Viral stocks were prepared from the filtered supernatants of transfected CEMx174 cells and were used for animal inoculations.

For animal inoculations, both pig-tailed and rhesus macaques were used. Four animals of each species were inoculated with the uncloned virus stock (SIVstm/174). Two biologically active clones of SIVstm were also used for

animal studies. The clones were termed: 1) 5'37-3'16 and 2) 5'29-3'11. Virus stocks of these clones prepared as described above were used to inoculate two rhesus macaques and two pigatiled macaques each. Two pigtailed macaques and two rhesus macaques served as uninoculated controls. A summary of isolation data for these animals is shown below.

SIVstm Study - Virus Recovery

Inoculation Date: November 15, 1990

		Weeks after inoculation		
Monkey	Inoculum	3 wks	8 wks	13 wks
PDp	SIVstm/174	+	+	+
PHo	SIVstm/174	+	+	+
PPn	SIVstm/174	+	+	+
PUn	--	-	-	
PMn	SIVstm/174	+	NA*	
RDi2	SIVstm/174	+	NA	
RKd2	SIVstm/174	+	+	+
RUi2	SIVstm/174	+	NA	+
RVz1	--	-	-	
RBi2	SIVstm/174	+	NA	+

Inoculation Date: November 16, 1990

		Weeks after inoculation		
Monkey	Inoculum	3 wks	8 wks	12 wks
PGo	SIVstm 5'37,3'16	-	-	
PKn	SIVstm 5'37,3'16	+	-	
PZn	SIVstm 5'29,3'11	+	+	+
PLn	SIVstm 5'29,3'11	+	+	
PAo	--	-	-	
RUc2	SIVstm 5'37,3'16	+	+	
RPi2	SIVstm 5'37,3'16	+	+	
RKg2	SIVstm 5'29,3'11	+	+	+
RVi2	SIVstm 5'29,3'11	+	+	+
RZa2	--	-	-	

*NA - Cultures became contaminated

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Identification of SIV Antigens that Induce T Cell Immunity in SIV-infected Nonhuman Primates.

AXIS I: 1a, 1d, 2, 7b, 9, 19

AXIS II: 31, 64, 66, 83

PRC UNIT: Pathobiology & Immun

INVES1: Powell, Jonathan D.
DEGREE1: B.S.
DEPT1: Pathobiology & Immunobiology
STAFF1: O

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

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

INVES4: Vuchetich, Matthew
DEGREE4: M.S.
DEPT4: Pathobiology & Immunobiology
STAFF4: O

INVES5: McClure, Harold M.
DEGREE5: D.V.M.
DEPT5: Pathobiology & Immunobiology
STAFF5: C

INVES6: Sell, Kenneth W.
DEGREE6: M.D., Ph.D.
DEPT6: Pathobiology & Immunobiology
STAFF6: O

INVES7: Ansari, Aftab A.
DEGREE7: Ph.D.
DEPT7: Pathobiology & Immunobiology
STAFF6: C

SPECIES1: Macaca mulatta
NUM1: 20

SPECIES2: Cercocebus atys
NUM2: 20

NON-HOST INSTITUTION:

ABSTRACT: Whereas considerable knowledge has been gained concerning the virus-specific humoral response in human HIV-1 infection and nonhuman primate SIV infection, relatively little is known concerning the virus-specific cellular immune response. It is generally known that whereas humoral immune responses protect against initial exposure of individuals to virus infections, it is the cellular immune response that leads to eventual eradication of virus infections by elimination of virus-infected cells. This is particularly important for viruses that replicate intracellularly and spread infection by cell to cell transmission. Our laboratory has previously defined an *in vitro* assay to measure the presence of SIV-specific T cell immunity in nonhuman primates naturally and experimentally infected with SIV. This assay consisted of co-cultures of highly purified T cells with autologous monocytes that had been pulsed with killed SIV preparations prior to co-culture. The data from this study clearly demonstrated the presence of virus-specific T cell immune response in both experimentally infected macaques and naturally infected mangabeys; however, the specific proteins and peptides of the SIV recognized by T cells from these SIV-infected mangabeys that remain clinically asymptomatic and from macaques that develop disease and eventually die are not known. It was reasoned that delineation of the specific proteins and peptides of the SIV recognized by T cells from these two species may shed light on the differential susceptibility of these two species to virus-induced pathogenesis. Toward this goal, our laboratory has set up a unique cellular Western blot assay. The SIVsmm virus preparation was subjected to electrophoretic separation and then transferred to nitrocellulose filters as routinely performed for Western blot assays. Two strips at each end of the blot were stained with a protein dye to mark the specific region of migration of individual separated viral proteins. Horizontal bands corresponding to the visualized protein band were then cut utilizing aseptic techniques. Small pieces of these individual bands were than incubated with monocytes from naturally infected mangabeys and experimentally infected macaques for 3 hours, followed by the addition of enriched population of autologous T cells. The proliferation of these T cells was measured by routine uptake of methyl-^{3}H-thymidine. Results demonstrate that marked proliferation occurred with proteins of 40, 25, and 15 kD relative molecular weight. No major differences in the response of T cells to individual bands of SIV were noted in cells from macaques or mangabeys. Further studies are in progress to delineate specific epitopes of each of these bands that are recognized by T cells form these two species.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: A Semi-Automated Computer Assisted Method for Measuring Peri-Implant Bone Support

AXIS I: 1a, 3, 7, 22

AXIS II: 42, 52, 63, 70, 80, 86

PRC UNIT: Pathobiology & Immun

INVES1: Reddy, Michael
DEGREE1: D.D.S., Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: 0

INVES2: Mayfield-Donohoo, M.T.
DEGREE2:
DEPT2: Pathobiology and Immunobiology
STAFF1: 0

INVES3: Jeffcoat, Marjorie K.
DEGREE3: D.M.D.
DEPT3: Pathobiology and Immunobiology
STAFF1: 0

NON-HOST INSTITUTION: University of Alabama at Birmingham (MR, MT-D, MKJ)

ABSTRACT: The purpose of this study was to develop a repeatable method for measurement of bone support about root form and blade implants. Ten phantoms were fabricated to simulate implants with osseous defects. Radiographs were taken in triplicate and digitized. Specialized software was written which placed a grid of known dimensions over the implant so that the top and the bottom of the grid were at the neck and the base of the implant, respectively. The investigators selected the edge of the bone at each point where the grid intersected the implant and the software automatically detected the implant edge. Bone loss was calculated in mm relative to the implant: (1) neck (2) side and (3) base. The software also outlined and displayed the defect on the computer monitor. Measurements were performed 5 times and the standard blades and root forms was .09±.07 mm and .03±.02 mm.,,respectively. There was no significant difference in the ability to measure bone loss in any direction or in the blade versus the root form (p>.17,NS). These results indicate that this semiautomated computer assisted method for measuring bone loss around implants is repeatable and may be of value for clinical trials using either root form or blade implants.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Isolation of Aerotolerant Campylobacter from Nonhuman Primates with Diarrheal Illness

AXIS I: 17a, 16c

AXIS II: 66

PRC UNIT: Pathobiology & Immun

INVES1: Richardson, Karen J.
DEGREE1: B.S.
DEPT1: Pathobiology and Immunobiology
STAFF1: O

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

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

INVES4: Wachsmuth, I.K.
DEGREE4: Ph.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: O

INVES5: Kielbauch, J.A.
DEGREE5: Ph.D.
DEPT5: Pathobiology and Immunobiology
STAFF5: O

SPECIES1: Macaca mulatta
NUM1: 285

SPECIES2: Macaca nemestrina
NUM2: 52

SPECIES3: Macaca arctoides
NUM3: 22

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

ABSTRACT: Campylobacter species are the most frequently isolated enteric pathogens from nonhuman primates housed at the Yerkes Primate Research Center. Following identification of a Group 2 aerotolerant Campylobacter (Gr2AC) from a rhesus monkey, we cultured 308 routine enteric specimens for Campylobacter using Campy-CVA plates incubated at 35°C. Campylobacter species were isolated from 145 specimen; 12 aerotolerant Campylobacter isolates from 10 macaques (7 rhesus, 1 cynomolgus, 1 stumptail, and 1 pigtail) with chronic diarrhea were isolated only on Campy-CVA. Histologic evaluation of specimens from 7 animals revealed mild to moderately severe chronic active colitis.

Phenotypic characterization of the 12 macaque isolates indicated they belonged to Gr2AC and this was confirmed by DNA hybridization. Ribotyping revealed 8 different strains among the 12 isolates. Subsequent isolates from 2 animal were the same strain. These data indicate that nonhuman primates may offer an opportunity to study this newly-recognized Campylobacter species, which has also been isolated from humans with a history of persistent diarrhea.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: National Cooperative Drug Discovery Groups for the Treatment of AIDS (EGY Group)

AXIS I: 1a, 7b

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

PRC UNIT: Pathobiology & Immun

INVES1: Schinazi, Raymond F.
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: O

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

SPECIES1: Macaca mulatta
NUM1: 25

NON-HOST INSTITUTION: Veterans Affairs Medical Center (RFS)

ABSTRACT: The objective of our study was to determine if four 2', 3'-dideoxynucleosides could prevent SIV infection in rhesus monkeys. Five groups of five animals were treated subcutaneously with phosphate buffered saline, 3'-azido-3'-deoxythymidine (AZT), 3'-azido-2', 3'-dideoxyuridine (AzddU or CS-87), 2',3'-didehydro-3'-deoxythymidine (D4T), and 3'-fluoro-3'-deoxythymidine (FDT, FddT, FLT). The drugs were administered every eight hours for one day prior to inoculation with 100 monkey ID_{50} of SIVsmm, and for 14 days thereafter at a dose of about 100 mg/kg per day. Pharmacokinetic studies had indicated that drug levels could be achieved with these drugs well above the median effective concentration against SIV in culture. To maximize the possibility of preventing infection, the animals were also treated intravenously just prior to virus inoculation. Animals were examined, weighed, and blood was collected every other week for 8 weeks. Virus antibody titer, CBC, chemistry, CD4/CD8 ratios, and virus culture was determined. All the animals were seronegative at 2 weeks after virus inoculation, but at 8 weeks all but one animal in the FDT group had seroconverted. Whereas, 78% of the animals tested were virus culture positive 6 months after virus inoculation, this animal was antibody and virus negative. The animals tolerated AZT, AzddU, and D4T well. FDT treatment resulted in diarrhea and severe bone marrow toxicity that was reversible. FDT treatment produced a reversible depression of RBC, SGOT, Hgb, MCV, and platelets. The results suggest that none of the nucleosides were effective in preventing infection in rhesus macaques. These studies may have implications for the drug prophylaxis of health care workers accidentally exposed to blood and fluids from individuals infected with HIV.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Immunogenicity of Human Melanoma Antigens in Nonhuman Primates and Production of Monoclonal Antibodies to Human Melanoma TAA.

AXIS I: 1a, 1d

AXIS II: 64, 76b

PRC UNIT: Pathobiology & Immun

INVES1: Seigler, Hilliard F.
DEGREE1: M.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: C

SPECIES1: Pan troglodytes
NUM1: 1

NON-HOST INSTITUTION: Duke University Medical Center

ABSTRACT: The objectives of this study are: (1) to determine the immunogenicity of human melanoma tumor associated antigens (TAA) in nonhuman primates and to examine the immunological benefit of antigen administration in combination with immune response modifiers such as IL-1, IL-2, interferon alpha, and others 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. Lymph node cells from a chimpanzee immunized with GD3 were immortalized by EBV transformation, and fused with SP2\0 murine myeloma. Four weeks after fusion, four hybrids which produced melanoma-reactive Igs were cloned twice and expanded. Characterization studies show 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. We are now beginning to produce the purified high molecular weight human melanoma TAA and will begin to examine the role for immune response modifiers IL-1, IL-2 and IL-4 in modulating response of nonhuman primates to this purified melanoma TAA. The results of these investigations will help to design strategies for use of specific active immunization with immune growth factors in human cancer patients.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Toxicity of Anti-AIDS Drugs on the Bone Marrow

AXIS I: 1a, 17

AXIS II: 31, 50, 66, 74c

PRC UNIT: Pathobiology & Immun

INVES1: Sommadossi, Jean-Pierre
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
STAFF1: 0

INVES2: McClure, Harold M.
DEGREE2: D.V.M.
DEPT2: Pathobiology and 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 modulating 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. Pharmacokinetics of anti-HIV drugs and modulation will be studied. Efficacy of selected drug combinations (anti-HIV and modulating agent) will be assessed in SIV-infected rhesus monkeys.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Pharmacokinetics of 3′-Azido-3′-Deoxythymidine and Its Catabolites and Interactions with Probenecid in Rhesus Monkeys

AXIS I: 1a, 2

AXIS II: 31, 50b, 66

PRC UNIT: Pathobiology & Immuno

INVES1: Sommadossi, Jean-Pierre
DEGREE1: Ph.D.
DEPT1: Pathobiology and Immunobiology
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

INVES4: Schinazi, Raymond F.
DEGREE4: Ph.D.
DEPT4: Pathobiology and Immunobiology
STAFF4: O

SPECIES1: Macaca mulatta
NUM1: 5

NON-HOST INSTITUTION: University of Alabama at Birmingham (J-PS), Veterans Affairs Medical Center (RFS)

ABSTRACT: The pharmacokinetics and metabolism of 3′-azido-3′-deoxythymidine (AZT) were investigated in rhesus monkeys after subcutaneous administration of 33.3 mg of AZT per kg of body weight alone or in the presence of 100 mg of probenecid per kg. In addition to unchanged drug, two catabolites, 5′-O-glucuronide (GAZT) and 3′-amino-3′/-deoxythymidine (AMT), were detected in plasma within 30 min. GAZT exhibited a kinetic profile similar to that of AZT, with elimination half-life of approximately 1 h, while AMT was more variable, with an apparent half-life of 1.6±1.5h. Approximately 90% of the toal administered dose was recovered in urine within 24 h as AZT, GAZT, AMT, and the 5′-O-glucuronide of AMT. AZT and AMT demonstrated similar cerebrospnial fluid (CSF) penetration 1 h after AZT treatment, while GAZT poorly crossed the blood-brain barrier. Concomitant administration of probenecid greatly altered the pharmacokinetics of AZT, GAZT, and AMT, resulting in prolongation of their apparent elimination half-lives, increased plasma concentrations, and marked reduction in renal clearances. In addition, the CSF/plasma concentration ratios for AZT and its catabolites were greatly increased, suggesting that probenecid inhibits efflux of AZT and its catabolites from CSF to plasma. The substantial levels of AMT in plasma suggest that this catabolite affects the pharmacodynamic properties of AZT in relation to its activity against human

immunodeficiency virus replication and cytotoxicity to host cells. Enhanced AMT levels in plasma in the presence of probenecid may decrease the therapeutic efficacy of the AZT-probenecid combination.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Laser Adjustable Synthetic Epikeratoplasty

AXIS I: 1a, 2, 3, 9, 25b

AXIS II: 48, 52, 63b, 70, 77, 86

PRC UNIT: Pathobiology & Immun

INVES1: Thompson, Keith P.
DEGREE1: M.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: 0

INVES2: Hanna, Khalil D.
DEGREE2: M.D.
DEPT2: Pathobiology & Immunobiology
STAFF2: 0

INVES3: Waring, George O.
DEGREE3: M.D.
DEPT3: Pathobiology & Immunobiology
STAFF3: 0

INVES4: Gailitis, Raymond P.
DEGREE4: M.D.
DEPT4: Pathobiology & Immunobiology
STAFF4: 0

INVES5: Ren, Qiushi
DEGREE5: Ph.D.
DEPT5: Pathobiology & Immunobiology
STAFF5: 0

INVES6: Maloney, Robert K.
DEGREE6: M.D.
DEPT6: Pathobiology & Immunobiology
STAFF6: 0

SPECIES1: Macaca mulatta
NUM1: 13

ABSTRACT: Refractive errors such as myopia, hyperopia, and astigmatism - conditions that require the use of corrective appliances such as glasses or contact lenses - affect over 140,000,000 Americans. Infantile and early childhood loss of a lens or removal of a cataract creates aphakic conditions with reduction of refractive power that threaten total vision loss. This investigation has studied the feasibility of permanently correcting optical refractive errors of the eye by attaching an optically clear, stable, predictable, adjustable, and removable biocompatible synthetic lenticule to the anterior cornea. Once a lenticule is attached to the cornea it is then precisely measured and reshaped with a prototype experimental imaging-laser system developed by this research team. The objectives of this study have been to evaluate the biocompatibility (i.e., ocular tolerance, lack of side effects, rate and stability of corneal epithelialization, and specific

biocompatibility with Bowman's layer of the cornea) of putative biomaterials (used for synthetic epikeratoplasty) in a non-human primate model. Following use of a pocket epikeratoplasty surgical technique the stable attachment of a lenticule in one monkey's eye has been followed since April, 1989. Rhesus monkeys (Macaca mulatta) have provided an in-vivo model with a Bowman's layer comparable to that found in human corneas. Only successful non-invasive synthetic epikeratoplasty attachment onto an in-vivo, non-human primate's Bowman's layer will make possible the transfer of this technology to techniques for treating refractive errors in human patients. Infants, children, and adults may then benefit from the results of this research. Remaining goals for in-vivo animal studies are the refinement of non-invasive attachment techniques (several are possible, each avoiding an incision into the cornea) and development of an associated biocompatible synthetic epikeratoplasty lenticule material necessary for non-invasive attachment.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: PCR-Aided Diagnosis of Occult SIV Infection in Nonhuman Primates.

AXIS I: 1a, 1d, 2, 7b, 9, 19.

AXIS II: 31, 64, 66, 83

PRC UNIT: Pathobiology & Immun

INVES1: Villinger, Francois J.
DEGREE1: D.V.M.
DEPT1: Pathobiology & Immunobiology
STAFF1: O

INVES2: Ansari, Aftab A.
DEGREE2: Ph.D.
DEPT2: Pathobiology & Immunobiology
STAFF2: C

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

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

INVES5: Jehuda-Cohen, Tamar
DEGREE5: Ph.D.
DEPT5: Pathobiology and Immunobiology
STAFF5: O

INVES6: De, Barun
DEGREE6: Ph.D.
DEPT6: Pathobiology and Immunobiology
STAFF6: O

SPECIES1: Cercocebus atys
NUM1: 40

SPECIES2: Macaca mulatta
NUM2: 20

NON-HOST INSTITUTION: Centers for Disease Control (B.D.)

ABSTRACT: The primary objective of this project was to investigate the presence of SIV infection in sooty mangabeys which by laboratory tests were shown previously to be seronegative, yet peripheral blood mononuclear cells (PBMC) from these animals appear to demonstrate immune function which could only be due to exposure to SIV infection; thus, PBMC from seronegative mangabeys, when cultured in vitro with polyclonal B cell mitogen (pokeweed mitogen), resulted in the secretion of antibodies in the supernatant fluid

that reacted with SIV antigen by ELISA and Western blot assays. In addition, $CD8^+$ T cells from these seronegative mangabeys markedly inhibited the replication of exogenously added SIVsmm virus to autologous $CD4^+$ cells *in vitro*. Both of these immune functions occur only in SIV-infected mangabeys and macaques. It was reasoned that such findings could be attributed to occult SIV infection in the seronegative mangabeys. To more definitively demonstrate the presence of SIV infection, the highly sensitive polymerase chain reaction (PCR) assay was set up. A series of primer pairs and probes based on the conserved sequence of the *gag* region of SIV and the previously published *gag* sequence of SIV/smH4 were utilized. Data from these studies showed that DNA samples from rhesus macaques experimentally infected with SIVsmm-9 and all sooty mangabeys tested (N = 42), both seropositive and seronegative, showed the presence of SIV. Of interest was the finding that the *gag* sequence present in naturally infected seropositive and seronegative mangabeys was distinct from that seen in experimentally infected macaques. There are three conclusions from this study. First, these data demonstrate that all sooty mangabeys in our colony are, in fact, infected with SIV and that SIV is most likely transmitted in this colony by other than sexual means. Second, the differences in the *gag* sequence of SIV in mangabeys and that in macaques experimentally infected with SIVsmm-9 indicate that the latter virus isolate is distinct and most likely a tissue culture variant of the SIV present in mangabeys. Third, we can now distinguish the predominant SIV strain of mangabeys from the disease-inducing SIVsmm-9 variant, using PCR techniques.

P51RR0165-30 1/1/1990 - 12/31/1990 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: Pathobiology and Immunobiology
STAFF1: 0

INVES2: Hanna, Khalil
DEGREE2: M.D.
DEPT2: Pathobiology and Immunobiology
STAFF2:

SPECIES1: Macaca mulatta
NUM1: 15

NON-HOST INSTITUTION:

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.

P51RR0165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Pre-chemotherapy Marrow Priming With Recombinant CSF's

AXIS I: Ia, Id, 2, 17

AXIS II: 50a, 76b, 88

PRC UNIT: Pathobiology & Immun

INVES1: Winton, Elliott F.
DEGREE1: M.D.
DEPT1: Pathobiology & Immunobiology
STAFF1: 0

SPECIES1: Maccaca mulatta
NUM1: 10

ABSTRACT: We have developed methodology for in vitro clonogenic assays and FACS analysis to be used in experiments in which rHuIL-3, rHuGM-CSF, or rHuIL-6 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 progenitors cells, and the effect on megakaryocyte ploidy were quantified. A marked effect on megakaryocyte ploidy was observed within 48 hours of rHuGM-CSF and rHuIL-6 administration. rHuIL-6 also leads to significant increases in circulating platelets. 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. Such use could involve priming the marrow donor prior to collection of marrow or blood stem cells with HGF's to augment the numbers of primitive hematopoietic cells collected, or administrating HGF's post chemotherapy or marrow transplant to accelerate regeneration.

DIVISION OF REPRODUCTIVE BIOLOGY

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P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: A High Resolution SE-I SEM Assessment of Diimidoester Fixed Chimpanzee Sperm

AXIS 1: 1a, 15, 23

AXIS 2: 74e

PRC UNIT: Reproductive Biology

INVES1: Apkarian, Robert P.
DEGREE1: MA
DEPT1: SEM Facility/Reproductive Biology
STAFF1: O

INVES2: Gould, Kenneth G.
DEGREE2: B. Vet. Med. Ph.D.
DEPT2: Reproductive Biology
STAFF2: C

SPECIES1: Pan troglodytes
NUM1: 3

ABSTRACT: Diimidoester (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 limited. 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).

The apparent value of this fixation methodology is the maintenance of immunological activity of surface components. We have demonstrated that polyclonal antibodies directed to sperm surface components which were conjugated to 10-18nm Gold particles can be imaged on the sperm surface of specimens prepared after fixation with diimidoester, critical point drying and chromium coating with continuous 2nm Cr film in a Denton DV602 turbo-pumped system. This methodology will be utilized to identify the localization and movement of sperm surface components associated with altered fertilizing capacity of primate sperm.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Basal Cortisol Levels in Young Chimpanzee Saliva.

AXIS I: 1a

AXIS II: 36, 41

PRC UNIT: Reproductive Biology

INVES1: Bard, Kim A.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: 0

SPECIES 1: Pan troglodytes
NUM1: 8

ABSTRACT: This study was designed to obtain a method for collecting baseline samples of salivary cortisol in young nursery-reared chimpanzees. During the summer of 1990, 4 different methods of collecting saliva were attempted; pipet/cotton ball, syringe, absorbent roll, and continuous suction. The first 3 methods produced collections of small amounts of saliva (50 microliters) over long durations (15 minutes). Continuous suction by means of vacuum pump aspirator provided the dual benefits of large collections in small amounts of time. Large amounts of saliva (200-300 microliters) are necessary to assay cortisol and short collection times are required (less than 5 minutes) due to the responsiveness of the adrenocortical system which results in fluctuation of cortisol levels. Baseline cortisol values were obtained on 8 individuals ranging in age from 3 months to 11 months. These levels are similar to the levels found in human infants.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Development of Self-Recognition 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: Anderson, James R.
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF2: 0

SPECIES 1: Pan troglodytes
NUM1: 5

Non-Host Institution: Laboratoire de Psychophysiologie, Université Louis Pasteur (JRA)

ABSTRACT: The goals of this study are to determine the age at which chimpanzees recognize their mirror image and to document mirror-directed behavior that many develop concurrently with this ability. This is research in progress. Five additional chimpanzees have been tested with the Gallup self-recognition paradigm (i.e., a colored mark applied to the forehead which is touched while looking in the mirror) in 1990. The criterion for self-recognition was found in all five of the subjects at the following ages: 5.1 years, 4.8 years, and three individuals of 3.8 years. Further data collections are expected to confirm these results. The results of the 9 subjects tested to date indicate that self-recognition in chimpanzees appears to be consolidated sometime after the age of 2 years. This is comparable to the age of onset of self-recognition in human infants.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Perception of Human Faces and Emotions by Young Chimpanzees (Pan troglodytes)

AXIS I: 1a

AXIS II: 36, 41

PRC UNIT: Reproductive Biology

INVES1: Bard, Kim A.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: 0

INVES2: Hopkins, W. D.
DEGREE2: Ph.D.
DEPT2: Behavioral Biology
STAFF2: 0

SPECIES I: Pan troglodytes
NUM1: 9

Non-Host Institution:

ABSTRACT: The aim of this study is to determine whether or not infant chimpanzees are asymmetric in processing emotion. The chimpanzee infants, held in the arms of an adult human, are presented with pictures of smiling and non-smiling human faces. Preferential looking techniques are used to detect the duration of gaze on each picture. This is research in progress. Nine infant chimpanzees have been tested to date. After the first round of 10 faces it appears that young chimpanzees can discriminate a smiling human face and a non-smiling human face. The analysis is in progress.

This study might show that hemispheric lateralization occurs in nonhuman primates. Thus, it might be concluded that lateralization of emotion occurs independent of lateralization of language. As more subjects are tested comparisons can be made between different aged individuals and the development of lateralization can be determined.

P5IRR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Cognitive Development and Temperament in Young Nursery-Reared Chimpanzees.

AXIS I: 1a, 21, 25

AXIS II: 36, 41, 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: 12

Non-Host Institution: NICHD, Laboratory of Comparative Ethology (SJS).

ABSTRACT: Each nursery-reared chimpanzee infant was tested approximately once a month, from the age of 3 months to 12 months, using the Bayley Scales of Infant Development. A total of 72 tests were conducted on 12 infants, 8 infants began testing during this period and 4 infants were given continuing assessments. This human-based test is used to assess temperamental responsiveness and manipulative abilities. This research is ongoing. Two scores were obtained from each chimpanzee's test: a human age equivalent and a mental development index (MDI). Chimpanzees, 3-7 months of age, performed at higher cognitive levels than humans at the same age, whereas the same chimpanzees at 8-12 months of age performed at lower levels than humans. The value of this study is to provide species comparisons of cognitive competence, to provide data on individual difference in emotional responsivity, and to provide a normative database to evaluate the effectiveness of behavioral interventions to be performed in the future.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Attachment in Nursery-Reared Chimpanzees: Ainsworth Strange Situation.

AXIS I: 1a

AXIS II: 36, 60, 71

PRC UNIT: Reproductive Biology

INVES1: Bard, Kim A.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: 0

INVES2: Platzman, Kathleen A.
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF2: 0

INVES3: Suomi, Stephen J.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: 0

INVES4: Swenson, R. Brent
DEGREE4: D.V.M.
DEPT4: Veterinary Medicine
STAFF4: C

SPECIES 1: Pan troglodytes
NUM1: 16

Non-Host Institution: NICHD, Laboratory of Comparative Ethology (SJS).

ABSTRACT: The quality of attachment in six additional nursery-reared chimpanzees was assessed using the Ainsworth Strange Situation. This research is ongoing. Each individual was tested with his or her favorite caregiver as the 'mother', and a completely unknown female as the stranger. The distribution of major attachment classifications in these and previously tested nursery-reared chimpanzees was similar to that found in human infants by Ainsworth. Specifically, 12 chimpanzees were classified as securely attached to their favorite caregiver, 4 were classified with insecure attachments. Attachment mechanisms in chimpanzee infants parallel those in human infants. Research from other cultures suggest that minimal exposure to novelty, frequency of separations from caregivers, and multiple attachments may all influence attachment at 1 year.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Neurobehavioral Responsivity of Neonatal Nursery-Reared Chimpanzees

AXIS I: 1a, 21, 25

AXIS II: 36, 60, 71

PRC UNIT: Reproductive Biology

INVES1: Bard, Kim A.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: 0

INVES2: Platzman, Kathleen A.
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF2: 0

INVES3: Suomi, Stephen J.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: 0

INVES4: Swenson, R. Brent
DEGREE4: D.V.M.
DEPT4: Veterinary Medicine
STAFF4: C

INVES5: Lester, Barry M.
DEGREE5: Ph.D.
DEPT5: Reproductive Biology
STAFF5: 0

SPECIES 1: Pan troglodytes
NUM1: 9

Non-Host Institution: NICHD, Laboratory of Comparative Ethology (SJS), Bradley Hospital and Brown University (BML).

ABSTRACT: From January 1990 through December 31 1990, 9 chimpanzee infants were placed in the nursery due to inadequate maternal care. The neurobehavioral integrity of these infants was assessed with the Neonatal Behavioral Assessment Scale (NBAS) (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.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Behavioral States of Mother-Reared Chimpanzees.

AXIS I: 1a, 21, 25

AXIS II: 36, 60, 65, 71

PRC UNIT: Reproductive Biology

INVES1: Bard, Kim A.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: 0

INVES2: Swenson, R. Brent
DEGREE2: D.V.M.
DEPT2: Veterinary Medicine
STAFF2: C

INVES3: Platzman, Kathleen A.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: 0

SPECIES 1: Pan troglodytes
NUM1: 5

ABSTRACT: The behavioral states of sleep and waking (Wolff, 1987) are being coded from videotapes of 5 additional infants. This is research in progress. In the first week of life, chimpanzee neonates spend approximately 25% of an hour's observation in a quiet alert state, allowing for visual and auditory orientation to their mother and other environmental stimuli. Neonatal chimpanzees sleep approximately 65% of the time. Crying and fussy states do not occur frequently or last very long in mother-reared chimpanzee neonates. An active awake state, which is when the infant is not fussy but exhibiting motor activity, such as mountaineering on mother, occurred approximately 5% of an hour's observation. Nursing bouts occurred once or twice within each hour of observation and lasted 10 minutes. Future analyses will compare the distribution of behavioral states in mother-reared chimpanzees with nursery-reared chimpanzees and will compare neonatal chimpanzees to neonatal humans.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Foundations of Parenting in Chimpanzees: Intuitive Parenting.

AXIS I: 1a

AXIS II: 36, 60, 71

PRC UNIT: Reproductive Biology

INVES1: Bard, Kim A.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: O

INVES2: Papousek, Hanus
DEGREE2: M.D.
DEPT2: Reproductive Biology
STAFF2: O

INVES3: Suomi, Stephen J.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: O

SPECIES 1: Pan troglodytes
NUM1: 2

Non-Host Institution: NICHD, Laboratory of Comparative Ethology (SJS), Center for Social Pediatrics, Munich FRG (HP).

ABSTRACT: In order to investigate the foundations of intuitive parenting, 2 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. However, the amount of maternal attention to the baby is quantitatively different from that found in humans. These data will be used to determine the frequency and types of behavioral interaction to be used in future behavioral interventions for nursery-reared chimpanzees.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Social Learning of Tool Use in Chimpanzees.

AXIS I: 1a

AXIS II: 36, 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: Visalberghi, Elisabetta
DEGREE3: Ph.D.
DEPT3: Behavioral Biology
STAFF3: 0

INVES4: Fragaszy, Dorothy
DEGREE4: Ph.D.
DEPT4: Behavioral Biology
STAFF4: 0

SPECIES 1: Pan troglodytes
NUM1: 3

Non-Host Institution: CNR, Instituto di Psicologia (EV).

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; and 3) 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. These three additional chimpanzees were tested from 1/90 to 12/90. Analyses are in progress. Preliminary results indicate that young chimpanzees can learn to solve the tool task but even 3.5 year olds make errors given complex tools. Similar results have been found for 2-year-old human infants.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Steroidogenesis by the Postpartum Ovary

AXIS 1: 1d, 15, 23

AXIS 2: 60, 74

PRC UNIT: Reproductive Biology

INVES1: Bruot, Brent C.
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF1: O

INVES2: Wilson, Mark
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF2: C

SPECIES1: Macaca mulatta
NUM1: 7

NON-HOST INSTITUTION: Kent State University (BCB)

ABSTRACT: The purpose of this study is to investigate the steroidogenic activity of the corpus luteum and granulosa cells from animals within the first week after parturition. Ovaries from primiparous and multiparous rhesus monkeys were removed and the corpus luteum was enzymatically dispersed in collagenase. The luteal cells were incubated for 4, 8 and 24 hours in medium 199 at 37 C in a humidified atmosphere of 95% air - 5% CO_2. Basal, hCG and dibutyryl cAMP stimulated progesterone production were determined. Progesterone production increased significantly with time. Human chorionic gonadotropin and dibutyryl cAMP had no effect on progesterone secretion. There were no differences in progesterone production by luteal cells from multiparous and primiparous animals. These results suggests that luteal cells obtained from rhesus monkey ovaries up to one week postpartum were able to synthesize progesterone but were refractory to hCG and dbcAMP stimulation. Granulosa cells were cultured for up to 5 days with testosterone, FSH and/or IGF-1. Preliminary results suggest that the granulosa cells were not steroidogenically active. Furthermore, the granulosa cells failed to take up ^3H-CH_3-thymidine. These results suggest that the granulosa cells from ovaries one week after parturition were not actively dividing. Collectively, these results indicate that only the corpus luteum in the postpartum rhesus monkey ovary was steroidogenically active. Furthermore, the ovaries were refractory to tropic hormone and growth factor stimulation.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Survival International - Conservation Efforts in the New World.

AXIS I: 1a, 23

AXIS II: 34, 78

PRC UNIT: Reproductive Biology

INVES1: Dahl, Jeremy F.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: 0

SPECIES 1: Alouatta pigra
NUM1: Feral population

SPECIES 2: Ateles geoffroyi
NUM2: Feral population

ABSTRACT: In order to advance the conservation of nonhuman primates and their habitats in Central America (an area with one of the highest rates of deforestation in the world), a training and survey program was carried out in the Cayo District of Belize. During a 6 week period, a team of workers achieved a number of objectives: 1) Training and experience in forest survey and evaluation techniques was provided to Forest Officers of the Belizean Forest Service; 2) the nonhuman primate populations of two species, Alouatta pigra luctuosa and Ateles geoffroyi yucatanensis, were surveyed in a 25 sq. km. area of broad-leaf forest forming the western border of the Mountain Pine Ridge Forest Reserve; 3) an assessment was made of the area with respect to it's potential as a Wildlife Sanctuary; 4) observations were made on A. p. luctuosa with respect to daily activity patterns, reproduction, and fecal samples were collected and stored for analyses by RIA for steroid hormones. In addition to the two ceboid species, the area was found to have a varied and diverse wildlife indicative of a marginally disturbed rain forest fauna that included Tapirus bairdii, Felis onca, Dicotyles tajacu (Mammalia) and avian predators Buteogallus sp. and Leucopteris albicollis. Unfortunately, evidence was obtained that the region had been recently infiltrated by humans engaged in illegal activities that were damaging the habitat and archaeological sites. This emphasized to the local authorities the need for more extensive foot patrols, and field equipment was made available so that Forest Guards (trained in this program) could carry out such patrols.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Post Natal Growth in the Vervet Monkey

AXIS I: 1a, 23, 26

AXIS II: 60

PRC UNIT: Reproductive Biology

INVES1: Eley, Robert M.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: 0

INVES2: Ochieng, Francis O.
DEGREE2: BS
DEPT2: Statistics
STAFF2: 0

SPECIES 1: Cercopithecus aethiops
NUM1: 82

Non-Host Institution: Institute of Primate Research, National Museums of Kenya

ABSTRACT: African Green Monkeys (Cercopithecus aethiops) are used for a variety of biomedical studies and of late these have extended into the area of reproductive biology. However, little is known of their growth and development or reproductive biology. This is the latest in a series of studies which have characterized these aspects of this animal. In order to determine the post natal growth anthropometric values were collected from 54 animals (34 females, 20 males) ranging in age from 18 to 882 days with repeated measurements taken between 42 and 183 days later. Single measurements were also taken from an additional 23 animals (12 females, 11 males) of 5 to 8 years of age. Between 20 and 25 measurements (dependent on sex) were obtained on each occasion. These included weight and head, body and limb measurements (length, width and circumference as appropriate) and skinfold thickness. Data were analyzed by age and gender, yielding parameters for age and rate of change relationships. Rates of growth were higher in the first year than thereafter and were significantly higher in the males than in females. For example weight up to 120 days of age was 1 gm/day more in males than in females. Growth was completed by 5 years of age with weight and crown rump length 3.13 kg and 43.9 cm versus 5.15 kg and 49 cm for females and males, respectively. Each parameter except subcutaneous fat thickness was larger in males than in females.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Artificial Breeding of Chimpanzees

AXIS 1: 1a, 2, 23

AXIS 2: 60, 65

PRC UNIT: Reproductive Biology

INVES1: Gould, Kenneth G.
DEGREE1: B. Vet. Med. Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

INVES2: Dahl, Jeremy F.
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF2: 0

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. The hormonal pattern of the normal menstrual cycle has been monitored closely with the intent to identify those cycles which, while exhibiting a normal intermenstrual interval are, in fact, subfertile. This is readily monitored in the chimpanzee due to the presence of an evident perineal swelling which is under hormonal control. In addition, the effectiveness of artificial breeding is being increased by hormonal control of follicle development so that more than one follicle develops during the menstrual cycle and the period of time for which a potentially fertile oocyte is present is increased.

Basic information regarding control of follicle development in the chimpanzee is being obtained by use of ultrasound monitoring of follicle growth during the follicular phase of the menstrual cycle.

Data obtained from this work provides assistance in captive breeding of the great apes and, particularly with regard to identification and classification of 'subfertile' cycles has direct application to the human.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Artificial Breeding in Chimpanzees and Ano-Genital Swelling Patterns.

AXIS I: 1a, 2, 9, 15, 23

AXIS II: 50b, 63h, 74e

PRC UNIT: Reproductive Biology

INVES1: Gould, Kenneth G.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

INVES2: Dahl, Jeremy F.
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF2: 0

SPECIES 1: Pan troglodytes
NUM1: 10

ABSTRACT: In order to promote and maximize the breeding potential of the captive colony of Pan troglodytes maintained at the Yerkes Regional Primate Research Center, an intensive effort is made to identify females with fertility problems and return them to a fertile status. One method by which this can be achieved is by artificial insemination (AI) in conjunction with: a) careful monitoring of the ano-genital swelling patterns, and excretory LH and steroid levels; b) visualization of the ovary by ultrasound, and c) various hormonal treatments. A current focus of the AI breeding program is the application of a newly devised method of monitoring the swelling patterns which appears to enable: 1) prediction of the time of the preovulatory LH surge and synchronization of AI procedures; 2) prediction of an infertile type of cycle with inadequate progesterone levels during the luteal phase. By careful examination of over 40 ovarian cycles in 10 females, data have been collected that substantiate the applicability of the method, and one pregnancy has been established. For a majority of cases when AI does not result in a pregnancy, the timing and technique of the AI procedure is consistent with a successful fertilization but subsequent implantation and/or establishment of pregnancy appears to be the cause of the infertility. This is consistent with the relatively low levels of urinary pregnanediol predicted for this sub-set of infertile cycles. The research is being extended, therefore, to examine ways in which: a) the infertile pattern of cyclicity can be converted to the fertile pattern; b) supplementing progesterone levels during the luteal phase of infertile, but ovulatory, cycles.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Artificial Breeding in Chimpanzees and Nipple Stimulation.

AXIS I: 1a, 2, 15, 23

AXIS II: 36, 50b, 71

PRC UNIT: Reproductive Biology

INVES1: Gould, Kenneth G.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

INVES2: Dahl, Jeremy F.
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF2: O

SPECIES 1: Pan troglodytes
NUM1: 10

ABSTRACT: The reproductive success of certain captive female Pan troglodytes is significantly reduced consequent to prolonged post-partum amenorrhea (pPA) after infant removal or weaning. Research by others has shown that auto-stimulation of the nipples (ANS) can cause pPA, and that ANS can be extinguished by administration of pergolide mesylate (a dopamine receptor agonist). To maximize the breeding potential of the colony at the Center, pergolide has been used in conjunction with artificial insemination procedures to return pPA individuals to a fertile status. To extend our understanding of the effect of ANS behaviors, an attempt has been made to: 1) document the behavior of animals exhibiting pPA with respect to ANS and the effect of pergolide administration on the behavior; 2) extend our understanding of the effect of ANS on fertility by evaluating the influence of low levels of ANS on ovarian and swelling cyclicity for individuals which have resumed ovarian cycles but remain infertile. It was hypothesized that ANS behaviors might be causally implicated in the distinction between two recently described types of cycle only one of which appears to be fully fertile and lead to pregnancy. Preliminary results from observations on 6 females indicate that: A) pergolide administration to pPA subjects always produces some sort of ovarian activity but some individuals appear to override the effects of the drug by increasing ANS and preventing completion of a fertile cycle; B) non-pPA individuals exhibiting low levels of ANS behavior appear to either disrupt the follicular and/or the luteal phase, or increase ANS after ovulation and disrupt the luteal phase alone. Consequently the work is being extended to evaluate pergolide administration on non-pPA subjects exhibiting ANS in an attempt to produce fully fertile cycles.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Identification of HIV in Chimpanzee Semen

AXIS 1: 1a, 2, 23

AXIS 2: 60, 65

PRC UNIT: Reproductive Biology

INVES1: Gould, Kenneth G.
DEGREE1: B. Vet. Med. Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

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

SPECIES1: Pan troglodytes
NUM1: 4

ABSTRACT: As a result of interest in the localization of HIV in semen and in the route of entry of the virus into semen, chimpanzees infected with HIV have been evaluated for the presence of the virus in semen samples. Subsequent to recovery of virus from the normal semen, the animals will be vasectomized and alteration of virus load determined. At the present time, probably as a result of the age of the animals and the relatively small semen samples recovered, together with low virus load in the animals, positive recovery of HIV from the animals has not been achieved on a routine basis. When virus recovery is achieved and should correlations be observed between virus content and vasectomy, micropuncture of the epididymis will be undertaken to identify those cells in the epididymis associated with HIV delivery into the seminal plasma.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Endocrine Control of Epididymal Function in the Primate Male

AXIS 1: 1a, 23

AXIS 2: 74, 83

PRC UNIT: Reproductive Biology

INVES1: Gould, Kenneth G.
DEGREE1: B. Vet. Med. Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

INVES2: Young, Leona G.
DEGREE2: Ph.D.
DEPT2: Reproductive Biology
STAFF2: O

SPECIES1: Pan troglodytes
NUM1: 6

ABSTRACT: There remains a significant need for development of effective male contraceptives. As part of our approach to this problem we are identifying those components of semen which are secreted under androgen control and which influence the fertilizing capacity of primate spermatozoa. We have obtained information on the pattern and duration of spermatogenesis in the adult male chimpanzee. That information is derived from direct evaluation of testicular biopsies and from measurement of the amount and distribution of tritiated thymidine within the developing sperm cells as measured by autoradiography. In addition , the time course and duration of pituitary suppression subsequent to administration of GnRH analogue to the adult male has been measured. Individual proteins identified as being under androgen control and having an influence on sperm fertilizing capacity will be used as the target for immunological blockade, resulting in reversible, specific contraception without the side effects of testicular inhibition or reduction of spermatogenesis.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Preservation of Bone Mass in Hypogonadal Female Monkeys with Recombinant Human Growth Hormone Administration

AXIS I: 1a, 15, 23, 26

AXIS II: 60

PRC UNIT: Reproductive Biology

INVES1: Mann, David R.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: O

INVES2: Gould, Kenneth G.
DEGREE2: Ph.D., D.V.M.
DEPT2: Reproductive Biology
STAFF2: C

INVES3: Rudman, Christopher G.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: O

INVES4: Akinbami, Mukaila A.
DEGREE4: Ph.D.
DEPT4: Reproductive Biology
STAFF4: O

SPECIES1: Macaca fascicularis
NUM1: 35

NON-HOST INSTITUTION: Morehouse School of Medicine (DRM, MAA) and Genentech, Inc. (CGR)

ABSTRACT: This study examined the effect of human recombinant growth hormone (GH) supplementation on bone loss in female monkeys made hypogonadal with a gonadotropin releasing hormone agonist (GnRH-Ag). Animals were randomly assigned to three treatment groups: vehicle, GnRH-Ag, and GnRH-Ag and GH. After an initial 5-mo pretreatment period during which all animals were maintained on a normal monkey chow diet containing a high level of calcium (1%), animals were shifted to a lower calcium diet (0.1%) for 5 mo before the beginning of treatment and were maintained on this diet throughout the remainder of the study. Monkeys were treated continuously for 10 mo with 25 ug/day of a GnRH-Ag or vehicle. GH was administered by intramuscular injection 3 times/week at a dose of 100 ug/kg BW/day. Animals treated with GnRH-Ag were amenorrheic throughout the treatment period, and serum estradiol and progesterone levels were below minimum levels of detection. Vehicle-treated animals continued to cycle throughout the study. Monkeys treated with GnRH-Ag alone showed a significant decline (12%) in bone mineral density (BMD) of the lumbar spine. BMD was reduced below pretreatment levels from 6 mo of GnRH-Ag treatment through 2 mo posttreatment in this group. In

contrast, GH supplementation preserved BMD in GnRH-Ag-treated monkeys. BMD did not change significantly in the GH supplemented or in vehicle-treated groups. Serum osteocalcin concentrations were elevated above pretreatment values after 6 and 9 mo of GnRH-Ag treatment alone or with GH supplementation, but did not change in vehicle-treated animals. GH also increased serum IGF-1 levels. In response to the lower calcium diet, serum PTH levels increased approximately 200% in vehicle-treated monkeys and animals treated with GnRH-Ag alone. GH attenuated this increase in serum PTH. The data indicate that the level of calcium in the diet of adult monkeys can be reduced more than 10-fold without affecting lumbar BMD provided ovarian function is normal, but if animals are made hypogonadal with a GnRH-Ag, bone mass declines. GH supplementation prevented bone loss resulting from the loss of ovarian function. GH supplementation may influence both the rate of bone resorption (via lowering PTH levels) and the rate of bone synthesis thus preserving bone mass.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Neonatal Testosterone and Primate Sexual Development

AXIS I: 1a, 15, 23, 26

AXIS II: 36, 60

PRC UNIT: Reproductive Biology

INVES1: Mann, David R.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: O

INVES2: Gould, Kenneth G.
DEGREE2: Ph.D., D.V.M.
DEPT2: Reproductive Biology
STAFF2: C

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

SPECIES1: Macaca mulatta
NUM1: 10

NON-HOST INSTITUTION: Morehouse School of Medicine (DRM).

ABSTRACT: The overall objective of this study is to define a potential role for neonatal testosterone in sexual and behavioral development. We have examined whether animals treated neonatally with a gonadotropin releasing hormone agonist in 1984 to suppress gonadotropin and testosterone secretion show a transient or permanent retardation of reproductive function as adults. We have previously reported that treated monkeys exhibited retarded peripubertal testicular development and testosterone secretion. The subnormal testicular volumes observed in these monkeys persisted into yr 5 of life; but by yr 6, seasonal changes in testicular volume did not differ between control and treated animals. The hypogonadotropic-hypogonadal condition observed in treated animals persisted into yr 6. Generally speaking, serum LH and testosterone levels were persistently lower in treated animals than controls through 6 yr of age. While sperm counts did not differ between control and treated monkeys, skeletal maturation in treated animals appears to be permanently retarded. At 6 yr of age, both crown-rump and tibia length was shorter in treated animals; and bone maturation scores were near adult levels. Thus, events that signal sexual development are delayed in animals deprived of neonatal testosterone secretion, but effects of this insult on skeletal maturation appear to be permanent.

Recently in an attempt to define the possible causes of the hypogonadotropic-hypogonadal condition, we challenged these animals at 6 yr of age with GnRH (two iv pulses of 50 ng/kg BW separated by 1 h), naloxone (1 mg/kg BW, iv) and NMDA (5 mg/kg BW, iv). Both controls (N=4) and treated

monkeys (N=6) showed significant serum LH ($P < 0.001$) and T ($P < 0.001$) responses to GnRH, but there were no differences between the two groups. Naloxone increased ($P < 0.001$) serum LH more than 2.5-fold over the first 30 min after injection in both groups of monkeys, and this resulted in a significant elevation ($P < 0.001$) of serum T, but again there were no significant differences in either response between groups. In contrast, treated monkeys did not show a serum LH or T response to NMDA whereas in controls serum LH was elevated ($P < 0.05$) above pretreatment values 15 min after NMDA injection and serum T levels were increased ($P < 0.05$) above basal values over the 1 h period following NMDA administration. These data suggest that the persistent hypogonadotropic hypogonadism in adult monkeys treated neonatally with a GnRH agonist may result from a subnormal sensitivity of the CNS to one or more excitatory neurotransmitters (e.g., aspartate or glutamate). In contrast, this condition does not appear to result from an elevation of tonic opioidergic inhibition of LH secretion or reduced pituitary responsiveness to GnRH. Thus, abolishing the neonatal surge of T with a GnRH agonist may permanently alter development and differentiation of CNS centers that are either involved in GnRH secretion or govern this process.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Effect of Neonatal Blockade of the Pituitary-Testicular Axis on Sexual Maturation in Male Monkeys

AXIS I: 1a, 2, 15, 23

AXIS II: 60

PRC UNIT: Reproductive Biology

INVES1: Mann, David R.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: 0

INVES2: Gould, Kenneth G.
DEGREE2: Ph.D., D.V.M.
DEPT2: Reproductive Biology
STAFF2: C

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

SPECIES1: Macaca mulatta
NUM1: 10

NON-HOST INSTITUTION: Morehouse School of Medicine (DRM).

ABSTRACT: We have found that blockade of neonatal activation of the pituitary-testicular axis with a GnRH agonist (Ag) retarded peripubertal testicular development and the pubertal rise in testosterone (T) secretion in male monkeys (J. Clin. Endocrinol. Metab. 68:600, 1989). The objective of the present study was to determine whether this early postnatal gonadotropin and T deficiency temporarily or permanently affected pituitary and testicular function in these animals. Animals were treated continuously (minipump) with a Ag (Wyeth-Ayerst Labs, Wy-40972, 10 ug/day, N=6) or vehicle (N=4) for the first 4 postnatal months. We have previously reported changes in endocrine and reproductive parameters in these monkeys through the onset of puberty (3.5 y of age). In the present study, we monitored endocrine changes, testicular function, and developmental parameters over the next 2 years. Animals were group-housed outdoors with access to indoor quarters throughout the study. The subnormal testicular volumes observed in Ag-treated animals at 3.5 y of age persisted through the subsequent breeding season. This was associated with a subnormal seasonal rise in serum LH and T. However, by the following season testicular volumes and serum LH and T levels in Ag-treated monkeys were comparable to those in controls. The frequency of response to electroejaculation was lower in Ag-treated animals than in controls at 3 (21.4% versus 62.5%) and 4 (69.4% versus 85.4%) y of age, but by 5 y had reached control levels. The 3 Ag-treated monkeys that did not show a significant pubertal rise in T at 3 y of age and from which we were unable to recover semen samples, exhibited an ejaculatory response during the subsequent

year. Sperm count and body weight did not differ significantly between treated and control animals at 3, 4 or 5 y of age, but crown-rump length at 5 y of age was less ($p=0.02$) in Ag-treated monkeys than in controls. These data suggest that the early postnatal period is a critical period in the maturation of the hypothalamic-pituitary-testicular axis in primates. Events which signal sexual development are delayed in animals deprived of neonatal T secretion, but effects on testicular development appear to be temporary and eventually reach control levels. Blockade of neonatal activation of this axis in male primates may also retard the normal course of skeletal growth.

P51RR00165-30 1/1/1990 - 12/31/1990 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

INVEST1: 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.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Nonreproductive Mating of the Chimpanzee

AXIS I: 1a, 15, 23

AXIS II: 36, 72, 74e

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: O

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. Several versions of the traditional laboratory pair-test, the free-access test (FAT) are used, including the FAT with delayed introduction of subjects (FAT_D), and two versions of the restricted-access test (RAT). The FAT_D is used to test the hypothesis that increased male sexual initiative in the FAT, both during the menstrual cycle and during pregnancy, is caused by the immediate introduction per se of the female partner. This hypothesis is based on the relatedness species-typical forms of courtship and greeting behavior following a period of separation. The RAT with male control over access (RATm) is also used to test the hypothesis that the male's mating initiative is artificially stimulated by specific aspects of testing in the FAT. The RAT with female control over access (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. The results are relevant to basic issues regarding the regulation of mating in primates. Clarification of the basis for mating initiative in chimpanzees should also 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.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Behavior and Physiology of the Gibbon

AXIS I: 1a, 15, 23

AXIS II: 36, 74e

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: O

INVES3: Gould, Kenneth G.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: C

INVES4: Collins, Delwood C.
DEGREE: Ph.D.
DEPT4: Reproductive Biology
STAFF4: O

SPECIES1: Hylobates lar
NUM1: 9

ABSTRACT: The objectives of this research are 1) to determine whether a hypothesis regarding the ultimate (evolutionary) causation of differences in reproductive behavior, anatomy and physiology, derived from research on the polygamous great apes, extends to the monogamous gibbon, and 2) to determine the relationship among sex hormone levels, female genital swelling, duetting (vocalizations), test conditions and pair-bond duration on the proximate activation of reproductive behavior in this lesser ape. Oppositely sexed pairs of gibbons will be studied behaviorally in commodious enclosures in conjunction with measurement of female genital swelling and radioimmunoassay and bioassay of sex hormones in serum, urine and feces of the female during natural menstrual cycles and pregnancy. In order to detect subtle behavioral changes during the menstrual cycle that may not be apparent in traditional laboratory pair-tests, we will also use pair-tests in which sexual access is controlled separately by the male and female through the performance of an operant task. The mating system of the gibbon represents one end of a continuum with respect to intermale competition for estrous females (and female choice of a male at estrus), a continuum associated with several aspects of reproductive function in the great apes. Since intermale competition for estrous females in the gibbon is minimal or totally absent, similar to the gorilla, we hypothesized that male courtship and sexual initiative, penile visibility, female genital visibility and duration of

significant female genital swelling during the cycle, preovulatory copulation and relative testis size would all be relatively low, in relation to the great apes, i.e., similar to the gorilla. We also hypothesized that sexual activity would be 1) infrequent or absent during pregnancy, as a result of relatively high paternity certainty, 2) somewhat greater during the menstrual cycle in newly established pairs than in long established ones, associated with formation of the pair-bond and 3) somewhat greater during the cycle following daily periods of extended social and spatial separation, due to re-affirmation of the pair-bond. Research on the gibbon represents an excellent opportunity to assess comparatively, the relevance of a monogamous sexual relationship to the regulation of reproductive behavior, anatomy and physiology of the extant hominoids. Depending on the results, the research could also provide indirect evidence regarding the nature of the human mating system.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Improved Behavioral Well-Being of Chimpanzees by Varied Feeding Strategies

AXIS I: 1a, 21

AXIS II: 36, 72

PRC UNIT: Reproductive Biology

INVES1: Nadler, Ronald D.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

INVES2: Erwin, J.
DEGREE2: Ph.D.
DEPT2: N/A
STAFF2: N/A

INVES3: Herndon, J.G.
DEGREE3: Ph.D.
DEPT3: Neurobiology
STAFF2: C

SPECIES1: Pan troglodytes
NUM1: 16 (Housed at SEMA, Inc., Rockville, MD)

ABSTRACT: Three experiments were conducted to determine if different feeding strategies used with young, individually caged chimpanzees, influenced their behavioral well-being, i.e., the concordance between activity levels of species-typical behavior in the laboratory and in the wild. Eight individually caged chimpanzees, aged 2-5 years were used in each experiment. In Experiment 1, 1 vs 3 meals per day was assessed during 4 4-week blocks in an ABBA design. In Experiment 2, lab chow vs lab chow plus 1 ear of corn on alternate days was assessed 1 hour post-feeding for 6 weeks. In Experiment 3, lab chow vs lab chow plus 1 ear of corn was given daily for 6 4-week blocks and was assessed 1 hour post-feeding during 4 4-week blocks in an ABBA design with 2 4-week blocks intervening between the 2 B segments of the design. Data were recorded on posture, position in space, environmental exploration, self-directed and other-directed behavior. There was considerable variability within and between subjects and few overall treatment effects other than those related to food contact per se. In Experiment 1, feeding was more equally distributed throughout the day with 3 meals in comparison to 1 meal. In Experiments 2 and 3, there was considerably more time involved with food 1 hour after feeding lab chow plus corn in comparison to feeding lab chow alone. The current study on young chimpanzees, together with comparable ones by others on adults, supports the proposal that feeding strategies are a useful approach for altering the behavior of captive chimpanzees. Since chimpanzees in the wild spend the majority of their waking hours engaged in foraging, food-processing and ingesting food, increasing food-related behavior in captivity can be regarded as an improvement in behavioral well-being, as defined above.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Behavioral Responsiveness to Strangers in Young Chimpanzees.

AXIS I: 1a, 21

AXIS II: 36, 60

PRC UNIT: Reproductive Biology

INVES1: Nadler, Ronald D.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

INVES2: Miller, L. Cheryl
DEGREE2: M.A.
DEPT2: Behavioral Biology
STAFF2: 0

INVES3: Bard, Kim A.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: 0

INVES4: Juno, Charles J.
DEGREE4: Ph.D.
DEPT4: Behavioral Biology
STAFF4: 0

SPECIES1: Pan troglodytes
NUM1: 16

ABSTRACT: Earlier studies of responses of primate infants to strangers were frequently confounded with separation from the attachment figure and/or removal to an unfamiliar setting. In the present study, young chimpanzees were tested in a familiar setting with a human female caretaker who served as an attachment figure. Two strangers were introduced: a human female, approximately the size of the caretaker, who refrained from initiating interactions and a larger human male, who repeatedly approached and initiated contact with the subjects. A somewhat more intense response was elicited by the larger, more assertive male stranger, but neither stranger elicited severe distress. The behavior of the chimpanzees is better described as wary, rather than fearful. These results may be attributable to the continued presence of the caretaker in contrast to previous studies reporting severe distress to strangers when chimpanzees are tested alone. A wariness of strangers in nursery-reared chimpanzees may develop by 6 months of age and diminish somewhat by 2 years of age under the conditions of this study.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Hand Preferences in Captive Gorillas, Orangutans and Gibbons.

AXIS I: 1a, 21

AXIS II: 36, 41

PRC UNIT: Reproductive Biology

INVES1: Nadler, Ronald D.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

INVES2: Olson, David A.
DEGREE2: M.D.
DEPT2: Reproductive Biology
STAFF2: 0

INVES3: Ellis, Jane E.
DEGREE3 Ph.D.
DEPT3: Behavioral Biology
STAFF3: 0

SPECIES1: Gorilla gorilla
NUM1: 12

SPECIES2: Pongo pygmaeus
NUM2 13

SPECIES3: Hylobates lar
NUM3: 9

ABSTRACT: Hand preference was assessed in 12 gorillas, 13 orangutans and 9 gibbons by using a floor retrieval task and a mesh-fence retrieval task. Hand preference was also assessed in 8 gorillas and 8 orangutans using a task involving the unfastening of a hasp. A bipedal requirement during testing (mesh retrieval task) facilitated detection of hand preferences. A significant left-hand preference was found for the gibbons with 6 of 6 gibbons preferring their left hand on the mesh-fence retrieval task. Similarly, a significant right-hand preference was found for the gorillas with 10 of 12 gorillas preferring their right hand on the mesh retrieval task. The data for the orangutan suggest a bimodal distribution on all tasks. Since the gibbon and the gorilla in the wild engage in bipedal locomotion more frequently than the orangutan, one possible interpretation for these results correlates the degree of bipedal behavior of a species in it natural environment with its readiness to exhibit a unilateral population-level hand preference.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Prolonged Lactational Infertility During Adolescence

AXIS I: 1a, 2, 15, 23, 36

AXIS II: 60, 71

PRC UNIT: Reproductive Biology

INVES1: Wilson, Mark E.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

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

SPECIES 1: Macaca mulatta
NUM1: 6

ABSTRACT: Adolescent rhesus monkey mothers experience a prolonged period of lactational infertility following their first parturition. Studies were continued this year to determine the responsiveness of adult and adolescent nursing mothers to various doses of LHRH in terms of pituitary and ovarian hormone secretion. At ~22 weeks post-partum mothers were fitted with an iv catheter which attached to a portable infusion pump. The pump delivered a bolus injection of LHRH once per hour for a three week period in one of three doses. The pump was encased in a primate vest, worn by the mother allowing unrestricted movement for the mother and permitting her infant to nurse ad libitum. Data collected to date indicate that pulsatile administration of LHRH at a dose of 50 ng/kg/hr stimulates the pituitary - gonadal axis such that increased E2 secretion is observed within two days of treatment. Ovulations, indicated by a rise in serum progesterone, have occurred by day 14 from the initiation of treatment in multiparous females treated with a 50 and 100 ng/kg/hr dose. These data suggest that suckling -induced suppression of the reproductive system is not primarily mediated at the level of the pituitary but rather from a reduction in endogenous LHRH activity. Nevertheless, the possibility remains that a secondary effect of nursing is to render the pituitary temporally insensitive to LHRH stimulation, particularly in primiparous mothers. Continuation of these dose-response studies will more fully address this question. Another study initiated this year determined the role of estradiol (E2) negative feedback inhibition of LH and FSH secretion during lactational infertility. Adolescent and adult mothers were ovariectomized within 2 weeks following parturition. Females were treated with subcutaneous implants of estradiol to maintain serum levels at ~25 pg/ml. E2-treatment periods lasted three weeks and were punctuated by 3 weeks of "no E2" treatment. Thus the design allows an analysis of the relative role of E2 negative feedback as lactation progresses and the intensity of the suckling stimulus diminishes. Data analyzed to date indicate that at a period during lactation, when the reproductive system is still suppressed in gonadally intact nursing mothers, E2 effectively suppresses bioactive LH secretion (>3

ng/ml) in both multiparous and primiparous mothers. In contrast, in the absence of E2, bioactive LH concentrations are not suppressed (>150 ng/ml). Further analyses of samples will determine whether a smaller dose of E2 will effectively suppress LH in primiparous mothers and not multiparous mothers. These data suggest that the nursing-induced suppression of LH is mediated, at least in part, to E2 negative feedback inhibition of gonadotropins and not to a non-gonadal restraint. Taken together, these studies will help describe the mechanism regulating contraceptive aspects of nursing and to define problems of infertility in adolescent females.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Nocturnal Melatonin Secretion and Reproductive Capacity in Females.

AXIS I: 1a, 2, 15, 23, 26

AXIS II: 54b, 60, 71

PRC UNIT: Reproductive Biology

INVES1: Wilson, Mark E.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

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

SPECIES 1: Macaca mulatta
NUM1: 6

ABSTRACT: Studies were initiated in August this year to determine if high amplitude nocturnal melatonin concentrations induced infertility in female rhesus monkeys. Certain conditions of hypothalamic amenorrhea/infertility in women are associated with high nocturnal concentrations of melatonin in serum. In order to determine if there is a causal relationship between this parameter and fertility, female rhesus monkeys were studied through one complete ovulatory menstrual cycle. On the first day of menses following ovulation, females received a daily subcutaneous injection of melatonin at 1600, 2000, and 2400 hr to elevate the circulating concentrations of melatonin during the night time. Females were treated until the onset of their next menstruation. Analyses revealed that the elevation in nocturnal melatonin in serum had no effect on reproductive function as evidenced by the occurrence of ovulation with a normal corpus luteum and circulating levels of estradiol, LH, and progesterone. These data demonstrate that high amplitude nocturnal melatonin concentrations in serum do not result in infertility.

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Common Neuroendocrine Mechanisms for Growth and Puberty.

AXIS I: 1a, 2, 15, 23, 26

AXIS II: 54b, 60, 71

PRC UNIT: Reproductive Biology

INVES1: Wilson, Mark E.
DEGREE1: Ph.D.
DEPT1: Reproductive Biology
STAFF1: C

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

INVES3: Tanner, James M.
DEGREE3: MD
DEPT3: Reproductive Biology
STAFF3: O

SPECIES 1: Macaca mulatta
NUM1: 12

ABSTRACT: Studies were initiated in August this year to determine if there is a common neuroendocrine mechanism regulating both pubertal growth and reproductive maturation. Immature females were treated with a clinical grade somatostatin analogue (Sandoz) and their prepubertal growth patterns, as well as parameters of sexual maturation, were compared to age-matched controls administered saline. Growth rates have been slowed by the analogue treatment, by its suppression of growth hormone and insulin-like growth factor -I secretion. Continued analyses of these females will determine how growth tempo is altered and if this affects the timing of reproductive maturation. 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.

DIVISION OF ANIMAL RESOURCES AND VETERINARY MEDICINE

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R. Brent Swenson, D.V.M., Chief of Veterinary Medicine and Senior Veterinarian

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K.S. Paul, D.V.M., Assistant Veterinarian, Division of Animal Resources and Research Associate, Division of Pathobiology and Immunobiology, Yerkes Center

Consultants

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E. Keener, M.D., Consultant in Medicine, Private Practice in Neurosurgery, Atlanta, Georgia

P51RR00165-30 1/1/1990 - 12/31/1990 Yerkes Regional Primate Research Center

TITLE: Tana River Primate Project

AXIS I: 1a, 8, 11

AXIS II: 34, 36, 54b

PRC UNIT: Animal Res & Vet Med

INVES1: Else, James
DEGREE1: D.V.M., M.P.V.M.
DEPT1: Animal Resources
STAFF1: C

INVES2: Leakey, Richard E.
DEGREE2:
DEPT2:
STAFF2: O

INVES3: Gould, Kenneth
DEGREE3: B.V.M., Ph.D.
DEPT3: Reproductive Biology
STAFF3: C

INVES4: Struhsaker, Thomas
DEGREE4: Ph.D.
DEPT4:
STAFF4:

INVES5: Smith, Euclid O.
DEGREE5: Ph.D.
DEPT5: Behavioral Biology
STAFF5: C

INVES6: Njuguna, Stephen
DEGREE6: Ph.D.
DEPT6:
STAFF6:

SPECIES1: Colobus badius
NUM1: 800 (wild)

SPECIES2: Cercocebus galeritus
NUM2: 1600 (wild)

NON-HOST INSTITUTION: University of Florida (TS), Kenya Wildlife Services (RL), and National Museums of Kenya (SN)

ABSTRACT: The Tana River National Primate Reserve is the home for two highly endangered primates, the Tana River Red Colobus (Colobus badius rufomitratus) and the Tana River Crested Mangabey (Cercocebus galeritus galeritus). Both species have experienced dramatic declines over the past decade which resulted in the establishment of the Tana Primate Project in 1987. A series of

integrated studies were subsequently initiated, the research findings of which were evaluated in 1990 and a proposed park management plan prepared. This has been submitted to various funding and development agencies to obtain support to implement the management plan.

P51RR00165-30 1/1/1990 - 12/31/1990 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: Animal Res and Vet Med

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: Bard, Kim A.
DEGREE3: Ph.D.
DEPT3: Reproductive Biology
STAFF3: O

INVES4: Gordon, Thomas P.
DEGREE4: M.S.
DEPT4: Behavioral Neuroendocrinology
STAFF4: C

INVES5: Strobert, Elizabeth A.
DEGREE5: D.V.M.
DEPT5: Veterinary Medicine
STAFF5: C

SPECIES1: Pan troglodytes
NUM1: 82

ABSTRACT: A dedicated group of chimpanzees has been identified and used to establish a stable, self-sustaining breeding population to guarantee the future availability of these animals for behavioral and biomedical research programs as part of a cooperative project with four other domestic institutions. Because of the past success of this program, breeding activities are now carried out at a maintenance level rather than a "production" level, but the production rate will be increased if a need for increased numbers of animals (such as for candidate AIDS vaccine testing) should occur.

Related research is also being carried out in early detection of labor using telemetry methods, gamete preservation to improve artificial breeding techniques and 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 reproduction. There were 8 live births in 1990.

INVESTIGATORS WITH PUBLIC HEALTH SERVICE SUPPORT

CORE: OTHER: X

NAME	TYPE	AGENCY	GRANT/CONTRACT	TOTAL FUNDS	% RPRC USED
Bakay, Roy A.E.	FED	NIH	NS-24340	163,460	95
Bard, Kim A.	FED	NIH	RR-06158	97,769	100
Bruot, Brent C.	FED	BRSG	SO7RR-07023	945	100
Fritz, Michael E.	FED	NIH	DE-08917	768,248	20
Gust, Deborah A.	FED	NIH	MH-46676	58,288	100
Hanson, Stephen R.	FED	NIH	HL-31469	184,265	100
	FED	NIH	HL-31950 (Scripps Subcontract)	110,927	20
	FED	NIH	HL-31950 (Scripps Subcontract)	83,461	100
Harker, Laurence A.	FED	NIH	HL-41357	178,386	45
	FED	NIH	HL-41619	166,850	45
	FED	NIH	HL-31950 (Scripps Subcontract)	156,378	20
Howell, Leonard L.	FED	NIDA	DA-05346	113,571	100
Lambert, Scott R.	FED	NIH	EY-08544	99,513	14
Mann, David R. Morehouse School of Medicine	FED	NIH	HD-26423	121,944	35
Rumbaugh, Duane M. Georgia State Univ.	FED	NIH	HD-06016	667,307	34
Sommadossi, Jean-Pierre Univ. of Alabama	FED	NIH	HL-42125	360,387	1
Waring, George	FED	NIH	EY-07388	120,399	50
TOTAL PHS SUPPORT			This page:	$ 3,452,098	
			Grand (Cumulative) Total:	3,452,098	

PART II, SECTION B1 GRANT NUMBER: P51RR00165-30

INVESTIGATORS WITH SUPPORT OTHER THAN PUBLIC HEALTH SERVICE

CORE: X OTHER:

NAME	TYPE	AGENCY	GRANT/CONTRACT	TOTAL FUNDS	% RPRC USED
Bernstein, Irwin S.	FED	NSF	BNS-86-16691	206,791	100
Fultz, Patricia N.	IND	Behringwerke	---	63,654	82
	IND	Pasteur Vaccins	---	54,300	58
Gould, Kenneth G.	FED	CONRAD	CSA-89-051	11,656	100
	FDN	Woodruff Funds	---	15,000	100
	FDN	INCOME	GC-635740	1,537	100
Metzgar, Richard S.	IND	Stratacyte Corporation	---	2,500	50
Nadler, Ronald D.	FED	NSF	BNS-87-08406	68,600	100
Wallen, Kim	FED	NSF	BNS-89-19888	120,000	100
Wilson, Mark	OTH	URC-Emory	---	7,000	100

TOTAL NON-PHS SUPPORT This page: $551,038
Grand (Cumulative) Total: 551,038

INVESTIGATORS WITH SUPPORT OTHER THAN PUBLIC HEALTH SERVICE

CORE: OTHER: X

NAME	TYPE	AGENCY	GRANT/CONTRACT	TOTAL FUNDS	% RPRC USED
Dahl, Jeremy F.	FDN	Jefferson, Jr. Memorial Fund	---	5,000	100
Eberhard, Mark L. Centers for Disease Control	FDN	McConnell Clark Fdn.	---	111,449	50
	FDN	McConnell Clark Fdn.	---	5,000	100
Gouzoules, Harold T.	FED	NSF	BNS-87-19230	100,000	100
	OTH	Emory Univ.	---	9,300	100
Greene, Bruce M. Univ. of Alabama	FDN	McConnell Clark Fdn.	---	98,000	10
Hanson, Stephen R.	IND	---	---	10,000	100
Kennedy, Philip R. Georgia Tech	FDN	Emory-Ga. Tech.	66-89TC	30,000	50
	PVAS	APA	KA1-8901	30,000	90
Lambert, Scott R.	FDN	Knight's Templar Eye Fdn.	---	15,835	5
Malizia, Anthony A.	OTH	Private	---	25,000	100
Mann, David R. Morehouse School of Medicine	IND	Genentech	---	215,299	50
Martin, David E. Georgia State Univ.	FED	VA	RRDS-B299-3RA	33,000	2
McCarey, Bernard	IND	---	---	100,000	12
Thompson, Keith P.	IND	GE Medical Systems	---	221,500	80
Winton, Elliott F.	IND	Sandoz	---	178,836	90
TOTAL NON-PHS SUPPORT			This page:	$1,188,219	
			Grand (Cumulative) Total:	1,188,219	

PART II, SECTION C BOOKS/PAPERS/ABSTRACTS GRANT NUMBER:P5RR00165-30

CORE: XXX OTHER:

Number Published:	Books:	0	Papers:	24	Abstracts:	21
Number in Press:	Books:	0	Papers:	23	Abstracts:	1

Anderson, D.C., Fultz, P.N., Ansari, A.A., Klumpp, S.A., Ribas, J.L., and McClure, H.M.: Naturally occurring SIV infection in a colony of Macaca arctoides. Eighth Annual Symposium on Nonhuman Primate Models for AIDS, New Orleans, LA, November 28-30, 1990, p.133 (Abstract).

*Ansari, A.A., Jehuda-Cohen, T., Powell, J.D., Villinger, F., Mayne, A., Lockwood, E., Gordon, I., and McClure, H.M.: Cellular and cytokine requirements for the in vitro synthesis of SIV-reactive antibodies by polyclonal activation of PBMC from infected yet seronegative nonhuman primates. Eighth Annual Symposium on Nonhuman Primate Models for AIDS, New Orleans, LA, November 28-30, 1990, p.108 (Abstract).

*Ansari, A.A., Powell, J.D., Jensen, P.E. Jehuda-Cohen, T., McClure, H.M., Anderson, D., Fultz, P.N., and Sell, K.W.: Requirements for simian immunodeficiency virus antigen-specific in vitro proliferation of T cells from infected rhesus macaques and sooty mangabeys. AIDS 4:399-407, 1990.

*Bernstein, I.S.: An idiosyncratic approach to the study of relationships. In: Interpretation and Explanation in the Study of Animal Behavior, Vol. I, Interpretation, Intentionality, and Communication, M. Bekoff and D. Jamieson, eds., Westview Press, Boulder, CO, pp.35-55, 1990.

*Bernstein, I.S.: Puberty is not an event: testosterone changes in adolescent male rhesus monkeys. Am. J. Primatol. 20:173-174, 1990 (Abstract).

*Boothe, R.: Experimentally induced and naturally occurring monkey models of human amblyopia. In: Comparative Perception, Vol. I, Basic Mechanisms, M. Berkley and W. Stebbins, eds., John Wiley & Sons, Inc., New York, pp.461-486, 1990.

*Boothe, R.G., Quick, M.W., Joose, M.V., Abbas, M.A. and Anderson, D.C.: Accessory lateral rectus orbital geometry in normal and naturally strabismic monkeys. Invest. Ophthalmol. Visual Sci. 31:1168-1174, 1990.

*Boothe, R., Tigges, M., Wilson, J., Quick, M., Neuner, G. and Eggers, H.: Monkey model of treatments for infantile aphakic amblyopia. Invest. Ophthalmol. Visual Sci. (Suppl.) 31:279, 1990 (Abstract).

Fultz, P.N., and Anderson, D.C.: The biology and immunopathology of simian immunodeficiency virus infection. Curr. Opin. Immunol. 2:403-408, 1990.

Fultz, P.N., Anderson, D.C., McClure, H.M., Dewhurst, S., and Mullins, J.I.: SIVsmm infection of macaque and mangabey monkeys: correlation between in vivo and in vitro properties of different isolates. Develop. Biol. Standard. 72:253-258, 1990.

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natural infection with simian immunodeficiency virus and simian T-cell leukemia virus type I in a breeding colony of sooty mangabey monkeys. AIDS 4:619-625, 1990.

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Fultz, P.N., Stricker, R.B., McClure, H.M., Anderson, D.C., Switzer, W.M., and Horaist, C.: Humoral response to SIV/SMM infection in macaque and mangabey monkeys. J. Acquir. Immune Defic. Syndr. 3:319-329, 1990.

*Gordon, T.P., Gust, D.A. and Wilson, M.E.: Factors modulating the seasonal onset of ovulation in nonlactating rhesus monkeys. Am. J. Primatol. 20:194-195, 1990 (Abstract).

*Gould, K.G.: Fertility in the great apes. Zoo Biol. 9:89, 1990 (Forward).

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*McClure, H., Anderson, D., Gordon, T., Ansari, A., Fultz, P., Klumpp, S., Emau, P. and Isahakia, M.: Natural SIV infections in nonhuman primates. Abstracts of the XIIIth Congress of the International Primatological Society, Nagoya and Kyoto, Japan, July 18-24, 1990, p.182 (Abstract).

*Nadler, R.D.: Homosexual behavior in nonhuman primates. In: Homosexuality/Heterosexuality: Concepts of Sexual Orientation, D.P. McWhirter, S.A. Sanders and J.M. Reinisch, eds., Oxford University Press, New York, pp.138-170, 1990.

*Nadler, R.D.: Sexual behavior and the concept of estrus in the great apes. Abstracts of the XIIIth Congress of the International Primatological Society, Nagoya and Kyoto, Japan, July 18-24, 1990, p.158 (Abstract).

*Nadler, R. D., Metz, B., Ferrer, A. C., Erwin, J. and Herndon, J. G.: Improved behavioral well-being of individually caged chimpanzees by varied feeding strategies. Am. J. Primatol. 20:214-215, 1990 (Abstract).

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*Savage-Rumbaugh, E.S.: Cognitive, linguistic, and postural development contrasts between female co-reared Pan troglodytes and Pan paniscus. Abstracts of the XIIIth Congress of the International Primatological Society, Nagoya and Kyoto, Japan, July 18-24, 1990, p.144 (Abstract).

*Savage-Rumbaugh, E.S.: Implications of the cognitive and linguistic abilities of the bonobo for theories of the development of hominid culture. Abstracts of the XIIIth Congress of the International Primatological Society, July 18-24, 1990, Nagoya and Kyoto, Japan, July 18-24, 1990, p. 172(Abstract).

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*Savage-Rumbaugh, E.S., Sevcik, R.A., Brakke, K.E., Rumbaugh, D.M. and Greenfield, P.M.: Symbols: their communicative use, comprehension, and combination by bonobos (Pan paniscus). Adv. Infancy Res. 6:221-278, 1990.

*Smith, E.O.: Dispersal and migration in nonhuman primates: an overview. Abstracts of the XIIIth Congress of the International Primatological Society, Nagoya and Kyoto, Japan, July 18-24, 1990, p.132 (Abstract).

*Tigges, J., Herndon, J.G. and Peters, A.: Neuronal population of area 4 during the life span of the rhesus monkey. Neurobiol. Aging 11:201-208, 1990.

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Wallen, K., Eisler, J., Gelmis, A., Tannenbaum, P., Tate, K. and Mann, D.: Hormonal and behavioral suppression with a Nal-Lys GnRH antagonist in group-living male rhesus monkeys. Am. J. Primatol. 20:241-242, 1990 (Abstract).

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*Wilson, M.E. and Gordon, T.P.: Pubertal decline in nocturnal melatonin in female rhesus monkeys is not influenced by serum estradiol concentrations. Abstracts of the Endocrine Society, 72nd Annual Meeting, Atlanta, Georgia, June 20-23, 1990, #1479 (Abstract).

IN PRESS

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*Bernstein, I.S.: The correlation of kinship and behavior in nonhuman primates. In: Kin Recognition, P.G. Hepper, ed., Cambridge University Press, New York (In Press).

Bernstein, I.S.: Aggression. In: Encyclopedia of Human Biology, Vol. 1, R. Dubecco, ed., Academic Press, San Diego (In Press).

*Bernstein, I.S.: An empirical comparison of focal and ad libitum scoring with commentary on instantaneous scans, all occurrrence and one-zero techniques. Anim. Behav. (In Press).

*Bernstein, I.S., Ruehlmann, T.E., Judge, P.G., Lindquist, T. and Weed, J.L.:

Testosterone changes during the period of adolescence in male rhesus monkeys (Macaca mulatta). Am. J. Primatol (In Press).

*Else, J.G.: The current status of the DeBrazza monkey (Cercopithecus neglectus) in Kenya. In: Proceedings of EAWLS Wildlife Conference (In Press).

Fultz, P.N.: HIV infection of chimpanzees: an animal model for asymptomatic HIV carriers and vaccine efficacy. In: Annual Review of AIDS Research, W.C. Koff, F. Wong-Staal, and R.C. Kennedy, Eds., Marcel Dekker, Inc. (New York), (In Press).

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Fultz, P.N., Siegel, R.L., Brodie, A., Mawle, A.C., Stricker, R.B., Swenson, R.B., Anderson, D.C., and McClure, H.M.: Prolonged $CD4^+$ lymphocytopenia and thrombocytopenia in a chimpanzee persistently infected with human immunodeficiency virus type 1. J. Infect. Dis. (In Press).

*Gould, K.G. and Vogel, K.: A comparison of cryoprotective media for freeze preservation of chimpanzee sperm. Am. J. Primatol. (In Press).

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Comparative Cognition, H.L. Roitblat, ed., Lawrence Erlbaum Associates, Hillsdale, NJ (In Press).

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*Tigges, M. and Tigges, J.: Parvalbumin immunoreactivity of the lateral geniculate nucleus in adult rhesus monkeys after monocular eye enucleation. Visual Neurosci. (In press).

*Wilson, J., Tigges, M., Boothe, R. and Quick, M.: Correlations between anatomy, physiology, and behavior for monocular infantile aphakia in monkeys. Invest. Ophthalmol. Vis. Sci. Suppl. 32: (Abstract) (In Press).

*Wilson, M.E.: Factors determining the onset of puberty. In: Sexual Differentiation: A Lifespan Approach: Handbook Neurobiology, A. Gerall, H. Moltz, and I. Ward, eds., Plenum Press, New York, vol. 10 (In press).

*Wilson, M.E., Gordon, T.P., Chikazawa, K., Gust, D., Tanner, J.M., and Rudman, C.G.: Effects of growth hormone on neonatal growth in nursing rhesus monkeys. J. Clin. Endocrinol. Metab. (In press).

* Center Support Acknowledged
** (Not previously reported)

PART II, SECTION C BOOKS/PAPERS/ABSTRACTS GRANT NUMBER:P5RR00165-30

CORE: OTHER: XXX

Number Published:	Books:	3	Papers:	78	Abstracts:	76
Number in Press:	Books:	0	Papers:	59	Abstracts:	21

Abraham, D.A., Eberhard, M.L., Lange, A.M., Yutanawiboonchai, Y., Dickerson, J.W., Swenson, R., and Trpis, M. Protective immunity against larval Onchocerca volvulus: Identification of susceptible rodent and primate hosts and induction of immunity in a model system. 39th Annual Meeting of the American Society of Tropical Medicine and Hygiene, New Orleans, LA, November, 1990 (Abstract).

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* Center Support Acknowledged
** (Not previously reported)

PART II, SECTION C BOOKS/PAPERS/ABSTRACTS GRANT NUMBER: P51RR00165-30

PUBLICATIONS SUPPORTED BY RECEIPT OF SPECIMENS: X

Number Published:	Books:	0	Papers:	21	Abstracts:	14
Number in Press:	Books:	0	Papers:	15	Abstracts:	0

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* Center Support Acknowledged
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