VOLUME 1

Nonhuman Primates in Biomedical Research: Biology and Management

EDITED BY:

Christian R. Abee
Keith Mansfield
Suzette Tardif
Timothy Morris

American College of Laboratory Animal Medicine Series

Nonhuman Primates in Biomedical Research

Volume 1: Biology and Management

Second Edition

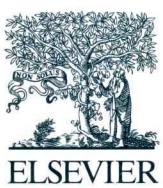
Edited by

Christian R. Abee
University of Texas, MD Anderson Cancer Center, Michale E. Keeling Center for Comparative Medicine and Research, Bastrop, Texas

Keith Mansfield
Novartis Institutes for Biomedical Research, Cambridge, Massachusetts

Suzette Tardif
University of Texas Health Science Center, Barshop Institute of Longevity & Aging Studies, San Antonio, Texas

Timothy Morris
School of Veterinary Medicine and Science, University of Nottingham, United Kingdom



ELSEVIER

AMSTERDAM • BOSTON • HEIDELBERG • LONDON • NEW YORK • OXFORD • PARIS
SAN DIEGO • SAN FRANCISCO • SINGAPORE • SYDNEY • TOKYO

Academic Press is an Imprint of Elsevier

Academic Press is an imprint of Elsevier
32 Jamestown Road, London NW1 7BY, UK
225 Wyman Street, Waltham, MA 02451, USA
525 B Street, Suite 1800, San Diego, CA 92101-4495, USA

First edition 1995
Second edition 2012

Notice

No responsibility is assumed by the publisher for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions or ideas contained in the material herein. Because of rapid advances in the medical sciences, in particular, independent verification of diagnoses and drug dosages should be made

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library

Library of Congress Cataloging-in-Publication Data
A catalog record for this book is available from the Library of Congress

ISBN: 978-0-12-415833-7 set
ISBN: 978-0-12-381365-7 volume 1
ISBN: 978-0-12-381366-4 volume 2

Typeset by TNQ Books and Journals

Printed and bound in Canada

12 13 14 15 10 9 8 7 6 5 4 3 2 1

Nonhuman Primates in Biomedical Research

Volume 1: Biology and Management

Second Edition

American College of Laboratory Animal Medicine Series

Steven H. Weisbroth, Ronald E. Flatt, and Alan L. Kraus, eds.:
The Biology of the Laboratory Rabbit, 1974

Joseph E. Wagner and Patrick J. Manning, eds.:
The Biology of the Guinea Pig, 1976

Edwin J. Andrews, Billy C. Ward, and Norman H. Altman, eds.:
Spontaneous Animal Models of Human Disease, Volume 1, 1979; Volume II, 1979

Henry J. Baker, J. Russell Lindsey, and Steven H. Weisbroth, eds.:
The Laboratory Rat, Volume I: Biology and Diseases, 1979; Volume II: Research Applications, 1980

Henry L. Foster, J. David Small, and James G. Fox, eds.:
The Mouse in Biomedical Research, Volume I: History, Genetics, and Wild Mice, 1981; Volume II: Diseases, 1982; Volume Ill: Normative Biology, Immunology, and Husbandry, 1983; Volume IV: Experimental Biology and Oncology, 1982

James G. Fox, Bennett J. Cohen, and Franklin M. Loew, eds.:
Laboratory Animal Medicine, 1984

G. L. Van Hoosier, Jr., and Charles W. McPherson, eds.:
Laboratory Hamsters, 1987

Patrick J. Manning, Daniel H. Ringler, and Christian E. Newcomer, eds.:
The Biology of the Laboratory Rabbit, 2nd Edition, 1994

B. Taylor Bennett, Christian R. Abee, and Roy Henrickson, eds.:
Nonhuman Primates in Biomedical Research, Volume I: Biology and Management, 1995; Volume II: Diseases, 1998

Dennis F. Kohn, Sally K. Wixson, William J. White, and G. John Benson, eds.:
Anesthesia and Analgesia in Laboratory Animals, 1997

James G. Fox, Lynn C. Anderson, Franklin M. Loew and Fred W. Quimby, eds.:
Laboratory Animal Medicine, 2nd Edition, 2002

Mark A. Suckow, Steven H. Weisbroth and Craig L. Franklin, eds.:
The Laboratory Rat, 2nd Edition, 2006

James G. Fox, Muriel T. Davisson, Fred W. Quimby, Stephen W. Barthold, Christian E. Newcomer and Abigail L. Smith, eds.:
The Mouse in Biomedical Research, 2nd Edition, Volume I: History, Wild Mice, and Genetics, 2007; Volume II: Diseases, 2007; Volume III: Normative Biology, Husbandry, and Models, 2007; Volume IV: Immunology, 2007

Richard E. Fish, Marilyn J. Brown, Peggy J. Danneman and Alicia Z. Karas, eds.:
Anesthesia and Analgesia in Laboratory Animals, 2nd Edition, 2008

Jack R. Hessler and Noel D.M. Lehner, eds.:
Planning and Designing Animal Research Facilities, 2009

Mark A. Suckow, Karla A. Stevens, and Ronald P. Wilson, eds.:
The Laboratory Rabbit, Guinea Pig, Hamster and other Rodents, 2011

Christian R. Abee, Keith Mansfield, Suzette Tardif and Timothy Morris, eds.:
Nonhuman Primates in Biomedical Research, 2nd Edition, Volume I: Biology and Management, 2012; Volume II: Diseases, 2012

Kathryn Bayne and Patricia V. Turner, eds.:
Laboratory Animal Welfare, 2012

Preface

Biomedical research using nonhuman primates continues to provide important insights into the pathogenesis and treatment of diseases that impact human health. In recent years, translational research has become an increasingly emphasized area in biomedical research. This emphasis on translating discoveries made in basic research into treatments that are useful to patients requires animal models that allow scientists to predict human responses. Nonhuman primates have long been recognized as important models for translational research due to their phylogenetic proximity to human beings and their similarity in responses to treatment and pathogenesis of disease when compared to patients subsequently observed in clinical trials. For these reasons, the American College of Laboratory Animal Medicine (ACLAM) recognized the need for an authoritative textbook on the biology, management, and diseases of nonhuman primates used in biomedical research.

The first edition of *Nonhuman Primates in Biomedical Research* was edited by B. Taylor Bennett, Christian R. Abee, and Roy V. Henrickson as part of the textbook series sponsored by the American College of Laboratory Animal Medicine. It was published in two volumes, *Biology and Management* (1995) and *Diseases* (1998). The completion of the first edition required more than 10 years to plan, develop, edit, and publish. It has served as a seminal text in the field because it provided readers with the collective knowledge of experts in veterinary medicine, laboratory animal medicine, comparative medicine, and primatology as these disciplines are applied to the care and use of nonhuman primates in biomedical research. The first edition is no longer in print and used copies have become collector's items selling for more than the original purchase price. This provided the Publications Committee of the American College of Laboratory Animal Medicine with strong justification to approve the development of this second edition of this important text.

Planning for the second edition of *Nonhuman Primates in Biomedical Research* began in 2006. Although much of the information in the first edition remains useful, there have been major advances in our understanding of the biology, veterinary medical care, pathology, and research uses of nonhuman primates. Planning for the second edition began with the return of Christian Abee as an editor followed by Keith Mansfield, Suzette Tardif, and Timothy Morris as co-editors.

The editors reviewed the first edition to determine those chapters that should be repeated with careful attention to chapters that required major revisions and those that required less extensive updating. The editors agreed that the text should have a more international perspective and chapters should be added that describe research areas in which nonhuman primates play a critical role. Therefore, this second edition has added chapters that provide a more international perspective on regulatory oversight of the care and use of nonhuman primates and chapters that describe important model systems and research areas. High-resolution color images have been included in this edition that illustrate gross and microscopic lesions characteristic of diseases of nonhuman primates. Color illustrations have also been included of imaging techniques that can be used in both clinical veterinary medical care and research applications.

The editors assembled an outstanding group of chapter contributors with many chapter authors from the first edition contributing once again. Chapter manuscripts were peer reviewed by experts in the respective subject areas. The reviewers of chapters provided a very important contribution by helping to make certain that chapters were accurate and fair in their review of the subject areas. Reviewers are listed in each respective volume, but are not identified with the specific chapter they reviewed.

Nonhuman Primates in Biomedical Research 2nd edition provides a comprehensive and current review of the collective knowledge of the biology, management, diseases, and research uses of nonhuman primates. The information in these volumes will be useful to clinical veterinarians, veterinary pathologists, primate caregivers and colony managers, scientists who work with nonhuman primates, and others who wish to know more about nonhuman primates.

Chris Abee, Keith Mansfield, Suzette Tardif, and Timothy Morris

Acknowledgments

There are many people deserving of recognition for their many hours of dedicated service in planning, developing, and editing *Nonhuman Primates in Biomedical Research* 2nd edition. The editors wish to thank Laura Zapalac and Jennifer Kurtz at the Michale E. Keeling Center for Comparative Medicine and Research of the University of Texas MD Anderson Cancer Center for the many hours they devoted to scheduling editors' conference calls, maintaining spreadsheets that allowed the editors to follow the progress of each chapter through the arduous process of composition, chapter review, authors' revisions, first copyedit, and finally, submission of each chapter to Elsevier. We are also grateful to Rachel Tardif for her outstanding efforts in the initial copyedit of most of the chapters. Her work allowed the editors to identify and correct mistakes in chapter manuscripts prior to final copyediting by Elsevier. The editors want to give special thanks to Mary Preap at Elsevier for her gentle pressure to keep us as close as possible to our deadlines and her timely responses to the book editors' questions and requests. And finally, I would like to thank my co-editors, Keith Mansfield, Suzette Tardif, and Tim Morris for their tireless efforts to make certain that this second edition of *Nonhuman Primates in Biomedical Research* met the high standard expected of the American College of Laboratory Animal Medicine "Blue Book" series. The completion of this second edition was truly a team effort and a team accomplishment of the chapter contributors, the chapter reviewers, the book editors, administrative staff, and the staff at Elsevier.

Chris Abee

Reviewers

Karyn L. Armstrong Covance Research Products, Inc., Alice, TX

Lynne M. Ausmann Tufts University, Jean Mayer USDA Human Nutrition Research Center on Aging, Boston, MA

Michael B. Ballinger Amgen, Inc., Thousand Oaks, CA

Kathryn Bayne Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International, Frederick, MD

Mollie Bloomsmith Emory University, Yerkes National Primate Research Center, Atlanta, GA

Rudolf P. Bohm, Jr. Tulane University, Tulane National Primate Research Center, Covington, LA

Kathleen M. Brasky Southwest National Primate Research Center, Texas Biomedical Research Institute, San Antonio, TX

William E. Britz, Jr. Britz & Company, Wheatland, WY

Hannah Buchannan-Smith University of Stirling, Psychology, School of Natural Sciences, Scotland, UK

Thomas M. Butler Retired, Fair Oaks Ranch, TX

John Capitanio University of California, Davis, Department of Psychology, Davis CA

William Cole Retired, Lansdale, PA

Lita Drobatz GlaxoSmithKline (GSK) Pharmaceuticals, King of Prussia, PA

Bennett Dyke Retired, San Antonio, TX

Marisa Elkins St. Claire National Institutes of Health, National Institute of Allergy and Infectious Diseases, Rockville, MD

James J. Elliott Texas A&M University, Comparative Medicine Program, College Station, TX

Lynn Fairbanks University of California at Los Angeles, Semel Institute, Los Angeles, CA

John Finch Charles River Laboratories, Edinburgh, UK

John Fleagle Stony Brook University, Department of Anatomical Sciences, Stony Brook, NY

Jeffrey D. Fortman University of Illinois at Chicago, Biologic Resources Laboratory, Chicago, IL

Margaret H. Gilbert Tulane University, Tulane National Primate Research Center, Covington, LA

Colin Groves Australian National University, Canberra, ACT, Australia

Patrick W. Hanley The University of Texas MD Anderson Cancer Center, Michale E. Keeling Center for Comparative Medicine and Research, Bastrop, TX

Robert F. Hoyt National Institutes of Health, National Heart, Lung and Blood Institute, Bethesda, MD

Denis Lambrights GlaxoSmithKline (GSK) Biologicals, Rixensart, Belgium

Judy MacArthur-Clark Animals in Science Regulation Unit, Home Office, London, UK

Christopher L. Medina Abbott Laboratories, Comparative Medicine, Abbott Park, IL

Yasmina A. Paramastri Vanderbilt University Medical Center, Department of Pathology, Microbiology and Immunology, Nashville, TN

Sulli J. Popilskis New York Medical College, Department of Comparative Medicine, Valhalla, NY

Wendy Saltzman University of California at Riverside, Department of Biology, Riverside, CA

Michael Schillaci University of Toronto, Department of Anthropology, Toronto, Ontario, Canada

Mårten K.J. Schneider University Hospital of Zurich, Laboratory of Vascular Immunology, Division of Internal Medicine, Zurich, Switzerland

Mary Schneider University of Wisconsin-Madison, Departments of Kinesiology (Occupational Therapy Program) and Psychology, Madison, WI

M. Michael Swindle Medical University of South Carolina, Department of Comparative Medicine, Charleston, SC

Maureen Thompson Emory University, Yerkes National Primate Research Center, Atlanta, GA

Duane Ullrey Michigan State University, Departments of Animal Science and Fisheries & Wildlife, East Lansing, MI

Gary L. White The University of Oklahoma Health Sciences Center, Comparative Medicine, Oklahoma City, OK

Gregory K. Wilkerson The University of Texas MD Anderson Cancer Center, Michale E. Keeling Center for Comparative Medicine and Research, Bastrop, TX

Lawrence E. Williams The University of Texas MD Anderson Cancer Center, Michale E. Keeling Center for Comparative Medicine and Research, Bastrop, TX

Roman F. Wolf The University of Oklahoma Health Sciences Center, Comparative Medicine, Oklahoma City, OK

Simon Young AstraZeneca, Alderley Park, Cheshire, UK

Marcus Young Owl California State University, Long Beach, Department of Anthropology and Biological Sciences, Long Beach, CA

Contributors

Mark G. Baxter Friedman Brain Institute, Mount Sinai School of Medicine, New York, USA

Kathryn Bayne AAALAC International, Frederick, MD

Irwin S. Bernstein Department of Psychology, University of Georgia, Athens, GA

James L. Blanchard Comparative Medicine Program, Tulane University, Covington, LA

Mollie A. Bloomsmith Yerkes National Primate Research Center, Atlanta, GA

Rudolf P. Bohm, Jr Division of Veterinary Medicine, Tulane National Primate Research Center, Covington, LA

Saverio Capuano Wisconsin National Primate Research Center, Madison, WI

Angela Carville New England Primate Research Center, Southborough, MA

Donna J. Clemons Abbott Laboratories, Comparative Medicine, Abbott Park, IL

Kristine Coleman Oregon National Primate Research Center, Beaverton, OR

David K.C. Cooper Thomas E. Starzl Transplantation Institute, Department of Surgery, University of Pittsburgh, Pittsburgh, PA

Carolyn M. Crockett National Primate Research Center, University of Washington, Seattle, WA

David Elmore Charles Rivers Laboratories, San Diego, CA

Paul A. Flecknell Comparative Biology Centre, The Medical School, The University of Newcastle, Newcastle-upon-Tyne, UK

Elizabeth W. Ford The Scripps Research Institute, LaJolla, CA

Margaret H. Gilbert Division of Veterinary Medicine, Tulane National Primate Research Center, Covington, LA

James C. Ha National Primate Research Center, Department of Psychology, University of Washington, Seattle, WA

Dennis O. Johnsen Port Townsend, WA

David K. Johnson Cascade Biosciences Consultants, Inc., Sisters, OR

Stephen T. Kelley Department of Comparative Medicine, University of Washington, Seattle, WA

Brian J. Kelly Behavioral Sciences Department, Fitchburg State University, Fitchburg, MA

Liz Koutsos Mazuri Exotic Animal Nutrition, PMI Nutrition International LLC, St Louis, MO

Joshua A. Kramer New England Primate Research Center, Harvard Medical School, Southborough, MA

Vince Meador Anatomic and Clinical Pathology, Integrated Science and Innovation, Covance Laboratories Inc., WI

Jerrold S. Meyer Department of Psychology, University of Massachusetts, Amherst, MA

Nancy Minugh-Purvis Department of Pathology and Laboratory Medicine and Office of Professional Studies in the Health Sciences, Drexel University College of Medicine, Philadelphia, PA

Kathy L. Murphy Friedman Brain Institute, Mount Sinai School of Medicine, New York, USA

Timothy H. Morris The School of Veterinary Medicine and Science, The University of Nottingham, Leicestershire, UK

Marek A. Niekrasz Animal Resources Center, University of Chicago, Chicago, IL

Melinda A. Novak Department of Psychology, University of Massachusetts, Amherst, MA

Michael L. Power Nutrition Laboratory, Smithsonian Conservation Biology Institute, National Zoological Park, Washington, DC

Karen Rice Southwest National Primate Research Center, Texas Biomedical Research Institute, San Antonio, TX

Kasi E. Russell-Lodrigue Division of Veterinary Medicine, Tulane National Primate Research Center, Covington, LA

Steven J. Schapiro The University of Texas MD Anderson Cancer Center, Bastrop, TX

David Glenn Smith Department of Anthropology and California National Primate Research Center, University of California, Davis, CA

Suzette Tardif Barshop Institute of Longevity & Aging Studies, University of Texas Health Science Center, San Antonio, TX

Barbara Toddes Philadelphia Zoo, Philadelphia, PA

Jean E. Turnquist Department of Anatomy and Neurobiology, University of Puerto Rico Medical School, San Juan, Puerto Rico

Robert Wagner Division of Laboratory Animal Resources, University of Pittsburgh, Pittsburgh, PA, USA

Alex Wakefield Covance Laboratories Inc., Greenfield, IN

Craig L. Wardrip Animal Resources Center, University of Chicago, Chicago, IL

James L. Weed Division of Veterinary Resources, National Institutes of Health, Bethesda, MD

Gerhard F. Weinbauer Developmental and Reproductive Toxicology, Covance Laboratories, Kesselfeld, Muenster, Germany

Gary L. White The University of Oklahoma Health Sciences Center, Comparative Medicine, Oklahoma City, OK

Robert A. Whitney, Jr. RADM (0–8 Retired), US Public Health Service, Steilacoom, WA

Lawrence E. Williams Michale E. Keeling Center for Comparative Medicine and Research, Department of Veterinary Sciences, The University of Texas MD Anderson Cancer Center, Bastrop, TX

Roman F. Wolf The University of Oklahoma Health Sciences Center, Comparative Medicine, Oklahoma City, OK

Contents

Chapter 1

History of the Use of Nonhuman Primates in Biomedical Research

Dennis O. Johnsen*, David K. Johnson† and Robert A. Whitney, Jr‡

*Port Townsend, WA, †Cascade Biosciences Consultants, Inc., Sisters, OR, ‡RADM (0–8 Retired), US Public Health Service, Steilacoom, WA

Chapter Outline

Nonhuman Primates in Biomedical Research. DOI: 10.1016/B978-0-12-381365-7.00001-7

HUMAN AND NONHUMAN PRIMATES TO 1960

Roots of Modern Primatology

Nonhuman primates probably first became valuable to humans as pets, but they are also the oldest recorded animal subjects for scientific research (Hill, 1977). Nonhuman primate pet trading is known to have occurred in Egypt as long as 5000 years ago (Morris and Morris, 1966); their use for medical purposes came somewhat later, although still in respectably ancient times. Galen (130–200 AD) did anatomical studies on animals including monkeys (Cohen and Loew, 1984) and Vesalius (1514–1564) used barbary apes (*Macaca sylvanus*) in his studies of circulatory anatomy (Morris and Morris, 1966; Kavanaugh and Bennett 1984; Loeb et al., 1989). Ruch (1941) has also documented that monkeys and apes were studied from ancient times through the middle ages by Hanno, Aristotle, Pliny the Elder, Pliny the Younger, Petrus, Candidus, and others.

Darwin's research on evolution and particularly his notes on the behavior of the gorilla established his credentials as one of the first observational primatologists (Darwin, 1871). Also late in the 19th century, the British physician David Ferrier conducted comparative neuroanatomy studies of apes and monkeys (Morris and Morris, 1966). During the same time period, Pasteur discovered that the passage of the rabies virus through monkeys caused it to lose its virulence for dogs (Pasteur et al., 1884a,b). Some 20 years later, poliovirus was isolated by inoculating spinal cord material collected from fatal human cases intraperitoneally into monkeys (Landsteiner and Popper, 1908, 1909). The primatological knowledge that was generated came largely from relatively few behavioral and biomedical investigators working independently. With the institutionalization of nonhuman primate research, a profound change became possible.

First Primate Centers

Soviet Institute of Experimental Pathology and Therapy

According to Held and Gay (1983) and Lapin (1983), the first Commissar of Health in the USSR was persuaded by Mechnikov, a pioneer of modern Soviet experimental primatology, to establish a primate breeding station in 1923. Located in Sukhumi on the subtropical shores of the Black Sea in the then Soviet State of Georgia, the station was intended to be a quarantine, breeding, and holding center for nonhuman primates and to support a network of 50 medical and biomedical research institutions. It began operations in 1927 when it received the first shipment of hamadryas baboons (*Papio hamadryas*) and chimpanzees (*Pan troglodytes*) from Africa. At first, captive breeding was unsuccessful. However, there was improvement as experience in maintaining and breeding nonhuman primates was gained. Charting a course that has been followed elsewhere, activities of the Sukhumi station's service gradually expanded to encompass initiatives in independent research. In 1957, now under the auspices of the Academy of Medical Sciences of the USSR, the station became the Institute of Experimental Pathology and Therapy (IEPT) in recognition of its status as a full-fledged research institution. By 1990, the IEPT had production colonies of over 7000 animals consisting primarily of baboon and macaque species, a staff of about 1000 people, and research programs focusing on oncology, physiology, biochemistry, infectious diseases, and the biology of nonhuman primates (B. A. Lapin, personal communication, 1990). The institute also served as a principal source of nonhuman primates for the Virology Institute in Moscow and the Russian space program. It was also an international resource with productive research links to medical scientists in the USA and elsewhere (Figure 1.1).

The secession of Georgia from the former Soviet Union and the disturbances associated with the declaration of independence of Abkhazia seriously disrupted continued operations in Sukhumi. These problems forced completion in 1992 of a move of less than 100 miles to a satellite site in Russia near the city of Adler (D. M. Bowden, personal communication, 1993). Despite this adversity, the institute, now the Institute of Medical Primatology of the Russian Academy of Medical Sciences, remains not only one of the largest nonhuman primate research centers in the world but one of the most enduring as well.

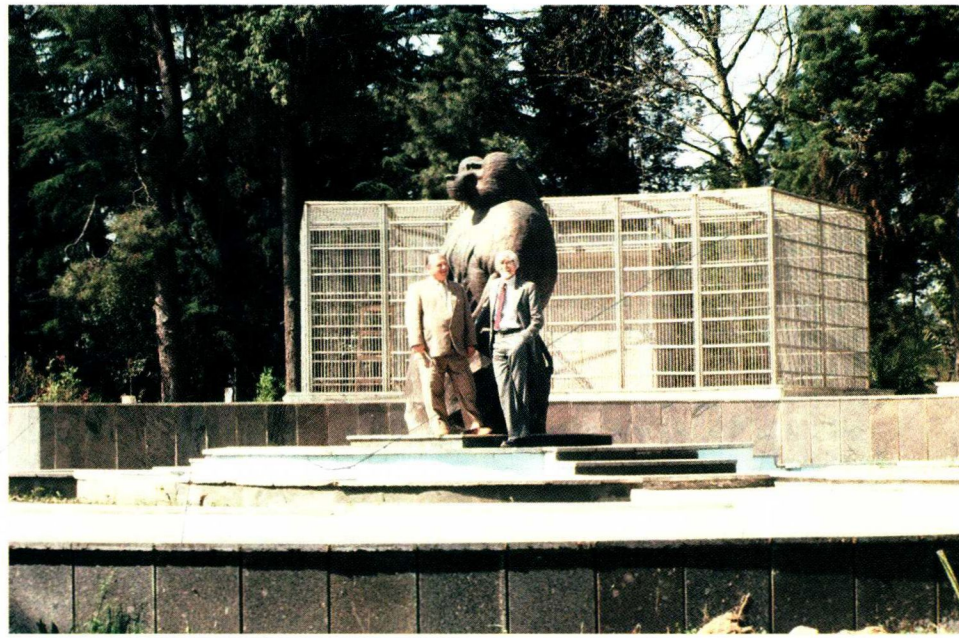


FIGURE 1.1 Drs Boris Lapin and Orville Smith at the IEPT in Sukhumi in 1987. Lapin, who became director of IEPT in 1958 and continued in that capacity after the move to Adler in 2010 had directed a major primate research center longer than anyone else. Smith was a longtime director of the Washington NPRC and studied the behavioral components of hypertension in baboons and collaborated extensively with investigators at IEPT and IMP.

Robert Yerkes and the Primate Laboratory of the Yale Institute of Psychobiology

Robert Yerkes, an accomplished comparative psychologist, had a vision for what the future held for nonhuman primate research and how to realize those dreams (Yerkes, 1916). Yerkes established the Primate Laboratory of the Yale Institute of Psychobiology at Orange Park, Florida, in 1930 (Bourne, 1971; Maple, 1979). His plan was to establish and develop "an institute of comparative psychobiology in which the resources of the various natural sciences should be used effectively for the solution of varied problems of life" (Yerkes, 1932). As early as 1919, he proposed the idea of establishing a nonhuman primate research institute for the systematic study of the "fundamental instincts" and "social relations" of nonhuman primates. Yerkes was a contemporary of other notable early investigators of the time such as Kohler and Kohts who were interested in nonhuman primate research (Maple, 1979). Interest in Kohts' perceptual and sensory work with chimpanzees in the Soviet Union may have contributed to the initiative for the establishment of the Sukhumi station (Yerkes, 1943).

Yerkes established his Orange Park station in 1930 with funds from Yale University and the Rockefeller and Carnegie Foundations. He received an initial gift of 13 chimpanzees from a breeding facility belonging to Rosalia Abreu in Cuba (Maple, 1979). The colony was expanded during the next several years with 16 additional chimpanzees from Africa, a gift from the Pasteur Institute. Laboratory studies were multi-categorical, encompassing neurophysiology, anatomy, pathology, nutrition, growth, and development (Bourne, 1971). Orange Park was the first organization of its kind in the western hemisphere.

In 1965, the laboratories in Orange Park were moved to Atlanta, Georgia, and the animals were re-established in the new Yerkes Regional Primate Research Center of Emory University.

Cayo Santiago and the Caribbean Primate Research Center

Clarence Ray Carpenter, a student of Yerkes and an accomplished field primatologist (Maple, 1979), has as one of his most enduring accomplishments the establishment of the Cayo Santiago Colony of rhesus monkeys. Rawlins and Kessler (1986) and Kessler (1989; M. J. Kessler, personal communication, 2007) have provided extensive accounts of the history of the Cayo Santiago Colony. Much of the following historical information is derived from those accounts.

Carpenter formulated plans in the early 1930s for establishing a population of both gibbons and rhesus macaques on an island in the American tropics. The possibility of conducting both behavioral and biomedical research on an island colony was basic to those plans. He interested a number of people, including the staff of Harvard's Museum of Comparative Zoology, the faculty of Columbia University's College of Physicians and Surgeons,

and the Columbia University/University of Puerto Rico's (UPR) School of Tropical Medicine in San Juan (later to become the UPR School of Medicine), in a planning effort. He selected Cayo Santiago, a 15.2-hectare (approximately 38-acre) island one kilometer off Puerto Rico's eastern coastal town of Humacao that was donated to the university by a wealthy Puerto Rican sugar cane and banking family.

With the help of a $60 000 grant from a private foundation, Carpenter set off for Indochina and India in 1938. He fared well in collecting the desired number of macaques. Survival of the 47-day sea voyage from Calcutta with the caged animals shipped as deck cargo was a testimonial to the enduring qualities of rhesus monkeys as well as to the care that they received. In late 1938, he released 409 rhesus monkeys, 14 gibbons, and three pig-tailed macaques on Cayo Santiago. Eventually only the rhesus monkeys remained.

Maintenance of the island and breeding were not without problems. Local fruits and vegetables did not provide an adequate diet and malnutrition was overcome only by feeding fox chow, the early precursor to monkey chow. Wells were dug, but the water was brackish. Cisterns and a system for collecting rainwater had to be constructed. A number of monkeys were lost through fighting or being denied access to feed by other animals. Under this pressure, some monkeys even escaped by swimming to the mainland. Various diseases also took their toll, but persistent efforts were successful in eventually eliminating tuberculosis.

Another problem was the lack of dependable financial support. In 1947, the UPR, which had assumed full responsibility for the project, actually offered it free to any institution that would support it. In 1948, a Puerto Rican neuroanatomist from the University of Michigan came to the rescue and succeeded in getting a $5000 grant to support his research and the colony as well. This was the first of many federal awards and marked the beginning of sustained federal support. In 1956, Cayo Santiago was incorporated into the NIH Institute of Neurological, Communicative Disorders, and Stroke's (NINCDS) Laboratory of Perinatal Physiology. The work of the laboratory focused on finding the cause and cure for neonatal asphyxia using rhesus monkeys as research models.

At the closure of the laboratory in 1970, the Cayo Santiago colony became a part of the UPR Medical Science campus's Caribbean Primate Research Center. The colony on Cayo Santiago has remained a favored site for naturalistic behavioral and noninvasive biomedical research for almost 70 years (Figure 1.2). It has also provided an extensive database on rhesus monkey genetics, thousands of rhesus monkey skeletons in the CRPC's osteological collection, and genetically well-defined animals that have provided founder stock for starting new breeding colonies at the center and elsewhere.

FIGURE 1.2 A male rhesus monkey patrolling his territory on Puerto Rico's Cayo Santiago Island, Caribbean Primate Research Center. Cayo Santiago is the longest standing primate breeding and research resource in the western hemisphere. The monkey is likely a direct descendant of Indian origin breeding stock that was introduced to the island by Ray Carpenter in 1938. *(Photo courtesy of R.G. Rawlins@rgrstockphoto.com)*

Virological Research in Nonhuman Primates

General

Technically, the modern use of nonhuman primates in biomedical research had its origins in Pasteur's work with rabies and the studies of others with smallpox and vaccinia in the late 1800s. Kalter and Heberling (1971) and Gerone (1974) have provided comprehensive reviews of virological research in nonhuman primates, including work on yellow fever and a variety of encephalitis viruses through the 1930s.

Polio

The Nobel prizewinning achievement of Landsteiner and Popper (1908, 1909) in isolating poliovirus in Vienna provided the real beginning of serious and widespread use of nonhuman primates in biomedical research. The unique susceptibility of nonhuman primates to this relatively new and frightening disease threat clearly established their special importance in research.

The intense efforts to develop a vaccine against polio that followed were unprecedented. They spanned the next 45 years, were international in scope, and involved a host of major investigators. However, it was a complex process that experienced serious setbacks. There were some promising early findings based on nonhuman primate studies using