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SERIES ON FERTILITY REGULATION

NANCY J. ALEXANDER

ANIMAL MODELS
FOR RESEARCH
ON CONTRACEPTION
AND FERTILITY

Animal Models for Research on Contraception and Fertility

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May 8-10, 1978

FOREWORD

There is little question that much of the progress in contraceptive research during the past 20 years has resulted from animal investigations. As fertility research becomes a greater political and scientific priority, more intensive laboratory research will be necessary if we are to improve and refine available contraceptive methods and to develop new approaches to fertility control that are safe, effective, acceptable, and inexpensive. At the present time, many public and private agencies have programs for contraceptive development and fertility research that rely heavily on animal studies.

The Program for Applied Research on Fertility Regulation (PARFR) provides scientific and technical assistance and financial support for contraceptive and fertility research. The program was established in 1972 at the University of Minnesota, in association with the United States Agency for International Development (USAID); in 1975 it moved to its present location at Northwestern University in Chicago. The primary objective of the program is applied research with the goal of developing safe, effective, and acceptable methods of fertility regulation, with particular emphasis on techniques suited to conditions and needs of individuals, as well as fertility control programs in developing countries. The program coordinates activities and utilizes the resources of other national and international agencies in order to carry out a scientific mission that complements, without unnecessary duplication, existing research programs. Specific PARFR efforts are directed toward the encouragement of relevant research and the funding of applied research projects in the United States and abroad.

Since 1972, PARFR has funded research projects in the following areas of fertility control: self-administered methods, long-acting female methods, non-surgical male methods, intrauterine delivery systems, postcoital and postovulatory methods, and female and male sterilization. In all of these areas, animal research occupies a significant role. Nonhuman primates have been particularly helpful in the elucidation of the efficacy and safety of new contraceptive methods prior to the initiation of studies in human volunteers.

In the past several years PARFR has organized and conducted scientific workshops on selected topics of fertility control. The intent of these workshops is to inform interested investigators of advances in research and to provide for discussion. In addition, these workshops have provided PARFR, AID, and other agencies with information on the directions of future research. Previous workshops have covered the following: hysteroscopic sterilization, the control of male fertility, advances in female sterilization techniques, risks as well as benefits and controversies in fertility control, reversal of sterilization, and pregnancy termination. The present program focuses on the importance of laboratory animals in contraceptive and fertility research. The choice of the appropriate animal for a particular study is an important investigative consideration. This symposium should aid in the

identification and evaluation of applications for currently available animal models for contraceptive research.

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PREFACE

For almost any study in reproduction and contraception, the use of animal models is a necessity not only in the testing of hypotheses but also in the development and testing of particular therapies before human clinical trials are begun. Since those interested in the field of reproduction come from diverse backgrounds, we hope that this volume may provide some guidance for the selection of a particular animal for a specific research project. In this regard, no animal can be ideal or universally suited to all areas of investigation, but particular species are individually suited for specific research objectives. To that end, this book contains an appendix which compares biologic and physiologic data from a variety of commonly used laboratory animals. A second goal of this book is to examine environmental and physiologic factors that can influence the suitability of various species for studies on reproduction. One paper will discuss how reproductive hormone levels can be altered simply by handling the animals at different times during the day or night. A second author shows that the position in utero can affect adult behavior even in an inbred strain of rats. We hope that such examples will encourage investigators to be more careful both in the design and interpretation of their experiments.

The book is divided into sections: (I) Factors that affect studies in reproduction, (II) Comparative aspects of reproductive processes, (III) Use of animal models for research on contraception and reproduction, (IV) Animal models for specific research questions, (V) Techniques applied to reproduction, (VI) Appendix. Some of the papers may express controversial view-points on the choice of models or appropriate research techniques. It is important that such differences in scientific opinions be aired so that further studies can provide a resolution to such questions.

An animal model is defined as a living organism with inherited, naturally acquired, or induced conditions useful for studies of phenomena occurring in man. Although animal models rarely provide final answers, they frequently offer an approximation of human conditions. Claude Bernard* (1927) has stated that without the use of comparative studies on animals, practical medicine could never acquire a scientific character; without the existence of animals, man's nature would be incomprehensible from the physiologic, pathologic, and therapeutic point of view.

In reproductive studies, investigators must remember 1) that people are slowly maturing creatures with a relatively long gestation period, a long life span, and few offspring and 2) that, because human beings are independent, one cannot control their environment and actions. Furthermore, in many cases it is not feasible to do studies on human beings because of the potential detrimental effects. Therefore, it is imperative that studies be done on animals with specific qualities that will provide information more rapidly and efficiently.

* Bernard C: *An Introduction to the Study of Experimental Medicine*. (Translated by H. C. Greene.) Riverside, NJ, Macmillan, 1961

The broad objectives of the National Research Council and its parent organization, the National Academy of Sciences, are to stimulate research and its application, to survey the broad possibilities of science and technology, to promote effective utilization of the scientific and technical resources of the country, and further the general interest of science. Within this framework, the Institute of Laboratory Animal Resources works to enlighten the research animal scientist, veterinarian, technician, and supplier and has—among others—specific aims of improving the supply of laboratory animals and the collection and dissemination of information on animals best suited for specific types of investigations. Hence, its sponsorship of this Symposium.

We would like to take this opportunity to recognize the special efforts of Drs. Michael Free, Gilbert Greenwald, Edward Mather, and Dolores Patanelli in preparing this volume and of Janina Ely, editor at the Oregon Regional Primate Center. We appreciate also the effective contributions of Nancy Muckenhirn and her associates on the ILAR staff.

Nancy J. Alexander, Chairman
Committee on Animal Models
of Fertility and Contraception

NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the Councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

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CONTENTS

Foreword by John J. Sciarra	ix
Preface	xi
 Part I. Factors That Affect Studies in Reproduction	 1
Obtaining and Caring for Research Animals <i>Charles McPherson</i>	2
Potential Sources of Variation Affecting Studies on Pituitary-Gonad Function <i>Claude Desjardins</i>	13
Circadian Mechanisms in Reproduction <i>Albert H. Meier, Nelson D. Horseman</i>	33
Control of Reproduction in Natural Populations <i>John J. Christian</i>	46
Animal Models in the Endocrinology of Reproductive Behavior <i>Julian M. Davidson, Gary D. Gray, Erla R. Smith</i>	61
 Part II. Comparative Aspects of Reproductive Processes	 83
Comparative Aspects of the Organization of the Testis and Spermatogenesis <i>Don W. Fawcett</i>	84
Accessory Sex Organs and Fluids of the Male Reproductive Tract <i>Ian G. White</i>	105
Animal Models in the Study of the Central Nervous System Regulation of Gonadotropin Secretion in the Female <i>Charles A. Barraclough, Phyllis M. Wise</i>	124
In Vivo Determination of Progesterone Production Rates <i>Rosemarie B. Thau</i>	142

Comparative Study of Mammalian Glycoprotein Hormones	151
<i>Darrell N. Ward, William T. Moore, Jr</i>	
The <i>In Vivo</i> Metabolism of Progestins: VI. Species Differences in the Metabolic Clearance Rate of Medroxyprogesterone Acetate and 6α-Methylprogesterone	165
<i>C. Wayne Bardin, Neal A. Musto, Peter D. Feil, Leslie P. Bullock</i>	
• Comparative Aspects of Antral Follicular Development During the Menstrual and Estrous Cycle	176
<i>Gilbert S. Greenwald</i>	
• Folliculogenesis in Primates: Process of Maturation and Atresia	187
<i>Marilyn J. Koering</i>	
Comparative Aspects of Gamete Transport in Mammalian Oviducts	200
<i>Richard J. Blandau</i>	
Fertilization and Blastocyst Formation	223
<i>John D. Biggers</i>	
Implantation	238
<i>Harry M. Weitlauf</i>	
 Part III. Use of Animal Models for Research on Contraception and Reproduction	 253
• In Vitro Assessment of Sperm Fertilizing Ability	254
<i>Benjamin G. Brackett</i>	
• Some Caveats of Mammalian Gamete Research	269
<i>J. M. Bedford</i>	
Fertility Regulation with Hormonal Antigens: Models for Evaluating Immunologic Methods	284
<i>Vernon C. Stevens</i>	
Immunobiology of Reproduction	300
<i>John E. Castro</i>	
Studies on the Antigenicity of the Zona Pellucida	314
<i>C. Alex Shivers</i>	
• The Effects of Chemicals on Spermatogenesis and Epididymal Maturation of Spermatozoa: Experimental Principles	326
<i>Larry L. Ewing, Robert J. Adams, Roger C. Cochran</i>	

Part IV. Animal Models for Specific Research Questions	345
Nonmammalian Models in Reproduction Research	346
<i>Ian P. Callard, Gloria V. Callard, Valentine Lance</i>	
Prolactin-Deficient Mice	360
<i>Andrzej Bartke</i>	
Androgen Insensitivity (Testicular Feminization) in Mice and Rats	366
<i>Leslie P. Bullock</i>	
The H^{re} Rat: A Model for Late Onset Seminiferous Tubule Failure in Man	372
<i>Neal A. Musto, Richard J. Santen, Claire Huckins, C. Wayne Bardin</i>	
Studies on Mammalian Spermatogenesis: The Baboon—A Model for the Study of Human Spermatogenesis	385
<i>Ajit K. Chowdhury</i>	
Changes in the Cervical Mucus of the Bonnet Monkey (<i>Macaca radiata</i>) During the Menstrual Cycle	396
<i>Nasir-ud-Din, Janet W. McArthur, Roger W. Jeanloz</i>	
Models for Cervical Transport of Spermatozoa	404
<i>Borje K. Gustafsson, Mushtaq A. Memon</i>	
Swine for <i>In Vivo</i> Studies on Capacitation	410
<i>Eric D. Clegg</i>	
A Comparison of Lemur Ovarian Cycles	417
<i>B. L. Lasley, Mark H. Bogart, Susan E. Shideler</i>	
Primate Models for Pregnancy Hormone Secretion in Man: Fetal, Maternal, and Placental Factors	425
<i>Gary D. Hodgen</i>	
Bats as Models in Studies on Folliculogenesis, Menstruation, Early Pregnancy, and Sperm Survival	437
<i>John J. Rasweiler IV</i>	
Armadillos for Studies of Delayed Implantation, Quadruplets, Uterus Simplex, and Fetal Adrenal Physiology	447
<i>B. L. Lasley, Nancy M. Czekala, Kay C. Nakakura, Susan G. Amara, Kurt Benirschke</i>	

Endocrine and Morphologic Effects of Pinealectomy in White-Tailed Deer	452
<i>Edward D. Plotka, U.S. Seal, Marc A. Letellier, Louis J. Verme, John J. Ozoga</i>	
Animal Model for Fallopian Tube Blockade	467
<i>Ralph M. Richart, Robert S. Newwirth</i>	
Choice of Animal Models for Oral Contraceptive Research	471
<i>Richard A. Edgren</i>	
Models for Vasectomy	475
<i>Linda L. Kosuda</i>	
 Part V. Techniques Applied to Reproduction	 479
Cannulation Techniques for Collection of Blood and Other Body Fluids	480
<i>Michael J. Free, Richard A. Jaffe</i>	
The Determination of Blood Flow in Reproductive Organs	496
<i>Richard A. Jaffe, Michael J. Free</i>	
Methods of Semen Collection	510
<i>George E. Seidel, Jr</i>	
Freezing of Spermatozoa	521
<i>B. G. Crabo, E. F. Graham</i>	
Preservation of Mammalian Germ Plasm by Freezing	528
<i>Peter Mazur</i>	
Techniques for the Prospective and Retrospective Diagnosis of Ovulation	540
<i>C. J. Mahoney</i>	
Ovarian Function as Measured by Milk Steroid Assays	552
<i>Edward C. Mather</i>	
 Part VI. Appendix	 559
<i>Edward C. Mather, R. Allen Rushmer</i>	
Participants and Contributors	577
Index	587

***FACTORS THAT AFFECT
STUDIES OF REPRODUCTION***