THIRD EDITION

Reproductive Physiology of Mammals and Birds

A. V. Nalbandov

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The Comparative Physiology of Domestic and Laboratory Animals and Man

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Preface

The physiology of reproduction is a composite science. For an understanding of the subject it is necessary to draw upon the accumulated knowledge of endocrinology, histology, embryology, anatomy, physiology, and genetics. To write a truly comprehensive treatise on reproductive physiology would require many volumes; such a work would be excellent for purposes of reference but unusable as a textbook. Accordingly, the present edition, like preceding editions, is limited to essential aspects of the subject. It was thought unnecessary to submerge the reader in the minutiae that are important to the mature specialist but distracting and puzzling to the beginner. This book allows the young scientist to become acquainted with the entire field and to decide for himself what is worth pursuing in detail.

The book emphasizes the diversity of the reproductive process by comparing the reproductive systems of different species. Quite often it is not possible to extrapolate from our knowledge of one species to another. It is becoming more and more apparent that much of the experimental work done on rats—hitherto the most widely used experimental animal—will have to be done over in order to be applicable to domestic animals or man.

Dr. Brian Cook of the Royal Infirmary, Glasgow, has written a new chapter on the chemistry of hormones involved in reproduction. This chapter includes a discussion of the theory and use of radioimmunoassay, a technique that is widely used at present.

I have followed the practice established in the previous editions of not documenting all statements (about 1,500 citations would be required to provide complete documentation). Although some readers have deplored the paucity of references, others feel that frequent citations of the literature are distracting. One instructor who uses this book requires his students to find documentation for statements that he considers important, and thinks that this practice is an excellent pedagogic device. I frequently cite the excellent articles on reproductive endocrinology published by the American Physiological Society in their *Handbook of Physiology* (Section 7). This work and the annual series *Recent Progress of Hormone Research* contain important new contributions as well as reviews by outstanding authorities in the field of reproductive endocrinology. Both are also an invaluable source of references to original research papers. A recent and unfortunate trend among younger colleagues is the tendency to ignore the older literature. As a result, their research frequently "rediscovers" phenomena that were recorded years ago. For this reason I have in many instances retained older data and references, in the hope that students will delve into the older literature.

Although comparisons between primates and nonprimates are frequently made in this book, experimental data for human reproduction are almost totally lacking. The reasons for this are the sanctions against purely experimental surgical incursions in humans, which makes them poor experimental subjects. Ovulation in ewes injected with an LH-releasing substance can be verified by actually counting the ova after laparotomy. On the other hand, results in women treated with an LH-releasing hormone must be inferred, and it is assumed that if blood progestin rises, ovulation has occurred. However, it is equally possible that the follicles may have luteinized without shedding the ovum.

Similarly, it is impossible to include large numbers of women or men of similar ages in single endocrine experiments, although this is routinely done with laboratory and domestic animals. For these reasons I have relied heavily on data from domestic and laboratory animals, without neglecting what I consider to be good data on human subjects.

As in previous editions I want to acknowledge the enormous debt I owe to the graduate students and postdoctoral fellows with whom I have worked, and who continue to provide stimulation both in the laboratory and in discussions. I gratefully acknowledge the help of Elizabeth Waldron in the preparation of this book.

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Introduction

The biological problem of the perpetuation of the species has been solved in a bewildering variety of ways in nature. Comparing across species one is struck by the diversity of reproductive systems and the comparative uniformity of other physiologic systems, such as respiration, digestion, and circulation. Evolution seems to have arrived at good solutions for some physiologic problems, modifying the basic principles only slightly or not at all in the species; by contrast, the reproductive process has been drastically modified in some species. As we shall see, these modifications extend from the anatomy of the female reproductive system to the neuroendocrine mechanism controlling reproduction. (Curiously, the evolutionary modification of reproductive processes is largely restricted to females; reproduction in males is remarkably uniform across species.)

The assumption that reproduction is the most important physiologic function and that diversity maximizes the chance of success in the competition between species is not tenable. No one mechanism of reproduction has an advantage over another simply because *all* species, including the primitive platypus and the didelphians, have been more or less equally successful in maintaining themselves over the ages. Moreover, other physiologic systems are equally vital to the survival of the species; inadequate circulatory or digestive systems, for instance, would not even permit young members of a species to reach reproductive age.

Some scientists resist accepting diversity in reproductive systems, insisting instead on finding a unified scheme that would fit all mammals. The danger of this thinking is that one is tempted to generalize from studies of single species, a temptation to which many scientists have succumbed in the past. That this cannot be done will be frequently illustrated in this book. Readers should be alert to this fact and beware of making unwarranted generalizations.*

Because this book deals with mammals and birds, we shall be concerned mostly with sexual reproduction of the dioecious type. Nevertheless, asexual reproduction, in the general sense of the term, occurs even in mammals and birds; all processes of growth are basically due to the asexual fission of somatic cells.

The two sexes involved in dioecious reproduction are highly specialized. The degree of specialization is the result of the complex synchronization of reproductive events, which, as a rule, follow predictable, well-regulated patterns. The details of these patterns differ in various species. Reproductive events are regulated by a complex of interlocking hormone systems, which are themselves locked into a neural control system. The neurohormonal control system provides a maximum of checks that ensure a normal and well-balanced functioning of the end organs affected by hormones, and this in turn results in synchronization of the functions of the sex mechanism. The neuroendocrine system and the anatomy and physiology of the sex mechanisms, both of which are largely controlled by the neuroendocrine system, are the main subjects of this book.

The processes of reproduction occasionally decline in efficiency because one of the hormonal, neural, or humoral links becomes impaired, or because they function out of phase, disrupting the sensitive mechanism of synchronization that underlies most reproductive events. When this happens, partial or complete sterility results. Because of its importance in domestic animals and humans, sterility is discussed later in the book. First, however, we shall consider some of the basic concepts of sex, the anatomy of the reproductive system, and the hormonal and other signaling systems that have evolved in the different species. The

*For a more detailed discussion of diversity in reproduction see Nalbandov, "The Fourth Hammond Memorial Lecture. Puzzles of reproductive physiology." *J. Repro. Fert.*, 34:1, 1973.

rat, the elephant, and the chicken all face basically the same problems in reproducing the species. Eggs must be matured and shed, and a signal must be given to the male that the latter event is about to happen in order to ensure the presence of viable sperm. These and subsequent events, such as pregnancy, parturition, and lactation, or the incubation of eggs by birds, depend on humoral and neural feedback mechanisms that form chains of events. It is essential to remember that no reproductive event ever stands alone, that any one event is only one link in a chain. Although thinking in terms of chains of events rather than isolated phenomena may be difficult at first, such an approach is necessary to understanding reproductive phenomena.

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The Biology of Sex

This chapter briefly summarizes present thinking on the subject of sex ratios. (Students interested in details should consult the works of Lawrence and Crew, in that order.) Sex ratios deviate from equality frequently and significantly; this deviation may be caused by a variety of factors, such as genetic selection, season, age of dam, parity of dam, and frequency of ejaculation by the male. Because the internal and external environment influences sex ratios, it is incorrect to assume that the "normal" sex ratio must be 50/50. The sex ratios of dogs, pigs, cattle, and rodents are normally high; those of horses, sheep, and chickens are normally low. The origin of sex chromosome aneuploidy is discussed and it is pointed out that reproductive or endocrine disorders are very common in both men and women with the genotypes XXY or XO. Whether sex chromosome aneuploidy occurs in other animals as frequently as in man is not known. The sex chromatin serves as a diagnostic feature of the genetic sex of embryos before sex differentiation as well as of normal and intersexual adult mammals.

INTRODUCTION

The word "sex" comes from the Latin word *sexus*, which means division (from *secare*, to cut or separate). Sex is not a biological entity, but "the sum of the peculiarities of structure and function that distinguish a male from a female" (*Webster's New International Dictionary*, second edition). Not all populations can be divided into two distinct groups of males and females, especially if one uses only one or two external sex characters as the basis of division. Populations are actually composed of individuals differing to a greater or lesser degree in the sum of their peculiarities of structure and function. In some instances the sexes overlap completely, making it impossible to distinguish them externally. For a clearer understanding of the continuous variation between the sexes, we shall distinguish between *genotypic* and *phenotypic* sex.

GENOTYPIC SEX

Genotypic sex is determined by the sex chromosomes received from the parents (Table 1-1). In man much work has been done on the genotypic (chromosomal) sex of individuals who show endocrine (including reproductive) and mental disorders. In individuals showing the Klinefelter syndrome, which is characterized by gonadal hypofunction, the genotype is usually XXY (instead of XY); in those showing Turner's syndrome, which is characterized by gonadal agenesis or aplasia, the genotype is frequently XO rather than XY or XX.

These unusual genotypes of the sex chromosome complex are called *aneuploidy;* they are ascribed to errors in chromosome division occurring during meiosis. If as the result of nondisjunction both X chromosomes go to the ovum, fertilization by a sperm will lead to the formation of either an XXX or an XXY zygote (maternal nondisjunction). In paternal nondisjunction some sperm will be of the genotype XY and others will have no sex chromosome (O). Fertilization of eggs of a normal genotype will result in zygotes of either the XXY or XO genotypes. As already noted, such aneuploid individuals very frequently show gonadal or endocrine defects.

Similar studies in other animals are lacking, and it is not known how frequently aneuploidy of sex chromosomes occurs in them. It appears that cases of gonadal disfunction or gonadal aplasia seen in domestic animals may possibly be due to aneuploidy, unless the profit motive in

Table 1-1. Sex chromosomes in male and female mammals and birds

	TYPE OF CHROMOSOME IN GAMETES	PROPORTION OF CHROMOSOME IN GAMETES
Female mammal	X only	All eggs carry X
Male mammal	X and Y	Half of sperm carry X, half carry Y
Female bird	X and Y	Half of eggs carry X, half carry Y
Male bird	X only	All sperm carry X

animal breeding has resulted in the elimination from the breeding population of families prone to aneuploidy. Research along these lines would be of great theoretical and perhaps practical significance and might explain why intersexuality is so frequently seen in some species (goats and pigs), but rare in others.

PHENOTYPIC SEX

To some extent genotypic sex may be compared to a genetic character controlled by a single gene—it is an all-or-none character. With respect to sexuality, the "sum total of peculiarities of structure and function" is either male or female. This implies, and to some extent correctly, that the characteristics of "maleness" or "femaleness" are unalterably fixed when the sperm fertilizes the egg and are not subject to environmental modification, just as the genetic whiteness of an albino animal is not subject to environmental modification. Actually, the manifestation of sexuality is as variable as the somatic characters that are determined by multiple genes. This variability can be seen in the different degrees of masculinity or femininity normally found in a population. The degree of expression of one or the other sex is called phenotypic sex.

To explain how such an all-or-none character as sex can be subject to variability, C. B. Bridges advanced the *genic balance* theory of sex determination. This theory accepts the basic assumption that sex is determined at the time of fertilization by a combination of the sex chromosomes. In addition, the theory assumes that the autosomes carry genes for maleness and the sex chromosomes carry genes for femaleness. If the number of genes for maleness on the autosomes is large, then in the case of an XY male these genes overbalance the genes for femaleness carried on the sex chromosomes. Such a male may be phenotypically more masculine than a male that has received fewer maleness genes on its autosomes. It is postulated that though the XY type of sex determination is permanently fixed and is not subject to genetic variability