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Hormones and Sexual Behavior

Broad relationships exist between the gonadal hormones and behavior.

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Research on the relationships between the hormones and sexual behavior has not been pursued with the vigor justified by the biological, medical, and sociological importance of the subject. Explanation may lie in the stigma any activity associated with sexual behavior has long borne. In our experience, restraint has been requested in the use of the word *sex* in institutional records and in the title of research proposals. We vividly recollect that the propriety of presenting certain data at scientific meetings and seminars was questioned. Counteracting this deterrent is the stimulation which has come from colleagues in many disciplines to whom we have appealed for help, and the satisfaction we have felt in seeing a picture emerge as the pieces of the puzzle have been studied and fitted together.

Relationships in the Adult

Causal connections between gonadal hormones and the development of the capacity of infrahuman vertebrates to display sexual behavior have long been assumed, although the existence of such relationships in man is questioned (*1–3*). Doubt has also been expressed that a specific relationship exists between any one hormone (or class of hormones) and the behavior it facilitates in adults in general, from fish to man (*4–6*).

A number of explanations may be given for the uncertainty which exists. Human sexual activity is influenced by many psychologic factors, the social level, cultural background, and tradition. The many reports are not completely trustworthy. Physiological correlates with individual behavior are largely nonexistent, and controlled study in man as we know it in laboratory animals is impossible. In our opinion the many differences in behavior which in the growing child and adult are socially rather than hormonally determined have obscured the possible role of the hormones in maintaining the strength of the sexual drive. Even in lower mammals the same quantity of hormone elicits almost as many modes of response as there are individuals. This fact may have contributed to the doubt, to which we have alluded, that there is any great degree of hormonal specificity. In the human female, sexual responsiveness does not have the sharp relationship to folliculogenesis and to the functioning of the corpus luteum in the ovary that it does in most lower mammals (*7*). The degree to which this evolutionary change within the primates has been accompanied by an emancipation from the effects of hormonal action is not known.

The need for testicular androgen in the maintenance of sexual vigor in the male has been questioned by some students of the problem. In man (*5, 8*), the dog (*9*), the domestic cat (*10*), fishes (*6*), and birds (*11*), there is, in males, a persistence of sexual activity for some weeks or months after castration which has not been explained satisfactorily; a corresponding persistence is encountered rarely if at all in females below the primates. The restoration of sexual vigor by replacement therapy also requires weeks in the male and only hours or days in the female. The longer time lapse which occurs, regardless of the direction of hormonal change, suggests that the manner of hormonal action in the male is greatly different from that in the female rather than that the strength of sexual behavior is independent of the presence of testicular androgen.

Finally, in this brief consideration of the subject, there are the important studies of deviant sexual types by Hampson and Hampson (*1*), Money (*2*), and the recent report by Völkel (*3*). The data these clinical investigators collected led them to conclude that the establishment of gender role or psychologic sex can be independent of chromosomal sex, gonadal sex, hormonal sex, internal reproductive structures, and external genital morphology. They relate the process rather to "the many experiences of growing up, including those experiences dictated by his or her own bodily equipment" (*1*).

The interest of one of us (W.C.Y.) in the relationship of the hormones to

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sexual behavior goes back to an observation made during his graduate years at the University of Chicago when he was looking for signs that would be useful in the identification of female guinea pigs in heat. No active interest was taken, however, until more than 6 years later. During a lull at Brown University, Young, Hugh I. Myers, and Edward W. Dempsey, while waiting for what turned out to be the disapproval of an application for a small amount of money for work on the function of the epididymis, fell into a discussion of the abrupt and dramatic change that occurs in the behavior of the female guinea pig when she comes into heat. They wondered whether this change is associated with any structural change in the ovaries. Continuous day and night observation of the laboratory animals for several months was rewarded by the information Young and his co-workers were seeking. The beginning of heat was found to coincide closely with the beginning of the preovulatory growth phase of the Graafian follicle (*12*); it could be that the three investigators, none of whom had any training in psychology, had stumbled on the only spontaneously occurring macroscopic structural change associated with the alteration of a behavioral state in a mammal.

The reports that ovariectomized mice, rats, rabbits, and dogs copulated after the injection of follicular fluid or of the estrogens that were available at that time suggested that the same behavior would occur in the guinea pig. To the surprise of Young and his associates, irregular results were obtained. These led to the conclusion that a second substance must participate. With the help of Roy Hertz, who worked with the group that year, Dempsey took his cue as to the nature of this substance from the demonstration that the preovulatory growth phase in anestrous cats is stimulated by hypophyseal luteinizing hormone (*13*). Tests soon revealed that this gonadotrophin does not produce heat directly; they suggested that by stimulating preovulatory swelling, ovulation, and production of progesterone luteinizing hormone leads indirectly to the display of estrous behavior by animals previously injected with an estrogen (*14*). The progesterone as it turned out, was the second participating substance. Its synergistic action in combination with estrogens to bring latent mating behavior to expression has since been demonstrated in an impressive number of mammalian species (see *7*). Astwood (*15*) showed later that the hypophyseal gonadotrophin responsible for the production of progesterone is luteotrophin rather than luteinizing hormone.

Importance of Soma

The familiarity obtained with the behavior of the female guinea pig and later with that of the rat and male guinea pig revealed (i) that in repeated tests individual differences in behavior were remarkably consistent and reliable (*16, 17*); (ii) that in the female these differences, except perhaps for the male-like mounting behavior, are not related to the number of rupturing Graafian follicles (*18, 19*); and (iii) that in neither sex are the differences in the vigor of the behavior related to the quantity of administered hormones, provided of course a threshold has been exceeded (*17, 20*). These findings led to the realization that the nature of the latent behavior brought to expression by gonadal hormones depends largely on the character of the soma or substrate on which the hormones act (*19*). The substrate was assumed to be neural (*9*). Unknown to Young and his co-workers until 15 or 20 years later, Goodale (*21*) in 1918 had been impressed by the failure of ovaries implanted into capons to feminize their behavior and had written, "the character of sexual reactions seems to depend upon the substratum, while the gonad merely determines that it shall be given expression."

Factors Influencing Character of Soma

It follows from this principle that an investigator trying to account for the behavioral differences between individuals, instead of looking to the gonadal hormones, would do better to look to the factors which influence the character of the tissues on which these hormones act. The age of the animal was one of the first factors investigated, and data indicating that age is significant were obtained immediately. Responsiveness or reactivity of the tissues to injected gonadal hormones is lacking during early infancy and increases gradually to the level observed in the adult (*22, 23*).

The possibility of further changes as aging progresses has not been investigated. The thyroid was thought of as a factor influencing responsiveness, and Young and his co-workers found that female guinea pigs surgically thyroidectomized and given I^{131}, to suppress any accessory thyroid activity, ovariectomized, and injected with estradiol and progesterone were less responsive to the latter substances than control females (*24*). The many reports of the effects of thyroid hormone on the vigor of sexual behavior in the male are so contradictory (*7*) that prediction of the relation of this hormone to the animal's responsiveness to androgens, before adequately designed experiments have been carried out, would be unwise.

The belief that the genetic background is an influential determinant of the character of the soma was soon confirmed. Intact male and female guinea pigs of the highly inbred strains 2 and 13 exhibit significant differences in their behavior. The differences are displayed consistently after gonadectomy and injection of the same amounts of the appropriate hormones (*20, 23, 25*). The hereditary basis of sexual behavior was studied. For both male and female behavior a high degree of heritability was demonstrated. The inheritance is autosomal, of the sex-limited or sex-influenced type, and appears to be polygenic for most of the behavioral characteristics studied. Sexual behavior is not inherited as a unitary trait, and the elements composing the patterns of behavior show a surprising degree of independence of one another. In the male, phenotypic dominance of strain 13 was found for specific behavioral characteristics—for example, frequency of mounting. With respect to other characteristics, such as latency to ejaculation, strain 2 was dominant (*26*). In the female, the characteristics of frequent male-like mounting, vigorous lordosis, and responsiveness to injected estrogen appeared to have independent modes of inheritance and separate genetic bases (*27*).

Attention was drawn to the possibility that experiential or psychologic factors might have a role in the determination of the character of the soma by two young psychologists in the laboratory, Elliott S. Valenstein and Walter Riss, who could not accept the view that inheritance was accounting for the entire action. Again, the hunch was a good one. In a relatively short time after they directed their attention to the behavior of males raised in isolation from the day of birth, except for association with the mother, the necessity of contact with other animals for the ma-

Table 1. Loss of the ability of female guinea pigs to come into heat relative to the amount of androgen (testosterone propionate) injected in the prenatal period and to the length of the period of treatment.

Period of prenatal injection of androgen (days)	Total amount of androgen injected (mg)	Percentage failing to come into heat
15 to 30	40	0
15 to 40	50	12
15 to 45	55	36
15 to 60 +	70 +	27
20 to 65	70	45
25 to 40	40	23
30 to 45	40	67
30 to 55 or 65	50 or 60	92 or 91
35 to 65	55	60
40 to 65	50	33
50 to 65	40	0

turation of normal patterns of sexual behavior was demonstrated (*28*). These males were sexually aroused to the same degree as normal males and attempted to mount frequently. However, the males that had been raised in isolation displayed an inability to properly mount and clasp a female. Presumably as a result of this inability, intromission was rarely achieved. These behavioral deficiencies characteristic of males reared in isolation were not overcome by injections of testosterone propionate and therefore cannot be attributed to a hormonal deficiency. The effect of isolation on maturation of the behavior of the female is less pronounced, except, interestingly, that isolation has an inhibiting effect on the male-like mounting behavior displayed so commonly by the female guinea pig (*29*). The guinea pig is not alone in needing contact with other animals for the maturation of normal behavior. This need has been demonstrated many times in species as widely separated phylogenetically as ring doves, domestic turkeys, rats, cats, rhesus monkeys, chimpanzees, and man (*10*, *30*).

Table 2. Mean copulatory quotients (lordosis/mounts) for rats gonadectomized at different ages and tested after injection of estradiol and progesterone at 120 days.

Day of gonadectomy	Quotient
Females	
90	0.619
Males	
1	0.436
5	.218
10	.014
20	.029
30	.042
50	.026
90	.019

Special Influence of Early Hormonal Factors

Up to this point nothing in the work with young or adult animals had suggested that gonadal hormones serve to organize the tissues mediating sexual behavior in the sense of differentiation, as experimental embryologists use the word. Conceivably the action is organizational before birth or before sexual maturation, and activational in the adult.

We were aware that numerous investigators have obtained a full functional sex reversal (including breeding) in fishes and amphibians after administering heterotypical hormones during the embryonic and larval stages [see *31* for a few of the many reports reviewed by Young (*32*)]. More important for our thought was the statement by Dantchakoff (*33*) that female guinea pigs given testosterone prenatally had ovaries and two sets of duct systems. Oviducts, uterus, and vagina existed along with epididymides, ducti deferentes, seminal vesicles, prostate, Cowper's glands, and a penis, all differentiated and developed to varying degrees. An inverse relationship was found between penile structure and the degree of vaginal development. After injections of testosterone, masculine behavior was displayed. A repetition of Dantchakoff's experiment was dictated by the circumstance that no controls seem to have been used in her studies of this species, in which most normal females display male-like mounting as a part of the estrous reactions. Once a satisfactory method of administering the hormone had been developed by Myron D. Tedford, whose interest was mainly in the structural changes, pseudohermaphroditic females were produced routinely. The genital tracts were similar to those described by Dantchakoff, although probably encompassing a larger range of variations in structure. A marked display of masculine behavior was seen, as well as a lowered capacity to display feminine behavior (*34*)—an effect not observed by the earlier workers. Loss of the ability to come into heat was greatest when androgen treatment was started on day 30 of the 67- to 71-day gestation period, regardless of the duration of treatment and the total amount of androgen (*35*) (Table 1).

For us, these results produced an exciting moment. It was clear, first, that the gonadal hormones, or at least testicular androgens, have a dual role in the control of sexual behavior in the guinea pig. During the fetal period the hormones have an organizing action on the neural tissues destined to mediate mating behavior after the attainment of adulthood; during adulthood their role is one of activation. In other words, during fetal morphogenesis androgens exert a fundamental influence on the organization of the soma, determining whether the sexual reactions brought to expression in the adult will be masculine or feminine in character.

Second, it was clear that the rules of hormonal action are identical with those shown by the experimental embryologists to be applicable to the genital tracts (*36*). During the fetal period the gonadal hormones influence the direction of differentiation. During adulthood they stimulate functioning, be it contraction of smooth muscle fiber, secretion of epithelial cells, or endometrial sensitization for implantation.

The comparison can be extended. Evidence has been presented by experimental embryologists that, as the male develops, fetal testicular hormone is re-

Fig. 1. Female pseudohermaphrodite produced by injecting testosterone propionate into the mother during pregnancy. The treatment involved injection of 25 mg daily from post-coital day 40 through day 50; 20 mg from day 51 through day 70; and 10 mg from day 71 through day 90. There were no injections during the balance of the 166-day period of gestation. A prominent and well-formed phallus is visible to the right of the empty scrotal fold. The surgical scar in the right inguinal region resulted from a laparotomy which showed that there was no testis.

sponsible for differentiation of the Wolffian duct system (precursor of the male genital tract) and suppression of the Müllerian duct system (precursor of the female genital tract). In the female and in the castrated fetal male, in both of which testicular androgen is absent, there is development of the Müllerian duct system and regression of the Wolffian duct system. In our experiments the administration of an androgen to developing female fetuses was followed by the production of individuals in which there had been a stimulating action on the tissues (presumably neural) having the potential capacity for mediating masculine behavior, and a suppressing action on the tissues destined ordinarily to mediate feminine behavior.

In order to complete the analogy it was necessary to demonstrate that genotypic males castrated before the end of the period in which the organizing action of the fetal testicular hormone ordinarily occurs would display feminine behavior as adults. For us, such an operation on the young fetal guinea pig was not feasible. The best available evidence from tests of fertility and mating behavior indicated that this organizational period in the rat, a species with a short period of gestation, is postnatal (*37*) rather than prenatal, and that it ends at approximately the 10th day after birth. If the analogy could be extended, male rats castrated during this short period after birth should display feminine behavior, or at least elements of feminine behavior, when injected with estrogen and progesterone as adults.

An experiment designed to test this hypothesis has just been completed by Kenneth L. Grady, a graduate student. Male rats were castrated at 1, 5, 10, 20, 30, 50, and 90 days of age, and as a criterion, females were ovariectomized at 90 days. When they were 120 days old, and from then on, all animals were tested, after injections of estradiol and progesterone, for the display of feminine behavior in response to mounting by intact males. As we had expected, the experimental males displayed feminine behavior. Those castrated on day 1 or day 5 displayed significantly more receptive behavior than those castrated as late as day 10. Castration later than day 10 did not promote the retention or development of female behavioral characteristics (*38*) (see Table 2).

Tests of masculine behavior in male rats castrated soon after birth and tested as adults are currently in progress. When these tests are completed the model established by the experimental embryologists will have been duplicated for behavior. The results may be anticipated from an early study in which male rats castrated on day 1 exhibited a marked deficiency in copulatory ability as compared with those castrated on day 21 or later (*39*). If this proves to be a representative finding, our work on the two sexes will have produced complementary pictures of the organizational influences of androgen. On the one hand, females treated with androgen during the appropriate period show a regression or inhibition of feminine behavior and an accentuation of masculine behavioral traits. Males deprived of the principal source of endogenous androgen during a comparable period show accentuated feminine behavior and the absence of, or a greatly diminished capacity for, masculine behavior.

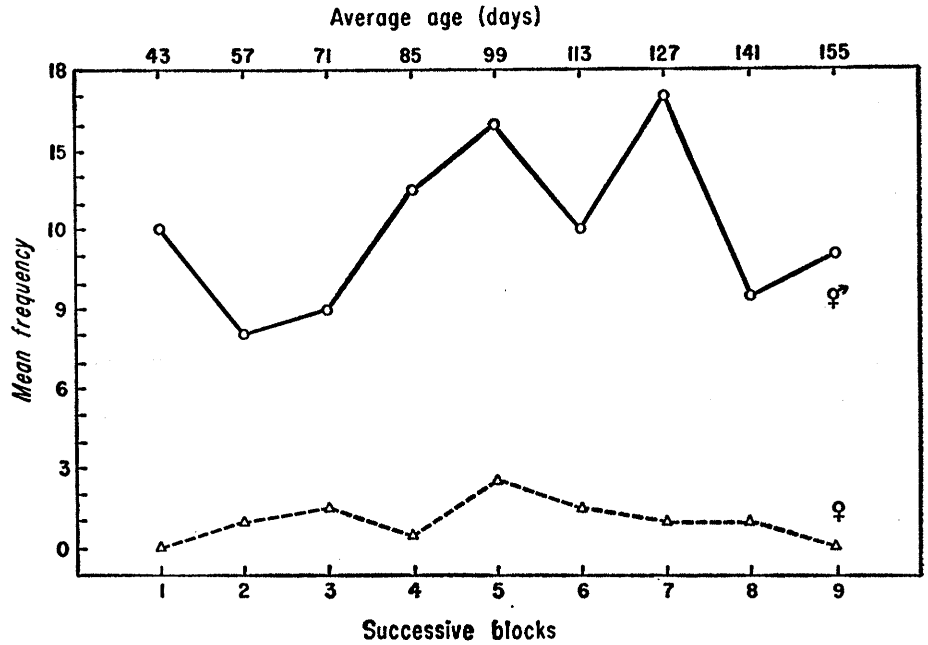

Fig. 2. Display of facial threat by female pseudohermaphroditic (solid line) and normal female (broken line) monkeys plotted relative to age. The abscissa is scaled in successive blocks of five trials.

Extension to Sex-related Behavior

When Phoenix, Goy, Gerall, and Young (*34*) were summarizing their data on the behavior of the female pseudohermaphroditic guinea pigs, they suggested that the organizing or sex-differentiating action of fetal gonadal substances may affect behavior beyond that which is primarily sexual in the sense of being directed solely toward the attainment of sexual aims. The rhesus monkey seemed better suited than the guinea pig or rat for a test of this hypothesis, so we proceeded accordingly.

Although an androgen treatment entirely compatible with the maintenance of pregnancy has not been worked out, we have succeeded in producing three female pseudohermaphroditic subjects with conspicuous genital alterations (Fig. 1). Two have been studied in considerable detail. We based our study of the early social patterns displayed by these individuals on the model established by Leonard Rosenblum during his graduate training at the University of Wisconsin. Accordingly, the pseudohermaphroditic females were allowed unrestricted social interaction with two untreated females for 20 minutes per day, 5 days per week, in a specially designed play room.

The results from 90 such observational sessions, covering the second through the fifth months of life, have been analyzed recently. A number of social behaviors, known to be sexually dimorphic and without any immediate instrumentality relative to mating, appear to have been influenced in the masculine direction by our prenatal treatments with androgen. The social behavior of the untreated females did not differ importantly from that described for normal females by Rosen-

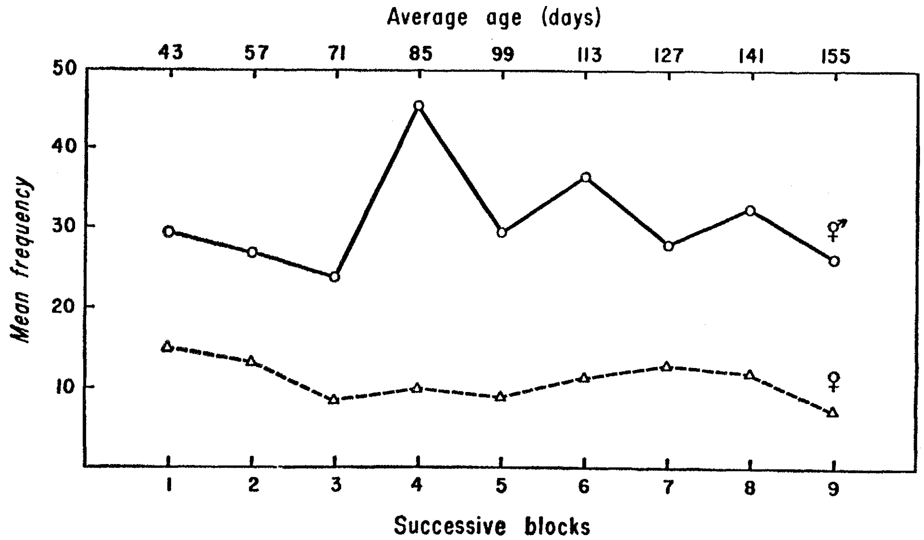

Fig. 3. Invitation to play by female pseudohermaphrodite (solid line) and normal female (broken line) monkeys, plotted relative to age. The abscissa is scaled in successive blocks of five trials.

blum, but the behavior of the treated females much more closely resembled his description of that of males. The pseudohermaphroditic females threatened, initiated play, and engaged in rough-and-tumble play patterns more frequently than the controls (Figs. 2–4). Like the males studied by Rosenblum, these pseudohermaphrodites also withdrew less often from the initiations, threats, and approaches of other subjects.

Analysis of the sexual behavior displayed by these pseudohermaphroditic females, although far from complete, already shows that it is not only in their patterns of withdrawing, playing, and threatening that they display a bias toward masculinity. In special tests with pairs of females, one pseudohermaphroditic and one normal, the pseudohermaphrodites consistently displayed more frequent attempts to mount, regardless of whether the normal female was brought to the hermaphroditic female's cage or vice versa. Their attempts to mount, while infantile and poorly oriented, are beginning to be integrated with pelvic thrusting and even, on a few occasions, phallic erection.

Our work with the primates has not progressed to a point where it may be considered definitive, partly because of the limited duration of the study and partly because of the very small number of subjects. We nevertheless consider the results to be highly encouraging and supportive of the general conclusions developed in our more extensive studies with the infraprimate mammals, concerning the action of the gonadal hormones.

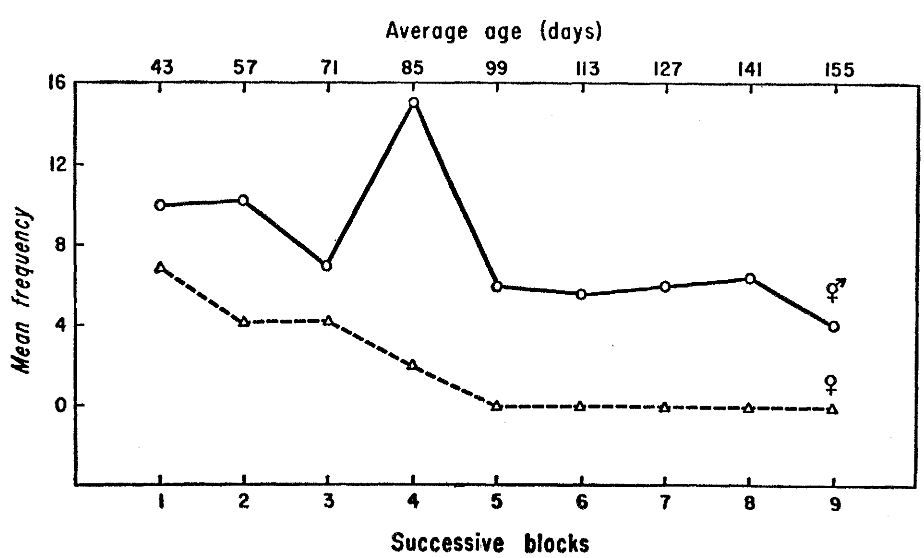

Fig. 4. Rough-and-tumble play by female pseudohermaphroditic (solid line) and normal female (broken line) monkeys, plotted relative to age. The abscissa is scaled in successive blocks of five trials.

Implications

Implied in the present discussion of data bearing on the organizing action of androgen on the neural tissues destined to mediate sexual behavior is the view that a part or parts of the central nervous system are masculine or feminine, depending on the sex of the individual. This concept is not new; it has been developing over the years in the writings of investigators whose approach has been entirely different from ours (*4*, *40*). What we have found adds support to this view and suggests something of the way in which masculinity or femininity is conferred on the nervous system.

An additional thought merits attention. It is that the principles of hormonal action in effecting this sexual differentiation of the developing brain provide a model to which we may look for a reexamination of the psychosexual incongruities discussed by Hampson and Hampson (*1*) and by Money (*2*) in their reviews and in their many articles published since the middle 1950's. We accept and, in our own work with lower mammals, have documented the importance of the subject's experience. However, explanation of the cases these investigators present need not lead to a rejection of the concept of a predetermined psychosexuality for the concept of a psychologic sexual neutrality at birth. If the endocrinology of the differentiation of the capacity to display masculine and feminine sexual behavior as we have worked it out for the guinea pig and the rat is applicable to man, the incongruities in the patients these workers examined can be explained without postulating a psychosexual neutrality at birth and attributing the gender role and sexual orientation solely to the individual's life experiences while growing up. In view of what we have learned an endocrinological basis which is consistent with the concept of psychologic bisexuality exists for the interpretation of most if not all of the cases they report. This is true of their hermaphrodites with ambiguous or masculinized external genitals and with a female sex chromatin pattern (comparable with our female pseudohermaphrodites); of the cryptorchid hermaphrodites with a male sex chromatin pattern, in which testicular function was clearly subnormal; of the simulant females with a male sex chromatin pattern but with the as yet unexplained feminizing testes; and of the "females" born with gonadal dysgenesis and an XO or XY chromosome pattern (Turner's syndrome). The large group of hyperadrenocortical patients with the female sex chromosome pattern probably would fit into this picture were the circumstances such that more information about the parameters of the excessive androgen production could have been obtained.

We realize as we venture into a clincal area that a question exists regarding the extent to which what we have found in the guinea pig, rat, and monkey is applicable to man. We call attention, however, to an interesting similarity revealed by Milton Diamond during his graduate work at the University of Kansas. After noting that testosterone does not induce masculinization of the adult female guinea pig while it is pregnant, he examined the clinical literature and found an apparent comparable lack of masculinization in pregnant human beings: 27 of 31 women who received androgenic hormones or gestagens in quantities sufficient to masculinize the female fetuses were not themselves virilized (*41*).

Direction of Future Research

As we have proceeded with our analysis of the relationships of the hormones to sexual behavior and, more recently, to sex-related behavior, we have always been aware that many questions remain to be answered. At the same time a picture is emerging, and, with good fortune in the selection of materials and techniques, much more of it will be revealed in the future.

Without discounting the influence of psychologic factors, which we know is great, or the need for carefully recorded observations of behavior, we expect that, increasingly, the materials and techniques used will be those of the neurologist and the biochemist. The directions many neurologists are taking are indicated by the various reports of efforts to locate the neurological sites of hormonal action and define the pathways of stimuli for the many responses that are given (see *42*).

Few biochemists have been attracted to the problem, but it is they who must clarify the mechanisms of hormonal action in organizing the tissues of the central nervous system during development and in bringing behavior to expression in the adult. They may be helped in such a search by the circumstance that cellular elements in the genital tracts, which differentiate and are activated under the influence of these same hormones, are at present more accessible for histophysiological study than those in tissues of the central nervous system. It is to be hoped that clues will come from the work of the many investigators whose studies are described in recent reviews (*43*).

The need for studies of sexual behavior in man is great. Methods for collecting trustworthy, meaningful data and means of ascertaining whether the many behavioral states are associated with hormonal action in the developing fetus and in the adult should be worked out. The possibility that such relationships exist and that typical and deviant behaviors have a physiologic as well as a psychologic basis may no longer be excluded.

Summary

From an attempt made 30 years ago to attain a limited objective, we have proceeded with what turned out to be a long-term investigation. Evidence has accumulated indicating that the gonadal hormones have a broad role in the determination of behavior. We have long known that they act to bring sexual behavior to expression, certainly in adult vertebrates below man. We now know, in addition, that during a period of organization and differentiation which is prenatal in the guinea pig and monkey and postnatal in the rat, the hormones act according to principles which appear to be identical with those operative during the differentiation of the genital tracts, and they effect a corresponding differentiation or organization of neural tissues.

The data thus far accumulated from a study of the behavior of two female pseudohermaphroditic monkeys suggest that this early hormonal action is also responsible for the establishment of much of the sex-related behavior which is a part of the masculinity or femininity of an individual but which is not related directly to the reproductive processes.

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Trends in Scientific Research

Rapid evolution of the frontiers is a hazard for scientists young and old.

Philip H. Abelson

Scientific research is in the midst of rapid evolution. New opportunities for research effort develop and are quickly exploited, and often their potential is soon exhausted. The rapidity with which changes occur poses problems for the student who desires to make a career in scientific research, either fundamental or applied. It also challenges the universities, for they have a responsibility to educate their students for the realities that may develop in the next 40 years. Therefore it is important to ask where science is heading and to attempt to identify the forces that are shaping its future.

I will begin by arguing that it is possible to identify major trends in many areas of science. Although no one can foresee in detail when or where specific scientific discoveries will be made, trends likely to have continuing influence for an extended period can be predicted. It was clear in the early 1930's that the invention of the cyclotron and of the Van de Graaff generator made atomic nuclei accessible to experimental studies. The characteristics of the cyclotron were such as to encourage optimism that higher energies could be obtained by constructing larger devices. By 1933 or 1934 it was obvious that a rich field for continuing study had been opened. Soon the discovery of useful artificial radioisotopes of sodium, phosphorus, and sulfur made it apparent that tracer isotopes would be important in the development of many areas of science, particularly in chemistry and biology.

Later, at the end of World War II, it was obvious that there would be a large effort in nuclear physics, because machines of higher energy could be constructed. The nuclear reactors developed during World War II were destined for intensive improvement and application to atomic power.

Perhaps less obvious were the beginnings of development of molecular biology. The first steps toward the recent successes in cracking the genetic code were taken shortly after the end of the war. At a course in viruses started at Cold Spring Harbor in 1946, many competent investigators, some of them physicists, were trained in new techniques. From this group came much of the impetus that set the intellectual stage for present activities.

Exhaustion of Research Possibilities in Some Fields

An important phenomenon in science is the exhaustion of fields of inquiry. Given a set of techniques and concepts, fields do become mined out. As an example from the borderline of chemistry and physics, consider the

The author is editor of *Science* and director of the Geophysical Laboratory, Carnegie Institution of Washington, Washington, D.C. The article is based on the Third Annual Klopsteg Lecture, which he delivered at Northwestern University 6 November 1963 under the title "Where Is Science Heading?" Parts of the article were included in talks to the University of Maryland chapter of Sigma Xi (25 April 1963) and the National Association of Science Writers in New York (11 September 1963).