

Embryonic Sex Differentiation and Sex Hormones (1947), by Carl R. Moore

In 1947, Carl Richard Moore, a researcher at the University of Chicago, in Chicago, Illinois, wrote *Embryonic Sex Differentiation and Sex Hormones*, which was published in the same year as a first-edition monograph. In the book, Moore argues that regulation of sex differentiation in mammals is not controlled by sex hormones secreted by embryonic sex organs (gonads), but is controlled by non-hormonal genetic factors. In support of his hypothesis, Moore describes the current literature on sex differentiation, and he reviews experiments on vertebrates and invertebrates and his own work with opossum (*Didelphis virginiana*) young.

The first section of the book, Moore discusses sex differentiation. He explains that once an organism approaches puberty or the beginning of its reproductive life, hormones secreted by the gonads influence the reproductive system's functions and development of secondary sex characteristics. However, Moore argues that scientists couldn't describe the physiological control over such development, which despite genetic sex determination, permits gradations of sex characteristics in degrees from typical male to typical female.

In the second section, Moore describes Frank Rattray Lillie's early twentieth century work with freemartins at the Marine Biological Laboratory in Woods Hole, Massachusetts. Born with a normal male twin, a freemartin is a sterile cow that has external female genitalia and internal male gonads. Lillie theorized that the freemartin is a genetic female whose internal sex differentiation was suppressed or antagonized by her twin's release of male hormones via their shared blood circulation. Lillie's study of freemartins led to the theory that gonadal sex hormones partly caused hermaphroditism. After a suggestion from Lillie, Moore began his research in 1916 to create hermaphrodites in the laboratory to test Lillie's theory. Moore reviews his experiments over the course of thirty years with rats, guinea pigs, and, opossums, studies that led him to conclude that hormones released by the embryonic gonads didn't cause the reproductive system to differentiate from other tissues, and that something else did, an interpretation contrary to Lillie's assertion.

In the third section, Moore reviews experiments in which researchers attempted to modify sexual development using living tissues and hormonal extracts from testes and ovaries. In the analysis of experiments using living tissues, Moore concludes that some animals, such as amphibians and some pigs, could develop just as freemartins in cows do. He next assesses experiments using hormonal extracts and concludes that while birds, fish, and amphibians, which are all non-placental animals, exhibit gradations of sex differentiation when exposed to hormonal extracts. Moore then describes experiments using hormonal extracts with placental mammals, and he reports that the experiments yielded a variety of atypical conditions. Moore concludes that those results could have been caused by the alteration of the hormones delivered in utero either by some interaction with the mother or because of an injury to the placenta. To investigate such possibilities, Moore began his research on the opossum in 1939, at the Marine Biological Institute.

The fourth section details Moore's experiments with opossums and the results from those experiments. Moore claims that he chose the opossum because he could avoid the risk of injuring opossums when he interacted with pregnant opossums while the young were in utero, and because the reproductive systems of opossum young are not differentiated at birth. Opossums are born after thirteen days of gestation and spend the next sixty-five to seventy days attached to the nipple located in the mother's pouch.

In his initial experiments, Moore treated the young with hormonal creams until thirty days after

birth. Moore concludes from these experiments that androgen cream stimulated the male reproductive system in both sexes, with a slightly greater effect in genetic males than in genetic females. The androgen cream, according to Moore, also stimulated female (Mullerian) ducts but did not inhibit ovarian development in females. Estrogen treatments, Moore asserts, did not change the differentiation of either sex, but did stimulate the growth of male (Wolffian) and female ducts in each sex.

Moore also treated opossum young with hormones that stimulate gonads (gonadotropins), and he states that such treatment failed to produce appreciable amounts of sex hormones from the gonads. He concludes that in opossum young, sex differentiation is visible at day thirty but the gonads are incapable of secreting hormones until day seventy in males and day 100 in females, gonadal hormones play a significant role in sex differentiation.

Moore then describes the procedures he used to surgically remove the gonads on opossum young without detaching them from the mother's nipples. He determines that even though the gonads are removed, the reproductive system of the opossum proceeds normally until the stage of development when the male and female systems are established. He cites the experiments as further evidence that the sex differentiation of the opossum does not depend on the hormonal secretion of the ovaries or the testes.

In the fifth section, Moore discusses his results and their implications for the study of sex differentiation in vertebrates more generally. He explains that in vertebrates, the embryonic gonads don't cause the formation of the male or female reproductive structures. Moore then hypothesizes that other factors modify reproductive structures in amphibians and birds. He suggests that prior experimental results that demonstrated a mismatch between the secondary sex characteristics and the genetic sex occurred because of the sensitivity of those structures in early periods of development. According to Moore, intersexual or hermaphroditic conditions, for which organisms have both testis and ovary, result from non-hormonal genetic factors in which neither the male nor the female factor establish dominance.

The final section of the book lists the ten points of Moore's argument. Moore asserts that embryonic sex glands don't cause sex differentiation in embryos, but findings published in the same year as his monograph confirmed Lillie's theory. Lee J. Wells, a former student of Moore's then at the University of Minnesota in Minneapolis, Minnesota, and Alfred Jost and Albert Raynaud, both in Paris, France, published papers in which they described how they produced hermaphrodites in their laboratories via fetal gonadectomies. Nevertheless, Moore's work enabled researchers to further study the role of embryonic gonads in sex differentiation.

Sources

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