Experimental Analysis of Hormone Actions on the Hypothalamus, Anterior Pituitary, and Ovary

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I. BRIEF HISTORY OF THE PROBLEM

The history of efforts to understand the factors that regulate cyclic gonadal function actually starts with research on a somewhat different problem. In the early 1900s, investigators such as Steinach (reviewed in Moore and Price, 1932) were interested in the problem of organ transplantation. Steinach attempted to transplant testes into intact female rats and ovaries into intact male rats. These transplants invariably failed to become functional or “take.” However, when the host animal was gonadectomized, transplantation of the heterologous gonad was said to be more successful. Somewhat later, Lipschütz (1925) transplanted ovaries into intact male guinea pigs. He stated that the time required to stimulate male mammary growth was much greater than when the graft was made in castrated males. Furthermore, ovarian grafts that failed to “take” (in terms of stimulating mammary gland growth) did so almost immediately when the male’s testes were removed. Lipschütz derived the idea that removal of the testes led to an “unbolting” of ovarian function.

The concept that there were antagonistic actions of the ovary and the testis flowed from these transplantation experiments. In 1926, Steinach and Kun extended this concept by claiming to demonstrate that the antagonistic actions...
of the gonads were exerted through their respective steroidal secretions. Moore and Price (1932) decided to thoroughly reexamine the question of direct antagonisms between the hormones secreted by the testes and the hormones produced by the ovaries. In the course of this reexamination, they came to the conclusion that failure of gonadal transplants to become functional in intact subjects had less to do with direct antagonisms between ovarian and testicular hormones than with suppression of pituitary activity by the transplanted gonads. After arriving at this conclusion, Moore and Price went on to hypothesize that gonadal secretion is regulated in normal animals by a reciprocal interaction between the gonads and the pituitary gland. The Moore–Price theory of the regulation of gonadal secretion has had, and continues to have, significant impact on the study of reproductive physiology. In its original form it consisted of four major principles.

1. Gonadal hormones stimulate homologous reproductive accessory tissues but are without effect on heterologous accessories. That is, androgen stimulates male, but not female, reproductive accessory tissues, whereas estrogen stimulates female, but not male, accessory tissues. Although this tenet is valid as a rough approximation, there is much evidence that demonstrates effects of androgens on uterus, vagina, oviduct, and breasts and effects of estrogens on seminal vesicles, prostate, epididymis, and coagulating, preputial, and Cowper’s glands (Burrows, 1949).

2. Gonadal hormones have no direct effect on the gonads of either the same or the opposite sex. Although this, too, is not entirely true (Parkes and Deanesly, 1966a; Armstrong and Dorrington, 1976), the general principle was neatly demonstrated by Moore and Price (1932). They gave hypophysectomized male rats testosterone and showed that testosterone did not stimulate growth of the regressed testis.

3. Secretions of the hypophysis stimulate the gonads to function both in terms of germ cell production and in terms of hormone secretion. This had been demonstrated previously by Smith and Engle (1927) who performed hypophysectomies successfully.

4. Gonadal hormones of either sex exert a depressant effect on hypophyseal function, and this results in a diminished quantity of hypophyseal sex-stimulating factor available to the organism. This point was considered by Moore and Price to be the key to the problem of hormonal antagonism posed by the transplantation experiments of Steinach and Lipschütz. One experiment that Moore and Price performed to support this notion is outlined in Table 1.

The conclusion drawn from the experiment described in Table 1 was that “oestrin” (an estrogenic preparation that probably consisted primarily of estrone and estradiol) did not induce damage to testicular function as long as sufficient quantities of gonadotrophic hormone (from implantation of multiple pituitaries) were present. Note that loss of testicular function occurred in