

## THE OVARY-STIMULATING HORMONE OF THE PLACENTA

## PRELIMINARY PAPER

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IT has been abundantly proved that the placenta contains the hormone of œstrus. This hormone, "œstrin", or the "female sex hormone", as it is designated by Frank,<sup>5</sup> was first studied in detail by Allen and Doisy.<sup>1</sup> They developed a method for the accurate biological assay of extracts containing the active principle. The assay is dependent on the characteristic property of the hormone to produce the phenomenon of œstrus in a fully castrated female rat. Since their original work on follicular fluid as a source of this œstrus-producing ovarian hormone, œstrin has been abundantly demonstrated elsewhere than in the ovary. Placenta, amniotic fluid, and the urine of pregnancy have been shown to contain very considerable amounts of the hormone.

Prior to the development of more accurate methods of assaying for œstrin, many earlier workers had proved that lipoidal extracts of placenta when injected into young females caused premature maturity of the uterus and vagina. A similar result was obtained with adult castrates.

Since œstrin is most readily obtained by taking advantage of the fact that it is freely soluble in fat solvents, and can be removed completely from aqueous suspension by the use of ether, workers in this field have for the most part confined their investigations to the lipid fraction of tissues or fluids studied. The demonstration that a water-soluble hormone having physiological properties quite distinct from œstrin may occur separate from or in conjunction with the latter is an outcome of the independent work of Smith and Engle<sup>9</sup> and of Zondek and Aschheim<sup>11</sup> on the ovary-stimulating action of implants of anterior pituitary substance. These investigators were able to show the most dramatic results in immature female rats and mice following the intramuscular injection of fresh

anterior pituitary gland or saline suspensions of the same. The effect of such treatment is to cause a most rapid development of the immature ovary. Smith and Engle report that the ovary of the experimental rat may be ten-fold the size of that of the control, and nineteen-fold in the case of the treated immature mouse. The increase in ovarian tissue thus produced is due for the most part to the rapid maturing of Graafian follicles. These apparently mature in a normal manner and superovulation results. But even of greater interest is the fact that as a result of the stimulation of ovarian activity, œstrin is liberated, producing its typical effects, *viz.*: hypertrophy of the genital tract and the phenomenon of œstrus. The work of these authors has therefore established that a hormone of the anterior pituitary gland can cause by direct stimulation of the ovary (liberating œstrin) all the effects of œstrin *per se*. There is this sharp distinction between the anterior pituitary principle and œstrin—anterior pituitary hormone has no effect on the castrate, whereas œstrin acts just as effectively in the castrate as in the normal female.

Zondek and Aschheim later demonstrated that implants of 0.1 gm. of placenta produced ovulation in immature mice. Blood serum and the urine of pregnancy were found to be similarly active, in doses of 0.5 and 1 to 2 c.c. respectively. They have also detected the ovarian stimulating principle in decidua, in the corpus luteum of pregnancy, in tubal mucous membrane, and in the blood of the new-born. They have prepared an œstrin-free product from the urine of pregnancy and have developed a method of biological assay of the principle dependent upon the production of hæmorrhagic follicles in the ovaries of 6 to 8 gm. immature mice. The pioneer work of Smith and Engle, and of Zondek and Aschheim, on the ovary-stimulating hormone of