

Letters to the Editor.

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The Ovary Stimulating Hormone of the Placenta.

THE production of prematurity in young female rats and mice by Smith and Engle in America, and by Zondek and Aschheim in Germany, through the use of the anterior pituitary gland transplant or emulsion has afforded a great stimulus to further investigation of the hormonal control of gonadal activity. The latter investigators have demonstrated that effects somewhat similar to those following pituitary gland implantations can be elicited in immature rats and mice by extract of pregnancy urine which has been rendered œstrin-free. They have likewise shown decidua, placenta, the corpus luteum of pregnancy, as well as pregnancy blood, to contain an ovary stimulatory hormone analogous to that of the anterior pituitary gland.

Dr. B. P. Wiesner, of the University of Edinburgh, experimented extensively with extracts of the placenta by the use of sulphosalicylic acid. He is of the opinion that his own experiments have demonstrated the existence in placenta of two hormones, one of which he called 'Rho I.', which is œstrogenic in action, causing prematurity phenomena in rodents; the other, 'Rho II.', has a luteinising action on the ovary and causes a state of pseudo-pregnancy (see Wiesner, *Edin. Med. Jour.*, February 1930, p. 73).

Dr. Wiesner visited my laboratory in September 1929, and asked me to take up the problem of concentration and purification of the ovarian stimulatory hormone of placenta which he has termed 'Rho I.'. The problem was, therefore, made a subject of special study in this laboratory, and the results of our investigations to date, which appear to be of great interest, may be summarised as follows:

1. The placenta (human or ox) contains an ovary-stimulating hormone the injection of which into immature rats and mice causes prematurity phenomena. (Confirming Zondek and Aschheim, and Wiesner.)

2. The active principle has been obtained in a fraction which is micro-crystalline in character. After repeated recrystallisations, 0.0015 mgm. of such a fraction has been found to represent one rat unit.

3. Active extracts which have been rendered protein- and lipid-free, as well as œstrin-free have been standardised in terms of rat units. The manifestation of prematurity phenomena (confirmed by microscopic sections of ovary, uterus, and vagina) has been the basis of the biological test.

4. Active extracts have been shown to withstand *in vitro* digestion with pepsin and trypsin without appreciable loss of their physiological activity.

5. It has been repeatedly demonstrated that potent extracts may be effective when administered by the oral route. The amount of extract, administered orally, required to produce definite stimulation of the immature ovary may be very little more than the effective subcutaneous dose.

6. The effects of daily injections, over long periods, of active extracts have been studied in relation to the histology of the genital tract and also in relation to pregnancy and lactation in the adult female rat.

7. Immature female rats, as a rule, become cyclic following the induction of prematurity phenomena.

8. Several instances of normal mating have occurred in treated rats thirty-five to fifty days of age.

9. Adult rats which have received two to ten rat units daily have manifested the normal cyclic changes, have been impregnated and produced litters of normal size at the normal gestation period, and have shown no impairment of lactation. Some of these rats are now in their third pregnancy since the injections began.

10. Clinical trial of the placental extract in a selected group of cases of ovarian hypofunction, with the collaboration of Dr. A. D. Campbell, has been productive of results which are most encouraging.

This phase of our work at McGill University is now a subject of intensive study. With the co-operation of the staffs of the Royal Victoria and Montreal General Hospitals, the following types of cases are being studied:

(a) Delayed puberty, (b) dysmenorrhœa, (c) amenorrhœa, (d) metropathia hæmorrhagica, (e) menopause, (f) toxæmia of pregnancy, (g) certain neurological and psychiatric cases, (h) thyroid dysfunction.

The extract, in liquid form, is being administered by mouth.

11. It is our opinion, in the light of experimental evidence, that the hormone of the placenta with which we are dealing is not identical with the anterior pituitary ovary stimulatory principle ('Rho I.' of Wiesner). It is produced, we believe, by an active process in the placenta itself. Its physiological effects on rodents are suggestive of the all-or-nothing law. It will activate an immature or hypofunctioning ovary, but has little effect upon the normal organ, and no effect on a castrated individual.

If we are correct in this assumption, then one should be able to demonstrate that the diseased placenta produces less of the active principle. Assay experiments which are now being made on placenta, both normal and pathological, obtained at various periods of gestation, will do much to settle this point.

J. B. COLLIP.

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The Crystalline Style of the Mollusca and a Carnivorous Habit cannot Normally Co-exist.

THE crystalline style of the Lamellibranchs and many Gastropods consists of a gelatinous rod formed of protein of a globulin type. It would, therefore, be readily digested by any extracellular proteolytic enzyme in the alimentary tract. Since the development of the carnivorous habit demands (with such rare exceptions as the one noted below) the presence of an enzyme capable of breaking down the flesh of the prey into soluble polypeptides and amino acids (for example, in Cœlenterates, Decapod Crustacea, and Cephalopods), it follows that a mollusc cannot normally both possess a style and be a carnivore.

A brief survey of those molluscs which possess a style will emphasise this point. The style is universally present in Lamellibranchs. Here feeding is by ciliary mechanisms, the food being selected according to size only. There is no extracellular protease in the gut, the only extracellular enzyme being that set free by the dissolution in the stomach of the head of the style and that acts exclusively on starch and glycogen (Yonge¹). Zooplankton may survive passage through the gut. Minute particles of animal matter (for example, blood corpuscles from fish) may be ingested and digested by wandering phagocytes which pass through the gut wall into the lumen and thence back