

If injected immature rats are sacrificed at various periods following the administration of the hormone, one notes first the rapid development of the Graafian follicles, associated with the changes in the mucous membrane of the vagina leading up to the œstrus desquamation of cornified epithelium. Corpora lutea then appear and one finds that the vaginal mucous membrane has now changed from the squamous to the cuboidal cell type. In our experience corpora lutea are not found in the ovaries of immature control rats. It is possible, therefore, to substitute the finding of corpora lutea in the ovary of immature animals injected with the placental hormone for the well-known œstrus phenomena usually made use of in biological testing. When the appearance of young corpora lutea is made the basis of a positive reaction the test animal may be sacrificed on the sixth or

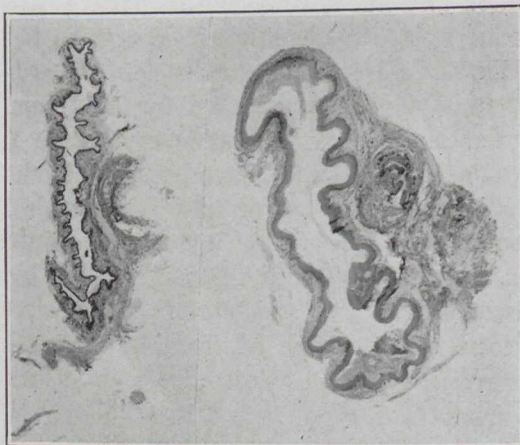


FIG. 4.—Cross section of vagina of immature rat.

FIG. 5.—Cross section of vagina of immature rat treated with placental hormone.

seventh day following the injection, or even later. It is possible, however, to have corpora lutea appear earlier, since a positive vaginal smear may on occasion be noted as early as the third day.

2. It has been shown that the same physiological effects may be produced in immature rats by oral administration of the hormone as by subcutaneous injection. The dosage by mouth necessary to produce these effects may not be more than two or three times the effective subcutaneous dose.

3. The hormone has been shown to be effective after moderate periods of exposure to the action of the digestive enzymes, pepsin and trypsin.

4. Injection of the active extract into adult castrates over a period of weeks is without effect. Injection of adult but vigorous normal females with two rat units daily has had very little effect on the normal œstrus cycle. In these experiments the animals were first submitted to a control period during which, by the taking of daily vaginal smears, the individual cycles were established. Œstrus occurs in most adult animals at regular intervals of four to six days. Apart from a slight extension of the period of cornification of the vaginal epithelium no effect was noted. Two pregnant animals receiving similar dosage daily, carried through a normal pregnancy, labour and lactation period, and, even though the injections were continued bi-daily, the animals again became pregnant following the introduction of a vigorous male, and a second time delivered a normal litter in the normal time. One would anticipate in the light of Smith's work, in which he caused termination of pregnancy in rats by pituitary transplants, that abortion might be induced by the above treatment. This may be a matter of dosage and the experiments are being repeated, using much larger doses in terms of rat units.

The injection of 12 rat units daily for three weeks produced no ill effect in a 2-kilo rabbit, and no marked change in the chemical constitution of the blood, apart from a slight increase in cholesterol.

5. The laboratory investigation making possible the production of a standardized extract containing the ovary-stimulating hormone factor, and its physiological effects having been studied in sufficient detail in certain animals, seemed to justify the view that clinical investigation of the effectiveness of the extract might now be started. On *a priori* grounds one may reason that only those individuals who give definite evidence of hypoaactivity of the ovary may be expected to receive benefit by the placental hormone. Therefore, in an experimental clinical study only such types of cases should be treated. Dr. A. D. Campbell is collaborating in this work and already a few typical patients with hypovarian signs and symptoms have been placed under treatment. The results so far obtained have been encouraging. (See the following paper in this issue).

One must remember that luteinization of the ovary has been produced by certain alkaline