

## Missouri Section.

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### The Luteinizing Substance of Pregnancy Urine.

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That pregnancy urine contains a luteinizing substance was first shown by Zondek.<sup>1</sup> From his later work<sup>2</sup> it appears that the luteinizing substance is different from the agent that causes ripening of the follicles, even though such a separation has not been made with urines of pregnancy.

Extracts prepared by us from pregnancy urine seem to produce both maturation of follicles and luteinization. In the immature mouse or rat premature estrus is effected by their administration. We have tentatively defined one mouse unit as the minimum amount that causes opening of the vagina and estrus on the twenty-second to twenty-fourth day of age, after being administered subcutaneously to 19-day-old mice in 6 equal portions during the course of 3 days. This criterion of activity seems to be quite satisfactory if one is assured of the absence of the estrogenic substances. Depending upon the degree of purification, the mouse unit has varied from 0.03 to 0.001 mgm. This amount produces a marked hyperemia and development of the ovaries and uterus but very little luteinization.

The daily administration of these extracts to adult female rats produces for the first 5 to 10 days an almost continuous state of estrus, due probably to stimulation of the follicular apparatus. Cornified cells then disappear from the smears, possibly as an effect of the extensive luteinization. The inhibition of estrus persists for 5 to 12 days following the cessation of the injections, the cycles then

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<sup>1</sup> Zondek, B., *Klin. Wschr.*, 1928, 7, 30.

<sup>2</sup> Zondek, B., *Klin. Wschr.*, 1930, 9, 1207.

reappearing with a slight prolongation of the diestrus interval. The ovaries of the treated animals are loaded with corpora lutea and weigh 4 or 5 times as much as those of the controls.

Kelly<sup>3</sup> has reported that the injection of pregnancy urine into pregnant guinea pigs invariably produces abortion. The administration of our extracts to rats greatly prolongs the gestation period.<sup>4</sup> This is true when the injections are started at any time between the fourteenth and nineteenth days of pregnancy. At autopsy the fetuses are usually dead and partially resorbed but fully developed and often of greater than normal size. The ovaries are much larger and more luteinized than those of control pregnant rats.

Since the luteinization is so pronounced it would seem reasonable to attribute the delay of parturition to this phenomenon. To test this idea we have administered the extracts to ovariectomized pregnant rats but in no case was the gestation period prolonged. Apparently, the presence of the ovary is necessary to produce this effect and since large quantities of theelin have no influence on the pregnancy, it seems probable that the corpora lutea are responsible for the retention of the fetuses.

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### Chromatophore Reaction to an Oestrogenic Hormone.

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Some 3000 tadpoles (*Rana pipiens*) were treated during 5 months with the oestrogenic hormone theelin obtained from the Biochemical Laboratory of Doctor Doisy. Several series of experiments were carried on simultaneously in which the tadpoles were exposed to different concentrations of theelin over varying periods of time. In other experiments 100 tadpoles were injected with the hormone.

In one series 250 tadpoles just emerged from the gelatin coating were placed in a 1000 cc. aqueous solution of theelin 0.0000003125 mg./cc. for 60 minutes. On successive days the exposure time was increased by 60 minutes for a period of 10 days. This time increment was kept constant during the rest of the experiment but the concentration of the hormone was doubled every 10 days until a

<sup>3</sup> Kelly, L. G., *Anat. Rec.*, 1931, **48**, 50 (supplement).

<sup>4</sup> Levin, L., Katzman, P. A., and Doisy, E. A., in press.