5993

Effects Produced by Intravenous and Intraperitoneal Injections of Urine of Pregnancy in Immature Female Rabbits.*

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Intraperitoneal injection of urine of pregnancy into mature female rabbits results in a direct luteinization of the unruptured follicles, while urine administered intravenously usually results in ovulation (Friedman[1]).

We have carried out a series of experiments in which we have studied the difference in the results obtained by these 2 modes of injection of urine of pregnancy in 18 immature female rabbits. The animals were divided into 2 groups; one group received urine of pregnancy intraperitoneally, while their litter-mate sisters received an equal amount of the same specimen intravenously. The animals were injected daily for 3 to 6 days. When an animal from one group was autopsied, its litter-mate control was likewise killed. In all cases we have studied serial sections of the ovaries.

In animals whose ovaries contained no mature follicles, but did contain smaller follicles with a follicular cavity, intravenous injection resulted in extreme growth of these follicles, which at autopsy appeared cystic. They usually contained some blood but never as much as was found in the animals which had been given urine intraperitoneally. There was practically no luteinization in these large follicles. In most cases the granulosa was not present. The *theca interna* was somewhat compressed in places, in others the cells showed a marked hypertrophy. There was no change in the very small follicles. Often the ovaries in these animals contained several extremely large follicles at one pole, while the remainder of the ovary was infantile. We believe that urine injected intravenously acts only on follicles which have a well developed follicular cavity, but never causes a stimulation of the smaller and more primitive follicles.

Urine injected intraperitoneally had a very different effect. The ovaries of these animals contained a large number of small blood follicles. None of these approached in size the large follicles obtained when the urine was injected intravenously, but they were

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[1] Friedman, M. H., *Am. J. Physiol.*, 1929, **90**, 617.

much more numerous. There was a marked direct luteinization of most of the follicles. and they all contained varying amounts of blood. The intensity of the luteinization varied with the amount of the blood present. For example, when a greater amount of blood was present on one side of the cavity, almost invariably there was also a greater amount of lutein tissue on that side. When there was only a small amount of blood in the follicle, it was almost invariably in or near the cumulus. This suggests that the first rupture of capillaries usually occurs at this position. This observation is based on the study of serial sections of more than 100 follicles in which only a small amount of blood was present and which showed an early stage of luteinization. In the animals which received intraperitoneal injections, the smallest follicles, which contained luteinized cells and free blood in the cavity, averaged 1.41 mm. in diameter, while the largest follicles, which did not contain any blood and did not show any evidence of luteinization, averaged 1.01 mm. in diameter. Luteinization has always been accompanied by free blood in the cavity of the follicle, except where the follicle has been completely luteinized.

5994

Small Doses of Anesthetics.

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It was previously noted that, while ordinary concentrations of sodium amytal diminished or abolished tone and activity of isolated intestine and uterus, minute doses seemed to be pressor.[1] Is the same "reversal" effect to be found in whole intact animals? Picrotoxin causes convulsions in mice. The convulsions may be stopped or prevented by a proper dose of anesthetic. Indeed a method for biological assay of the hypnotics has been based on this antagonism,[2] and picrotoxin has been suggested as an antidote for barbiturate poisoning.[3] Thus it seems that wherever the points

[1] Reynolds, C., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 656.

[2] Wieland, H., and Pulewka, P., *Arch. Exp. Path. u. Pharm.*, 1927, **120**, 174 and 186.

[3] Maloney, A. H., Fitch, R. H., and Tatum, A. L., *J. Pharm. and Exp. Therap.*, 1931, **41**, 465.