2. Schales, O., Schales, S., *J. Biol. Chem.*, 1941, v140, 879.

3. Barbour, H. G., Hamilton, W. E., *idem*, 1926, v69, 625.

4. Smith, H. W., *The Kidney*, 1951, p169, Oxford Press, N. Y.

5. Wilde, W. S., Malvin, R. L., *Am. J. Physiol.*, 1958, v195, 153.

6. Kaplan, A., Friedman, M., Kruger, H. E., *idem*, 1942, v138, 553.

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Fall in Uterine Histamine Associated with Ovum Implantation in Pregnant Rat.* (24634)

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A role for histamine as decidual cell inducer in the mechanism of ovum implantation has been proposed(1-4). Evidence includes: 1) induction of deciduomata (DCM) by intraluminal histamine(1,5). 2) inhibition of DCM by intraluminal histamine-antagonists (1). 3) induction of DCM by traces (30 $\mu\mu$) of intraluminal histamine releaser 48 '80(6). 4) induction of DCM by systemic (i.p. and i.v.) injections of histamine and of histamine releasers(6), 5) inhibition of systemically induced DCM by intraluminal histamine antagonists(6), 6) inhbiition of natural ovum implantation by intraluminal antihistamine(2). 7) mast cell depletion of rat endometrium immediately before nidation, and 8) intense infiltration of eosinophilic polymorphs before nidation (unpublished). This report measures histamine of uteri of rats during period of ovum implantation.

Methods and materials. Forty-five multiparous female rats (200 ± 20 g) were mated and examined for vaginal sperm before 9 a.m. the next morning. At intervals of 96, 120, and 144 hr after detection of sperm, groups of 5 rats were killed and their uteri removed and weighed. Histamine was extracted in 10% TCA(7). Uteri of 5 rats were pooled for each time-sample. Bioassays (4-pt) were carried out on atropinized guinea pig gut. Confirmation of histamine was by use of histamine antagonist (tripelennamine) at termination of assay. Three groups were done, all under same conditions.

Results. Figure shows values obtained; histamine concentration (μg/g) and total content (μg). Histamine concentration and content of uteri were markedly reduced between 96 hr and 120-144 hr.

Discussion. Since ovum implantation occurs in rats of this colony around 120-135 hrs after mating, and sperm were detected about 8 hr following mating, reduction in histamine concentration and content of gravid uteri took place just prior to implantation. This correlates with the fact that mast cell population of endometrium is reduced to almost zero during 80th to 120th hr after mating. Moreover this time interval fits the period between provocation of progravid endometrium and appearance of first nests of decidual cells(8). These findings add evidence for a role of histamine in the mechanism of nidation related to induction of decidual cell reaction. The release of histamine is effected by estrogens. Limited and preliminary histamine assays of 10% TCA extracts of uteri of spayed rats, 90 and 180 min after injection of 20 μg of estradiol show relase of histamine by estrogen(9). Spaziani and Szego(10) have recently demonstrated significant decrease of uterine histamine following single injection of estradiol-

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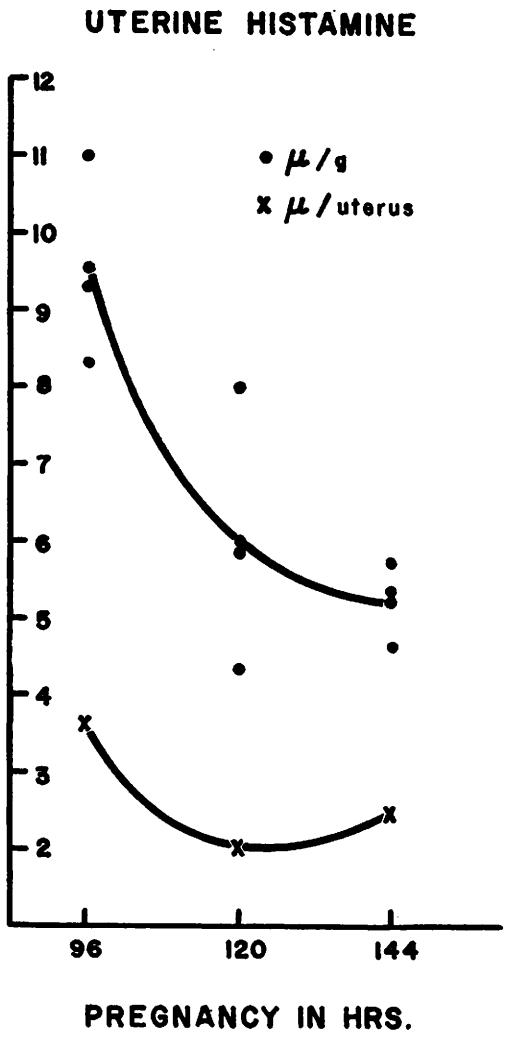

17. Studies recently completed in our laboratory show estradiol, estrone and estriol equally effective on a molar basis in releasing histamine.

Summary. Bioassay of uteri of pregnant rats reveal a significant reduction of concentration and content of histamine during 24 hr prior to actual implantation of blastocyst.

1. Shelesnyak, M. C., *Am. J. Physiol.*, 1952, v170, 522.
2. ———, *Rec. Progr. Hormone Res.*, 1957, v13, 269.
3. ———, *Bull. Soc. roy. belge Gynec. Obstet.*, 1957, v27, 521.
4. ———, *Mem. Soc. Endocrinol.*, 1958, v6, 84.
5. Chambon, Y., Lefrein, H., *C.R.S.B.*, 1952, v146, 821.
6. Kraicer, P., Shelesnyak, M. C., *J. Endocrinol.*, 1958, v17, 324.
7. Parrat, J. R., West, G. B., *J. Physiol.*, 1957, v137, 179.
8. Sachs, L., Shelesnyak, M. C., *J. Endocrinol.*, 1955, v12, 146.
9. Johnson, T. H., Shelesnyak, M. C., *ibid.*, 1958, v17, xxi.
10. Spaziani, E., Szego, C. M., *Endocrinology*, 1958, v63, 669.

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FIG. 1. Histamine concentration (μ/g) and content (μ/uterus) during early pregnancy. Curves connect means of 3 samples, each sample pool of 5 rats.

Detection of Depressant Components of Drug Activity. (24635)

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Seeking a rapid means of detecting subtle central depressant effects of drugs, we administered substances to mice followed by a subhypnotic dose of hexobarbital. In this, and in similar procedures(1,2,3), it is assumed that depressants will add to the effect of the barbiturate and induce loss of the righting reflex. To determine whether central depressant activity could be detected among drugs not ordinarily classified as CNS depressants, widely different types of compounds have been assayed with the results set forth below.

Method. Drugs were administered orally or intraperitoneally when necessary to unstarved, adult male albino mice (CF #1) in groups of 10, at 3 or more doses. Thirty minutes later, (or more, depending on time of peak activity of test drugs) a subhypnotic