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Received February 13, 1958. P.S.E.B.M., 1958, v98.

Uterine Growth Promoting Action of Relaxin. (23932)

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Previous reports indicate that relaxin may have an effect upon several metabolic alterations of the uterus of rat, guinea pig and human. These alterations include glycogen and water content(1,2,3), decidual tissue reactions(4,5) and myometrial activity(6-11). We recently reported that large doses of Relaxin augmented wet and dry uterine weights of non-ovariectomized immature rats, and that exogenous relaxin potentiated weight response of uterus of ovariectomized immature rat to a physiologic level of estradiol-17β (11).

These observations raise the question as to the effect of different dosages of relaxin on relative contents of nitrogen, water and non-nitrogenous solids as well as gross wet and dry weights of uteri of immature female rats. The present study is directly concerned with ascertaining these effects.

Methods. Two groups of intact immature albino female rats were injected daily for 3 days and necropsied on the fourth, one group of females 33 days of age at start of experiment, the other group 28 days old. The animals were neither ovariectomized nor otherwise treated so as to change the hormonal balance.

In each of the 2 age groups there were 8 subgroups receiving saline or different doses of relaxin‡ as shown in the table. The 3 daily doses were given subcutaneously in 0.50 ml fluid. At necropsy the animals were weighed, uteri dissected, blotted on paper, weighed, dried at 110°C for 24 hours, and reweighed. The nitrogen content of the dried uteri was then determined by the Kjeldahl method.

Results. Wet and dry uterine weights are summarized in Table I. Weights of animals

TABLE I. Weight Responses to Relaxin of Uteri of Rats not in Estrus Necropsied at 36 Days of Age and 31 Days of Age.

Treatment, total amt Relaxin in mg	Age in days: 31	36	31	36	31	36	31	36
	No. of rats		mg % wet wt		mg % dry wt		% water content	
Saline controls	10	15	45 ± 3.5	47 ± 2.6	7.4 ± .6	7.9 ± .5	85	85
.0002	7		47 ± 1.5		8.3 ± .6		82	
.001	10	10	51 ± 2.4	47 ± 4.6	8.1 ± .8	7.8 ± .6	86	83
.01	10	9	52 ± 2.4	47 ± 3.5	8.3 ± .6	7.1 ± .7	86	85
.1	17	8	58 ± 3.3	50 ± 4.6	9.7 ± .6	8.5 ± .7	85	85
1.0	10	7	64 ± 4.1	52 ± 4.6	8.4 ± .6	9.8 ±1.2	87	86
2.5		15		58 ± 3.2		10.7 ± .6		82
5.0	10	7	63 ± 6.0	66 ± 4.2	10.1 ±1.1	11.4 ± .9	84	86
10.0	8	9	67 ± 7.0	70 ± 3.9	10.6 ±1.6	11.5 ± .9	84	83

* Studies carried out during tenure of Lederle Medical Faculty Award.

† Supported by grant from U.S.P.H.S., N.I.H.

‡ The authors wish to acknowledge generous supplies of relaxin (Cervilaxin®) furnished by The Princeton Laboratories, Princeton, N. J.

TABLE II. Influence of Relaxin on Nitrogen Content of Uteri of Rats Necropsied at 31 and 36 Days of Age.

Treatment, total amt Relaxin in mg	31 days	36 days	31 days	36 days
	No. of rats		Nitrogen content of dry wt, %	
Saline	10	12	14	13
.001	10	10	15	13
.01	10	10	12	14
.1	10	10	12	12
1.0	10	10	13	13
2.0	10		14	
5.0	10	10	16	13
10.0	8	10	16	12

which had prematurely entered estrous cycles are not included in the averages in this table. Uteri of younger rats showed a greater relative increase in growth than older ones, especially in low dosage ranges. Older animals developed heavier uteri as shown by dry weights after minimum dosage of 0.1 mg, whereas uteri of younger animals responded measurably to 0.0002 mg. Thus it seems that rats 28 to 31 days of age are sensitive to extremely small doses of relaxin. As body weights of animals killed at 36 days of age average 82 g while those killed at 31 days averaged 66 g, the absolute uterine weights of the older animals were greater than those of younger rats for each given dosage.

Nitrogen determinations were done mainly on groups of 10 uteri from each of the original groups regardless of whether or not they manifested vaginal estrus, except for the 10 mg relaxin-treated 31-day-old group in which the results of 2 animals abnormally in estrus are not included.

Results of water and nitrogen determinations thus show a rather constant percentage of each within the limits of experimental error, regardless of age of animals or treatment received. Younger animals exhibit this constancy rather well, while older ones show it less significantly. It may thus be concluded that the increase in uterine weight seen in treated animals after 3 days of relaxin injection is not due to preferential increase in one of these factors, but rather represents a uniform increase in all components.

Summary. Experiments were performed to determine response of uteri of immature albino rats to subcutaneous injections of varying dosages of relaxin. Saline and 0.0002, 0.001, 0.01, 0.1, 1, 5, and 10 mg relaxin were injected into female rats 28 and 33 days old by dividing the dose into thirds and administering each third on 3 consecutive days. Necropsies were performed on the fourth day at ages 31 and 36 days, respectively, and the uteri weighed, dried and reweighed. Wet uterine weights, *i.e.* mg % of body weight, increased along a sigmoid pattern from 45 for saline to 67 for 10 mg in younger group, and from 47 for saline to 70 for 10 mg in older group. Water concentration remained relatively constant, varying between 82 and 87% of wet weights, with no correlation as to amount of relaxin received. Nitrogen content showed a similar response, ranging between 12 and 14% for 36-day-old animals, and 12 and 16% for 31-day-old animals.

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Received February 13, 1958. P.S.E.B.M., 1958, v98.