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The reactivity of the pregnant rat myometrium

SIR,—It has been demonstrated (Schofield, 1957) that the actomyosin concentration of the rabbit myometrium, measured by the tension developed to optimal electrical stimulation, increases from mid-term to parturition and that the synthesis of actomyosin is regulated by oestrogens (Csapo, 1950). For the greater part of pregnancy, the rabbit myometrium is progesterone-dominated and refractory to oxytocin (Schofield, 1957). A possible mechanism by which progesterone exerts its "blocking" action may be due to the greater effectiveness of calcium binding which the progestrone-dominated uterus shows when compared with the oestrogen-dominated uterus (Csapo, 1961). The present work was undertaken to assess the influence of the female sex hormones on the pregnant rat myometrium.

Wistar rats 13–15 weeks old were with males for 4 days and subsequently separated into groups at different periods of gestation; each group therefore represented a 4 day period of gestation as shown in Table 1. Those animals used on the day of parturition were killed within 6 hr of completion of delivery and further animals were used for 3 days post-partum. A group of 10 non-pregnant animals served as controls.

The animals were stunned, decapitated, and the uteri rapidly dissected into a dish of modified Krebs solution (Knifton, 1966) at 4°. One uterine horn from each animal was incised longitudinally and the foetuses removed. A strip of uterus 25 mm × 7 mm was cut, transferred to a 10 ml tissue bath and assembled for electrical stimulation and isometric recording as previously described (Knifton, 1966).

All experiments were made with the tissues adjusted to resting length. After a 30 min resting period to allow the pattern of spontaneous motility to become apparent, the minimum dose of oxytocin (Syntocinon, Sandoz) which caused a uterine contraction (oxytocin threshold) was determined. The tissue was then stimulated electrically at 1 min intervals at optimum voltage, each stimulus of 5 sec duration. When the contractions attained a steady state tension, the tissue was washed repeatedly in calcium-free Krebs solution and the time when the tension was reduced to 50% of the steady state tension (T50) was measured.

The results are summarized in Table 1.

The values for steady state tension increased as gestation advanced to reach a maximum at the time of parturition. When the mean steady state tension of each group is compared with that of the controls however, the difference in tension is not significant until the 17–20 day period of gestation. That is, the steady state

TABLE 1. THE RESPONSE OF THE PREGNANT AND POSTPARTUM RAT UTERUS TO ELECTRICAL STIMULATION AND OXYTOCIN. THE FIGURES SHOW THE MEAN VALUE (±S.E.) FOR EACH GROUP OF ANIMALS.

		Stage of gestation (days)					Stage post-partum (days)			
	Controls	1–4	5–8	9–12	13–16	17–20	Partn	P + 1	P + 2	P + 3
Steady state tension (g) ..	4·11 ±0·65	3·70 ±0·71	3·73 ±0·67	4·35 ±1·02	5·72 ±1·12	6·40 ±1·04	8·55 ±1·21	8·72 ±1·09	4·78 ±0·89	3·58 ±0·43
T50 (min)	4·05 ±0·77	3·55 ±0·95	4·73 ±1·07	6·77 ±1·59	7·03 ±1·23	6·70 ±1·67	1·58 ±0·28	3·01 ±0·50	3·43 ±0·64	3·74 ±0·77
Oxytocin threshold (mU)	0·91 ±0·51	0·57 ±0·42	1·54 ±0·33	3·00 ±1·16	2·34 ±1·17	0·98 ±0·39	0·31 ±0·17	1·14 ±0·45	0·53 ±0·25	1·16 ±0·41
Number of animals per group ..	10	7	8	8	9	13	11	13	10	12

tension in the 17–20 day group, the animals on the day of parturition and those the day after parturition is significantly greater ($P < 0.05$) than that of the controls. Two days after parturition, tension had fallen abruptly. It has been shown (Csapo & Corner, 1953) that, other factors being equal, the tension developed by the myometrium to optimal electrical stimulation is proportional to the actomyosin concentration, which reflects the degree of influence of oestrogens. This would indicate that in the rat, there is a fairly sudden rise in oestrogen output towards the end of gestation to reach a peak at parturition and an abrupt post-partum decline. The conclusion is endorsed by other work (Knifton, 1967) where it was shown that, in the rat, progesterone does not affect the tension developed by the myometrium to optimal electrical stimulation.

When compared with the non-pregnant controls, the sensitivity to oxytocin did not change significantly throughout gestation until the day of parturition when it increased ($P < 0.05$). There is also a difference in sensitivity to oxytocin ($P < 0.05$) between the parturient group and the group in mid pregnancy (9–12 days).

The degree of calcium binding in the myometrium, indicated by the time taken to reduce tension by 50% in calcium-free Krebs solution (T50), approximates to the oxytocin sensitivity at different stages of pregnancy. Calcium is bound most effectively during mid pregnancy; the difference between the 13–16 day group and the controls is significant at the 5% level. There is an abrupt decrease in calcium binding on the day of parturition which coincides with the sudden increase in sensitivity to oxytocin. These findings are in accord with the evidence reviewed by Daniel (1964) that when calcium is effectively bound in smooth muscle membrane, the tissue is relatively refractory to stimulation.

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