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Effect of Calcium Upon Uterine Activity and Reactivity.

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Since the original reports by Blair-Bell[1, 2] very little experimental study has been devoted to the effect of calcium on uterine motility, although in the clinical literature varying opinions have been expressed. This study was undertaken to repeat in part the experiments of Blair-Bell and to ascertain the relation of available calcium to the reactivity of the uterus to pitocin.

Ten postpartum dogs were used for this study. Uterine motility was recorded by the method of Rudolph and Ivy,[3] in which a balloon is placed in each uterine horn, appropriately inflated, and connected to a water manometer. After control tracings had been made the following solutions were administered intravenously: calcium, as a 10% solution of calcium chloride; sodium hexa-metaphosphate, a substance which combines with calcium in such a manner that it is unable to act physiologically; and pitocin (Parke, Davis & Company). After the effects of these had been observed, they were combined, as indicated below, and administered. Sodium pentobarbital was used as an initial anesthesia. After the dog had been prepared, analgesia was maintained by the subcutaneous injection of morphine sulfate at hourly intervals. This did not affect uterine motility. The results of the experiments on the dog were checked *in vitro* by using uterine strips obtained from guinea pigs in diestrus. Either oxygenated "normal" or calcium-free Locke's solution was used.

Dog's uterus in situ. In all instances (20 experiments) calcium, in doses of from 10-30 mg of calcium per kilo of body weight, was found to augment the motility of the dog's uterus *in situ*. Both the rate and amplitude of contraction, as well as coördination between the 2 horns, were increased. The opposite effect was noted when sodium hexametaphosphate (20 experiments) 10-25 mg per kilo was administered; in many instances the uterus was reduced to a state of complete quiescence which was sustained, frequently, for more than 20 minutes. The injection of suitable amounts of

[1] Blair-Bell, W., and Hick, P., *Brit. Med. J.*, 1909, **1**, 777.

[2] Blair-Bell, W., *Proc. Roy. Soc. Med.*, 1915, **8**, 71.

[3] Rudolph, L., and Ivy, A. C., *Am. J. Obst. and Gynec.*, 1930, **19**, 317.

calcium immediately restored normal rhythm and coördination.

The minimal effective dose (M.E.D.) of pitocin (which varied from 1 cc of a 1:10,000 solution per kilo to 1 cc of a 1:1,000 solution per kilo) was determined by injecting that amount which produced a definitely detectable increase either in rate, or amplitude of the uterine contractions, usually both. Larger doses, of course, produced tetany. When the M.E.D. of pitocin was given simultaneously with, or shortly after, the injection of calcium, the effect was invariably greater (20 experiments) than that produced by the pitocin alone. Conversely, when the M.E.D. of pitocin was given with, or shortly after, the injection of sodium hexametaphosphate, the effect was either markedly reduced or not observed at all. The latter reaction was the rule (15 experiments), the former the exception (5 experiments). After injecting an adequate dose of calcium the uterus responded to an M.E.D. dose of pitocin.

Guinea pig's uterus in vitro. When the guinea pig's uterus was placed in oxygenated Locke's solution the addition of calcium (1.5-3.0 mg to a 50 cc bath) caused augmentation. The addition of 0.05 to 0.1 cc of a 1:100 solution of pitocin augmented the contractions (12 experiments). When the 2 were added to the bath simultaneously an additive effect was observed. When the uterus was bathed (12 experiments) with oxygenated calcium-free Locke's solution pitocin in the doses given above either had no, or only a very slight effect. These results confirm those of Van Dyke and Hastings.[4]

This study substantiates previous findings concerning the oxytocic effect of calcium and, further, shows that in its absence the uterus is incapable of contracting in a normal manner or of manifesting its usual reactivity to pitocin. The activity and reactivity of the uterus under conditions in which the available calcium is diminished suggest the condition observed during early pregnancy and during the latter part of the menstrual cycle, and also following treatment with progesterone. There is no evidence showing that the two states of the uterus just referred to have a common basis, but the similarity is striking. This is now being investigated.

Conclusion. Spontaneous contractions of the postpartum dog uterus or the diestrous uterus of the guinea pig may be augmented by the administration of calcium or depressed or completely inhibited by diminishing the available calcium. In the latter instance the uterus is usually not only quiescent, but is also relatively refractory to pitocin.

[4] Van Dyke, H. B., and Hastings, A. B., *Am. J. Physiol.*, 1928, **83**, 563.