

Induction of Lactation in Rabbits with Reserpine.* (23590)

JOSEPH MEITES[†] (With technical assistance of Valerie Cholvin and Beth Alsup)

Department of Physiology and Pharmacology, Michigan State University, East Lansing

Sawyer(1) reported that when estradiol benzoate was injected subcutaneously into mature female rabbits for 2 days followed by a single intravenous injection of reserpine, milk was observed one week later in the lactiferous ducts of 15 out of 20 animals. Gaunt (private communication) has confirmed this finding, although in some of the rabbits only a pale watery secretion was seen. These observations suggested that reserpine may induce an increased secretion and/or release of prolactin from the anterior pituitary. In view of evidence that estrogen alone can increase pituitary prolactin content and initiate lactation in a number of species, including rabbits(2,3), it was of interest to determine whether the lactation induced in rabbits was in fact elicited by reserpine and not by the prior treatment with estrogen. It was also of interest to see whether reserpine could stimulate mammary development beyond that produced by estrogen alone.

Methods. Twenty-four mature female rabbits, predominantly New Zealand White in origin, were used in 3 separate experiments. These rabbits weighed 2.8-4.8 kg each and were fed a standard rabbit diet. In the first experiment, 8 rabbits were injected subcutaneously for 2 successive days with 0.2 mg estradiol[‡] daily, and on the third day 4 were injected intravenously with 1 mg reserpine/kilo body weight. The other 4 served as controls. One week later a slight amount of milk could be expressed from the nipples of 3 of the 4 reserpine-injected rabbits and from none of the controls. Milk could still be expressed from one of the reserpine-treated

rabbits almost one month after administration of the drug. In the *second experiment*, 4 rabbits were made pseudopregnant by a single intravenous injection of chorionic gonadotrophin, and 15 days later 2 of these rabbits were injected once intravenously with 1 mg reserpine/kilo body weight. The other 2 served as controls. Only the 2 reserpine-injected rabbits had milk when examined 5-7 days later, and the quantity of milk present in the mammary glands appeared to be somewhat greater than in the rabbits treated with the drug in the first experiment. Lactation persisted in one of the 2 reserpine-injected rabbits for more than a month after treatment. In the *third experiment*, 12 rabbits were injected with 0.2 mg estradiol daily for 10 days, and on the 11th day 6 rabbits were injected intravenously with the same dose of reserpine used in the previous 2 experiments, and the other 6 served as controls. One week later all the rabbits were killed and their mammary glands were removed for macroscopic and histological examination. Their pituitaries were also removed for prolactin assay. *Lactation* occurred in all 6 reserpine-treated rabbits but not in the controls. When the mammary glands were exposed it was apparent that those from the reserpine-treated rabbits were enlarged and milk could be seen in the lactiferous ducts (Fig. 1). On the other hand the mammary glands of the controls were so undeveloped that they were not readily visible macroscopically. Stained whole mounts of these mammary glands showed that when estrogen was followed by reserpine, there was extensive development of the lobule alveolar system comparable to that seen in pseudopregnant rabbits. Estrogen alone elicited mainly an extension of the duct system (Fig. 2). Histological examination revealed that the mammary alveoli of reserpine-treated rabbits were filled with secretion, whereas few alveoli were seen in controls and the ducts were dilated. A fuller description

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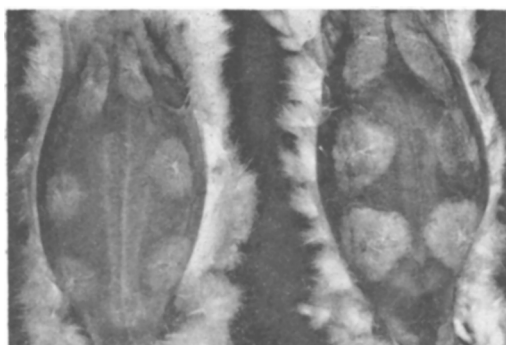


FIG. 1. Lactating mammary glands from 2 rabbits injected subcutaneously for 10 days with 0.2 mg of estradiol daily followed by a single intravenous injection of 1 mg reserpine/kilo body wt. The mammary glands of rabbits injected only with estradiol were not visible macroscopically.

of the histology of the mammary glands as well as the results of the prolactin assays will be published upon completion of this phase of the work.

Discussion. The results reported here confirm the findings of Sawyer(1) and Gaunt (private communication). Experiments currently in progress also indicate that daily administration of reserpine can initiate milk secretion in mature female rabbits without prior treatment with estrogen or induction of pseudopregnancy. There can be little question that reserpine can elicit mammary growth in addition to initiating lactation in rabbits. In none of the reserpine-treated rabbits was the degree of lactation induced comparable to that seen in rabbits after parturition. It is possible, however, that daily administration of reserpine to rabbits with fully-developed mammary glands would produce a much greater yield of milk than seen in the present study.

The mechanism(s) whereby reserpine initiates lactation in rabbits remains to be elucidated, although the results suggest that release and/or secretion of prolactin by the anterior pituitary are increased by the drug. Other factors from the pituitary favorable to mammary growth and lactation may also be released at increased rates by reserpine, although prolactin has been shown to be the only hormone capable of directly stimulating the mammary secretory cells to produce milk(4). That reserpine may induce an in-

creased release of prolactin from the pituitary is also suggested by the observation of Baraclough(5) that reserpine injections into rats during diestrus result in a maximum and prolonged decidual response following traumatization of the uterus.

It is of interest that several clinical investigators have recently observed that administration of chlorpromazine occasionally elicits lactation in women patients(6-9). A similar mechanism(s) to that of reserpine is probably involved. That reserpine may inhibit rather than stimulate other functions controlled by the endocrine system is suggested by reports that it may depress thyroid function(10) and interfere with the estrous cycle and conception in the rat(11,12). There is also evidence that reserpine may inhibit certain hypothalamic functions(13,14).

Summary. 1. Twenty mature female rabbits were injected subcutaneously with 0.2 mg estradiol daily for 2 or 10 days, followed by a single intravenous injection of 1 mg reserpine/kilo body weight into 10 animals. The other 10 rabbits served as controls. Nine of the 10 reserpine-treated rabbits came into lactation one week later while none of the controls produced milk. Four other rabbits were made pseudopregnant, and 15 days later 2 were injected as above with reserpine and 2 served as controls. Only the 2 reserpine-treated animals came into milk. 2. Macroscopic and histological examination of the mammary glands of reserpine-treated rabbits

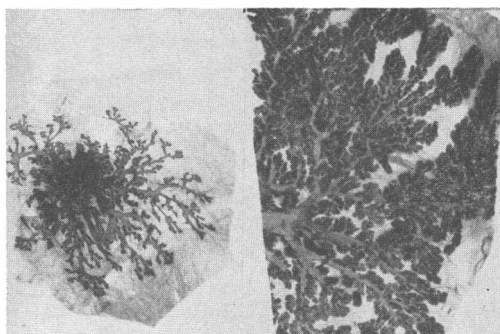


FIG. 2. *Left.* Whole mammary gland from a rabbit injected with estradiol for 10 days and killed 1 week later. *Right.* Half of mammary gland from a rabbit injected with estradiol for 10 days, followed by a single injection of reserpine and killed 1 week later.

previously injected with estrogen revealed extensive lobule-alveolar development with secretion in the alveoli, whereas controls injected only with estrogen showed an extension of the duct system with no alveolar growth. 3. It is probable that reserpine induced an increased secretion and/or release of prolactin and perhaps of other hormones favorable to mammary growth and lactation, but confirmation of this hypothesis awaits assay of pituitary hormones.

Addendum: Pituitary assays now completed reveal that reserpine induced a substantial increase in prolactin in both normal and estrogen-treated rabbits.

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Effects of Growth Hormone on Lactation and Body Growth of Parturient Rats.* (23591)

JOSEPH MEITES (With technical assistance of Valerie Cholvin and Beth Alsup)

Department of Physiology and Pharmacology, Michigan State University, East Lansing

Growth hormone (GH) has been demonstrated to increase milk yields in the parturient cow(1,2), sheep(3) and goat(4). Shaw *et al.*(5) reported that when GH was injected into cows on a limited ration, milk production fell for the first 3 days but this was followed by a return to normal levels of milk together with a striking increase in milk fat. This suggests that GH injections into lactating ruminants may preferentially divert nutrients to the mammary glands rather than be used for growth or maintenance purposes. Significant effects of GH on body weight of ruminants have not been reported.

It was of interest to determine whether injections of GH into parturient rats would (a) elicit increases in milk production similar to those observed in ruminants and (b) increase body weight. The ability of GH to

increase body weight in mature female rats which have reached growth stasis constitutes an established assay method for this hormone(6).

Methods. Mature female albino rats (Carrworth) of uniform age and weight and which had reached growth stasis were bred, and on the day of parturition their litters were reduced to 6 young per dam. On the 5th day after parturition, 20 rats were divided into 2 groups of 10 each. Ten were injected subcutaneously with 1 mg GH[†] daily in .1 cc distilled water, and the other 10 rats (controls) were injected only with the same volume of distilled water. This treatment was continued until the 17th day after parturition. The rats were maintained in an air-conditioned, temperature controlled room, and both dams and litters were weighed

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