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Induction of Mammary Secretion in Rats by Electrical Stimulation.* (26251)

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This laboratory has recently demonstrated that many agents can induce mammary growth and/or secretion in estrogen-primed rats, including adrenergic and cholinergic drugs(1,2), tranquilizers(3,4), morphine(5), carcinogens(2), rat hypothalamic tissue(6), electrical stimulation of the uterine cervix (5) and several nonspecific stresses(7). Most of these agents are believed to act through the CNS but others may directly stimulate the anterior pituitary to release prolactin and ACTH. Most of these agents have produced adrenal cortical stimulation as indicated by reduced thymus weight, and both prolactin and ACTH have been shown to be essential for initiating mammary secretion in intact, estrogen-primed rats(7). It was of interest to see whether direct electrical stimulation of the head, nasal mucosa, lumbar region and nipples could also release sufficient prolactin and ACTH to induce mammary secretion in estrogen-primed rats.

Methods. Virgin female rats (Carworth) weighing between 200-300 g were injected subcutaneously with 10 μg estradiol per day for 10 days to produce mammary lobule-alveolar development(4). For the next 5 days, 4 groups of 5 rats each were electrically stimulated for 30 seconds twice daily in the regions of the head, nasal mucosa, lumbar area and nipples, respectively. Ten control rats received injections of physiological saline twice daily. An electrodyne stimulator with fine needle point electrodes, set at a frequency of 20 cycles/second, was used. The electrodes used for different groups were the same. The alternating current was just detectable on the finger tips and produced only slight struggling by the rats. Electrical stimulation of the head was effected by piercing the 2 electrodes through the skin over the frontal bones; of the lumbar region by piercing the electrodes through the skin of the 2nd and 3rd lumbar vertebrae; of the nasal mucosa by placing the electrodes in the nasal openings; of the nipples by inserting one electrode in the dermis of the teat and the other in the skin surrounding the nipple. On the 16th day, all rats were killed and the right inguinal mammary glands were removed, fixed in Bouin's fluid, sectioned at 6-7 μ and stained with H and E stain. The sections were examined microscopically and assigned ratings of 0 to 3.00 in units of 0.25, depending on amount of mammary secretion observed. Adrenals, thymus, ovaries and uterus were also removed and weighed.

Results. The mammary glands of the saline-injected controls (Group 1) regressed from a lobule-alveolar system at 10 days to practically a bare duct system by the 16th day, with no evidence of secretion (Table I).

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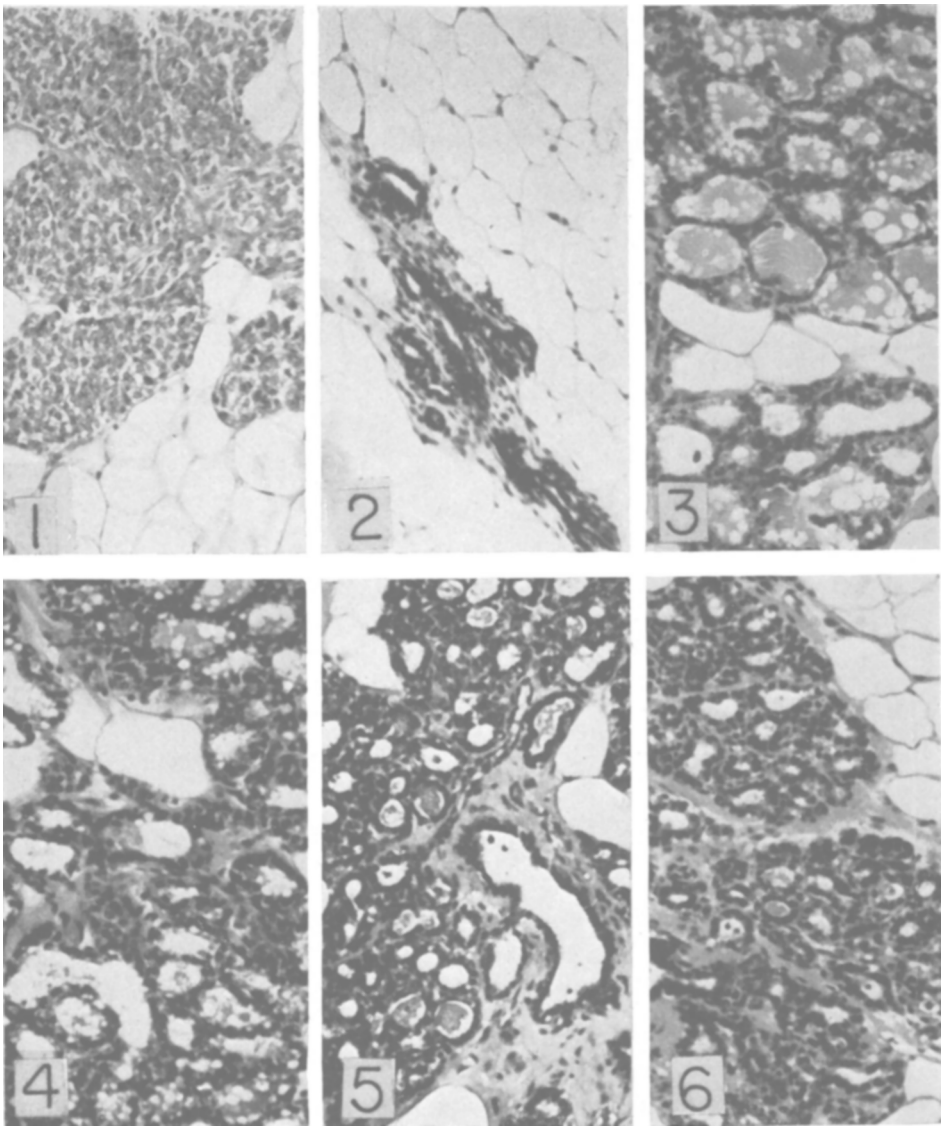

FIG. 1-6. Histological sections of mammary tissue from treated rats. (1) Estradiol 10 days. Note lobule-alveolar growth. (2) Estradiol 10 days, saline 5 days. Note mammary regression. Other rats were given estradiol 10 days, followed by electrical stimulation of (3) nasal mucosa, (4) lumbar area, (5) head, (6) nipples. ×125.

All electrically-stimulated rats (Groups 2-5) showed varying degrees of mammary secretion and maintenance of lobule-alveolar structure, which were more pronounced in the rats stimulated in nasal mucosa and lumbar region than in those stimulated on head or nipples (Fig. 1-6). No inflammatory or edematous reaction was observed at site of insertion of the electrodes. Thymus glands of all electrically-stimulated groups were significantly reduced in weight below control values, but none of the other organs showed significant weight differences.

Discussion. The present results agree with and extend previous work showing that electrical stimulation of the uterine cervix initiates mammary secretion in estrogen-primed rats(5). Stimulation of nasal mucosa and lumbar regions was more effective than stimulation of nipples or head. This

TABLE I. Effects of Electrical Stimulation on Initiation of Mammary Secretion in Estrogen-Primed Rats.

Group and No. of rats	Region stimulated for 5 days	No. with secretion	Avg secretion rating*
1 (10)	Controls, saline 2× daily	0	0
2 (5)	Head, stim. 2× daily	5	0.5
3 (5)	Nasal mucosa, stim. 2× daily	5	1.2
4 (5)	Lumbar area, stim. 2× daily	5	0.9
5 (5)	Nipples, stim. 2× daily	4	0.4

* Range = 0 to 3.00.

may be due to greater concentration of nerve fibers in the former sites. Frequent suckling of the nipples of virgin rats by fresh litters has been shown to induce mammary growth and lactation(8), and in postpartum rats to elicit release of prolactin and ACTH(9), but nipples of the estrogen-primed rats were not as well developed as in these rats. Since all electrically-stimulated groups showed increased adrenal cortical function as indicated by a significant decrease in thymus weight, and both ACTH and prolactin are needed to initiate mammary secretion in estrogen-primed rats(7), it can be concluded that both hormones were released by electrical stimulation.

It is of interest that pseudopregnancy has been induced in sexually mature rats by electrical stimulation of the skull(10) and uterine cervix(11); and in sexually mature rabbits by electrical stimulation of head and lumbar region(12). Sexual maturation in prepubertal rats has also been hastened by electrical stimulation of the uterine cervix (13). Thus in the rat, electrical stimulation of some tissues apparently induced release of FSH and LH in addition to ACTH and prolactin. It is probable that oxytocin and vasopressin are also released, but there is no evidence that either of these hormones can induce mammary secretion in rats(5,14).

The effects on the anterior pituitary are believed to be mediated through the autonomic and CNS. Thus, interruption of sympathetic pathways during electrical stimulation of the uterine cervix prevents pseudopregnancy in the rat (15), while transplantation of the pituitary to a non-cranial site(16) or injections of rat hypothalamic tissue(6) induces mammary secretion in estrogen-primed rats.

Summary. Mature virgin female rats were injected subcutaneously with 10 μg estradiol daily for 10 days to produce mammary lobule-alveolar development. For the following 5 days, all except 10 controls were electrically stimulated twice daliy for periods of 30 seconds on head, lumbar region, nasal mucosa and nipples. Control rats showed regression of the mammary glands to a bare duct system and no secretion, whereas almost all of the electrically stimulated rats showed variable degrees of mammary secretion and maintenance of lobule-alveolar structure. Adrenal cortical stimulation in all electrically-stimulated groups was indicated by significant decreases in thymus weight. It is concluded that electrical stimulation of these areas in the rat induces release of both prolactin and ACTH, probably through autonomic and CNS pathways.

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