

changes. Cells of unusual size, having an excentric nucleus and a large vacuole in the cytoplasm, were observed. These elements are very similar to the so-called "castration cells" or the cells observed after thyroidectomy. In many cases hemorrhages were seen in the anterior lobe, and large cysts lined with epithelium and filled with colloid were frequently observed.

These findings show that marked histological changes of a degenerative type may be produced in the hypophysis by the chronic administration of hypophyseal extracts.

7276 C

Production of Pseudo-Pregnancy by Mechanical Stimulation of the Nipples.

H. SELYE AND T. MCKEOWN. (Introduced by J. B. Collip.)

From the Department of Biochemistry, McGill University, Montreal.

We have previously described experiments on lactating rats in which we found that the nervous stimulus of suckling could maintain the dioestrus of lactation after all galactophores had been trans-cised.^{1,2} It was also observed that in such animals, from which escape of milk to the litter was prevented, the mammary gland did not undergo rapid involution, but remained in an actively secreting state for some time in spite of the accumulation of the products of secretion.

The escape of milk is therefore not an essential condition for the continuation of dioestrus or for the maintenance of secretory activity in the mammary glands. Accordingly, the questions arise whether the influence of suckling could produce dioestrus in the absence of actively lactating glands and whether, since suckling will maintain the secreting gland, it could lead to a regeneration once involution has set in.

In order to answer these questions we performed the following experiments on rats.

The animals used fall into 3 groups: first, adult virgin rats; second, animals whose litters have been weaned at the end of a normal lactation and which have been seen to be normally cyclic for at least 3 cycles; and third, lactating mothers deprived of their litters

¹ Selye, H., *Am. J. Physiol.*, 1934, **107**, 535.

² Selye, H., Collip, J. B., and Thomson, D. L., *Endocrinology*, 1934, in press.

on the third day postpartum and studied daily until one or 2 oestrus cycles had appeared. To all animals a strong suckling stimulus was applied, and in order to keep the young alive they were exchanged with the well nourished litter of a normally lactating mother on alternate days, the young of the normal mother being transferred



FIG. 1.
Mammary gland of an adult female rat. Only ducts are present.

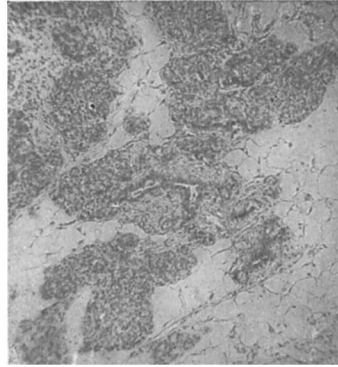


FIG. 2.
Mammary gland of the same rat in early stage of pseudo-pregnancy induced by suckling. Alveoli form around the ducts.

on these days to the experimental animal. Thus the rats under observation were continuously exposed to the suckling stimulus.

There were obvious technical difficulties. On the theory of cer-



FIG. 3.
Uterus of a rat during pseudo-pregnancy induced by suckling. Normal endometrium on the right, large placentoma invading the uterine cavity from the left.

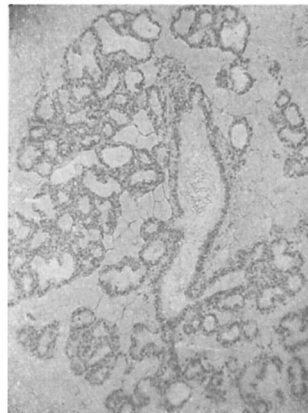


FIG. 4.
Secreting mammary gland with distended alveoli in a rat weaned for a short period, and then given litter again.

tain investigators, suggesting a hormonal basis for maternal instincts, it seemed unlikely that virginal or weaned animals would tolerate the presence of a young litter. But it was found that only rarely would an animal harm the litter, and this occurred no less frequently with lactating mothers than with virgins. In many instances, however, there was no suckling, either from the unwillingness of the animal to allow it or from the inability of the litter to find the relatively small nipples of virginal and weaned rats. Further, nipples frequently became necrotic from the strength of the stimulus, especially in virgins and in animals weaned for a long time.

It was found that the teats could be made more obvious by cutting the hair immediately around them and by teasing them out gently between 2 moistened fingers.

We attempted to expose 6 virgin rats to the stimulus of suckling as described above. Out of this group we found that active suckling occurred only in one case, and in this instance the nipples became necrotic and the animal had to be discarded. Considering that the nipples of a virgin are very much smaller than those of an animal that has at some time been pregnant, we continued our experiments on animals of the latter type.

These animals were taken from large cages in which numerous males and females were kept together. Their previous sex history had not been followed, but their having been pregnant at some time was indicated by the appearance of the nipples. Vaginal smears were taken daily from the day of selection, and only those animals which were regularly cyclic were used.

Of 25 animals given litters, active suckling occurred only in 15 cases. In this group again we observed that some of the nipples became necrotic and for this reason a few animals had to be discarded. There remained, however, a group of 8 animals, in some of which a partial necrosis of a few nipples had been observed in the earlier part of the experiment, but after a few days the teats took on the appearance and flexibility of those of a lactating mother, and from that time the mechanical stimulus of nursing caused no further damage.

These animals became continuously dioestrous, but in some cases an oestrus cycle occurred after the initiation of nursing. As biopsy specimens showed (Figs. 1, 2) the mammary gland developed to the same extent as it would in the course of pseudo-pregnancy. Numerous alveoli appeared around the ducts, but they showed little or no sign of secretion. The uteri became progestational in appearance.

In many cases large placentomata were found (Fig. 3). The ovaries contained one set of large corpora lutea similar to those of pregnancy. Maturing follicles were never observed. The average weight of the ovaries was about 80 mg., and that of the pituitaries 16 mg. These weights correspond closely to those that we find in the pregnant animals of our colony. In some cases silk threads were placed in the uterus, and the placentoma development typical of pseudo-pregnancy followed.

These findings lead us to the conclusion that the stimulus of nursing induced a condition resembling pseudo-pregnancy.

In the next series, a group of 5 rats was weaned on the third day postpartum, from which time vaginal smears were taken. A litter was given to 2 of these after the appearance of the first cycle, and to the other 3 after the appearance of the second cycle. Although the mammary glands had stopped secretion and had undergone severe atrophy in every case at that time, secretion started again in all animals under the influence of suckling (Fig. 4). Further, immediately on the return of the litter the cycles stopped and dioestrous set in, lasting 13 to 16 days, except in the case of one animal which was still dioestrous on the twenty-second day, at which time it was killed.

From these experiments it appears that mechanical irritation of the nipple may lead to a condition closely resembling, if not identical with, the pseudo-pregnancy produced by sterile copulation. It is interesting to note that this same stimulus which maintains secretion in the mammary gland of the normal lactating animal leads to the development of glandular epithelium similar to that seen in pregnancy, but with little or no secretion when applied to an animal in which the mammary gland has undergone involution.

In view of these findings the question arises whether the corpus luteum of lactation is not merely a corpus luteum of pseudo-pregnancy produced by the act of suckling. Although some workers have reported that placentomata may be produced during lactation in rodents by irritation of the uterine mucosa,³ we ourselves have rarely seen spontaneous deciduomata at this period.

Considering that almost all of our experimental animals showing pseudo-pregnancy also showed spontaneous placentomata, we feel that there must be a difference in the response of the animal to suckling, depending upon whether the stimulus is applied during or outside of lactation. This view is further substantiated by the fact that no obvious mammary growth is observed during lactation, but

³ Corner, E. W., and Warren, S. L., *Anat. Rec.*, 1919, **16**, 168.

secretion is active, while during pseudo-pregnancy the growth processes are very conspicuous, and little or no secretion occurs.

Summary. A condition resembling pseudo-pregnancy has been obtained in adult female rats, by the mechanical irritation of the nipple, produced by an actively suckling litter.

7277 P

Dependence of Continuous Bioelectric Currents upon Cell Oxidation.

H. F. ROSENE. (Introduced by E. J. Lund.)

From the Department of Zoology, University of Texas.

Lund has shown that bioelectric potentials are quantitatively linked with oxidations (frog skin, hydroids, etc.) and has advanced the theory that continuous bioelectric currents are established by redox systems in flux equilibrium within the cell.¹ The new findings

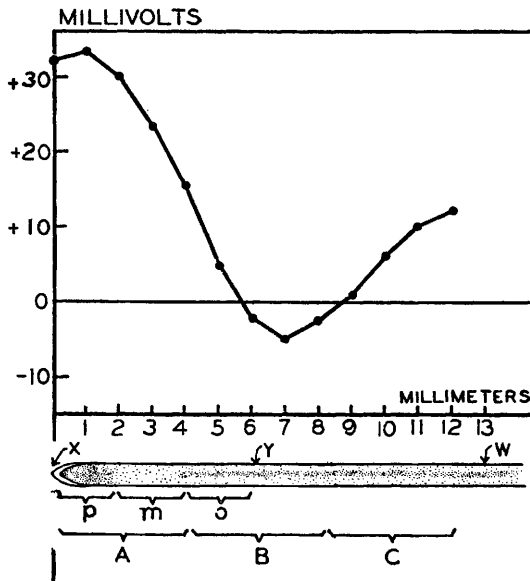


FIG. 1.

Typical curve of distribution of E. M. F. per unit length of root (*A. cepa*). Abscissa, position of positive electrode in millimeters from the tip. Root regions are drawn to scale. See text for further description.

¹ Lund, E. J., *Protoplasma*, 1931, **18**, 236.