pointed out, for instance, that "proteolipid" appears in extracts of wet ghosts, and this would be difficult to account for on a completely mechanical view. It seems most probable that the experimental extraction procedures employed do give an indication of relative stability of certain undefined lipid complexes in the red cell membrane. The data may therefore be regarded as evidence for the view that insusceptibility of camel cells to cobra hemolysin is due to a peculiar binding of lecithin which makes it inaccessible to venom enzymes. The idea has been advanced many times in connection with the old observation that the red cells of some species, notably the ruminants, are resistant to venom(4), but never examined experimentally. In any case, either the binding or the spatial orientation of red cell phosphatides, or both, would appear to be different in the camel. At the same time it is clear that detailed analysis of these lipids is desirable; the possibility exists, however unlikely, that the findings may be further related to a novel sort of phosphatide.

It is impossible to say whether phosphatide composition or structure may be related to the morphological features of size and shape. But it can be noted (a) that appreciable amounts of lecithin cannot be found in the red cells of the 3 species of true ruminants thus far examined, while the cells of this group as a whole are relatively small in size, and (b) that a peculiarity of lipid constitution appears to exist in the camel cell, which has an oval shape.

The method of extraction may perhaps, with suitable modifications, be applied to pathological tissues, *e.g.*, in human diseases involving the erythrocyte it is possible that lesions of the red cell membrane could exist that might be manifested in terms of the ease or difficulty with which bound lipids are liberated.

Summary. The red cells of the camel are like those of true ruminants in being resistant to lysis by cobra venom but dissimilar in appearing to contain lecithin. The idea that the resistance of camel cells to venom is due to the binding of lecithin so that it is inaccessible to venom enzymes has been tested in terms of comparative extractability into ether-ethanol mixtures of phosphatides from cells of man, ox, and camel. The lipids were liberated much less readily in the case of the camel, indicating that the lipid complexes are different and more stable.

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Effect of Reserpine* on Mammary Gland Involution, and on Other Organs in the Rat. (24416)

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A number of workers have reported recently on lactogenic effects of reserpine in several species, *i.e.* rabbits(1,2), rats(3,4) and man(5,6). However, in this laboratory, Tindal(7) has investigated mammogenic or

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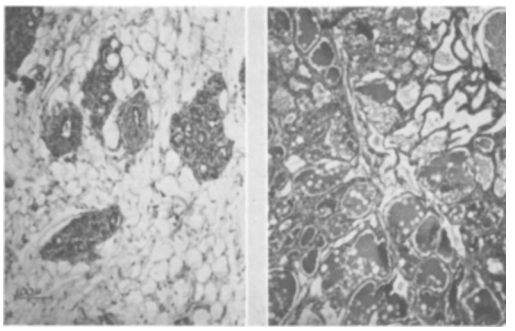

FIG. 1. Sections from left abdominal mammary glands of lactating rats treated with saline (left), and reserpine (right), 100 μg daily, for 9 days after removal of the pups on 4th day of lactation. Involution is retarded after treatment with reserpine.

lactogenic potency of this compound in rats, rabbits, goats and pigeons, without obtaining any positive effects. In view of the somewhat conflicting evidence with regard to effects of this substance on mammary gland, it was of interest to study the effect of reserpine on mammary gland involution in the lactating rat after weaning, as investigated by Benson and Folley(8). These authors have demonstrated that oxytocin, like prolactin, will inhibit mammary gland involution in rats after weaning, and it seemed possible, in view of the alleged lactogenic action of reserpine, that the administration of this substance would inhibit mammary regression in a similar manner.

Materials and methods. 24 Hooded Norway rats were used, 2-3 months old, undergoing first lactation. Stock colony diet(9) with addition of powdered milk, was fed *ad lib,* and food consumption was recorded daily. After parturition all litters were reduced to 9 pups on first day of lactation, and to 8 on second day. Litters were weighed daily to check lactational performance of the mother, and the mothers were also weighed daily. Pups were removed on 4th day of lactation, when treatment began. Reserpine was administered, as supplied, in a stabilised aqueous vehicle. The animals were divided into 3 groups of 8, one group receiving 50 μg reserpine daily; the second group 100 μg reserpine daily, and the third group served as a control and received 0.5 ml saline daily. The substance was in all cases administered as a single daily injection, subcutaneously, and treatment was carried out for 9 days, the animal being killed on the 13th day after parturition. Histological study of mammary tissue was then carried out exactly as described by Benson and Folley(8), the estimation of percentage parenchyma again being used as a quantitative method of assessing alveolar maintenance. In addition various other organs were removed, weighed, and preserved for further study.

Results. The mammary glands of both reserpine treated groups exhibited a very high degree of alveolar maintenance, which was particularly marked in the group receiving highest dose of reserpine. This is in contrast to the advanced state of regression observed in mammary glands of the saline treated group (Fig. 1). In Table I the values for percentage parenchyma of all 3 groups are given; the figure of 67.4 for the higher dosage group is remarkably high, being comparable to the best results obtained in this type of experiment, after treatment with a combination of prolactin and growth hormone (STH)(8).

Vaginae, uteri and ovaries. Uteri of untreated animals were significantly heavier than those from the reserpine treated groups, but there was no significant difference between weights of ovaries (Table I). Histological examination of uteri and ovaries from all 3 groups has also been carried out. No apparent differences could be detected in the ovaries, but the observations made on uteri indicate that ovaries differed functionally, and suggest an explanation for uterine weight differences. Thus, a number of uteri from untreated group exhibited a prooestrous or oestrous condition(10), a finding which was confirmed when the vaginae from the same animals were examined. In contrast, vaginae of all reserpine treated animals showed marked vaginal mucification, which compares favorably with results reported by Benson and Folley(8) after oxytocin administration, and appears to confirm the assumption that prolactin (LTH) has been released as a result of reserpine treatment. Evidence for luteotrophic activity following reserpine administration has previously been reported by Barraclough(11).

TABLE I. Effect of Reserpine Treatment on Mammary Gland Regression, Body Weight, Organ Weights and Food Consumption, in the Rat after Weaning at the Fourth Day of Lactation; 8 Rats per Group.

Treatment	% parenchyma at 13th day	% decrease in body wt over treatment period	Mean daily food consumption (g) over treatment period	Mean wt (mg)/100 g body wt				
				Thymus	Adrenals	Uterus	Ovaries	Thyroids
Saline, .5 ml daily	23.2 ± 3.4	1.0 ± .9	16.7 ± .6	131.8 ± 6.9	29.2 ± 1.0	191.5 ± 7.1	35.8 ± 1.9	12.7 ± .9
Reserpine, 50 μg daily	54.0 ± 4.6	3.0 ± 1.3	16.6 ± .6	100.1 ± 12.5	34.2 ± 1.5	115.2 ± 10.3	32.7 ± 1.2	12.3 ± 1.0
" 100 " "	67.4 ± 3.9	22.0 ± 2.9	8.9 ± .9	56.9 ± 5.3	41.8 ± 2.3	137.9 ± 6.7	33.4 ± 1.4	13.3 ± .6

Other organs. A study of organ weights of the 3 groups (Table I) reveals that reserpine has caused a highly significant increase in adrenal weight over the 9 day treatment period, as compared to control values, with a corresponding highly significant decrease in thymus weight. This is again particularly marked in the group receiving higher dose of reserpine. There is no significant difference between weights of thyroids of treated and untreated groups.

Body weight. The smaller dose of reserpine had little effect on food intake and body weight over the treatment period when compared to the control group. The higher dose, however, greatly affected appetite, the food intake being approximately halved, and a much larger percentage body weight decrease was apparent in this group over the treatment period (Table I).

Discussion. The results of this experiment appear to be in harmony with the conclusion of several authors that reserpine exerts a lactogenic effect under certain experimental conditions(1-6). Its effect in this experiment parallels that of synthetic oxytocin or a combination of prolactin and STH administered under similar circumstances(8). How this effect is obtained is not clear however. It is possible, as suggested by several authors (1,3,4) that reserpine stimulates release and/or secretion of prolactin by the anterior pituitary. On the other hand, since reserpine is considered to exert its general depressant effects by way of the central nervous system (12) it might be postulated that its lactogenic effect is due to its action in suppressing an inhibitory centre in the hypothalamus controlling release of prolactin. Such a centre has been postulated for the control of FSH release(13). Finally, of course, there is the possibility that the effect of reserpine is due to a direct action of the substance on the mammary gland, though this seems unlikely in view of the supplementary observations made on vaginae and uteri. Further experiments are in hand, however, to investigate these possibilities.

The pronounced effect of the compound on thymus and adrenal weights is of interest, and it would appear that in this experiment reser-

pine has markedly stimulated ACTH release. This is in agreement with the findings of Gaunt *et al.*(12) in the rat, and Harwood and Mason(14) in the monkey, though it has also been suggested that reserpine will block the stress induced release of ACTH in the rat, provided that steps are taken to block its initial stimulatory action (Wells, Briggs & Munson,15). These authors observed no change in adrenal weight as a result of reserpine administration, a finding also reported by Fluhmann(16).

The apparent effect of reserpine in causing a discharge of ACTH in this experiment is unlikely to have had any significant effect on mammary gland regression however, since it has recently been demonstrated that ACTH administration has only a slight effect on this process in normal lactating rats after weaning(17).

The absence of any effect on thyroid weight is probably of little significance in view of the comparatively short treatment period, though Fluhmann(16) has reported a marked decrease in thyroid weight following reserpine administration to young rats over a period of 44-49 days.

Summary. 1. The effect of reserpine on mammary gland regression after weaning in the rat has been studied. Two groups of 8 lactating rats received 50 μg and 100 μg of reserpine respectively for 9 days after removal of pups on 4th day of lactation. A third group of 8 animals which received saline injections served as a control. Histological examination of the mammary glands at the end of this period revealed that reserpine administration caused a marked inhibition of mammary involution, this being particularly pronounced at the higher dose level. 2. Reserpine also caused a pronounced decrease in food intake and a considerable loss in body weight at the higher dose level. 3. Both levels of reserpine administration resulted in a significant increase in adrenal weight and a concomitant decrease in thymus weight. Uterine weight was also reduced but ovarian and thyroid weight was unaffected. 4. Histological examination of vaginae and uteri revealed that whereas all reserpine treated animals showed evidence of LTH release (vaginal mucification), several of the untreated animals were cycling normally again, their uteri and vaginae exhibiting prooestrous or oestrous conditions. 5. These results are discussed in relation to the possible mechanisms by which reserpine may exert its effects.

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