EXPERIMENTAL STUDIES ON THE EFFECT OF ERGOCORNINE METHANESULPHONATE ON THE LUTEOTROPHIC FUNCTION OF THE RAT PITUITARY GLAND

By

G. H. Zeilmaker and R. A. Carlsen*

ABSTRACT

The effects of a single administration of 1 mg ergocornine methanesulphonate to female rats with functional corpora lutea have been studied. It was shown that: 1) Injection of ergocornine into hypophysectomized rats bearing an autotransplanted pituitary brought about morphological changes in the corpora lutea; 2) In intact rats bearing two isologous pituitaries a prolonged period of leucocytic vaginal smear was found following an ergocornine-induced oestrus, indicating that the secretion of luteotrophic hormone was resumed after drug treatment; 3) Administration of ergocornine to lactating rats temporarily inhibited milk production, the effect being prevented by treatment with luteotrophic hormone.

These studies indicate that the effects of ergocornine administration to intact female rats such as failure to develop decidual tissue as a response to uterine traumatization and the interruption of the leucocytic vaginal smear by oestrus, are the result of a temporary inhibition of the secretion of luteotrophic hormone by the pituitary. This brings about irreversible changes in the corpus luteum. The subsequent progesterone deficiency is responsible for the failure of the decidual tissue to develop and for the onset of oestrus three days after the administration of the drug.

It has been shown that a single administration of certain ergo-alkaloids in early (pre-nidation) pregnancy and pseudopregnancy causes a disturbance of the hormonal equilibrium in the rat and mouse. This disturbance is inferred

Supported in part by a grant C-3491 (C251) from the National Cancer Institute, U. S. Public Health Service.

* R. A. Carlsen was on temporary leave from Yale University School of Medicine (New Haven, U. S. A.) and participated in the studies dealing with lactating rats.
from a failure of the decidual tissue to develop and a reappearance of oestrus signs in the vaginal smear three days after injection of the drug, together with a resumption of the normal cyclic pattern of ovarian function (for reviews: Shelesnyak 1957; Carlsen et al. 1961).

As these effects could be prevented in the rat by treatment with exogenous progesterone, it was concluded that the uterus was not directly affected by the treatment (Shelesnyak 1954). Experiments on hysterectomized rats confirmed this conclusion (Zeilmaker & Carlsen, unpublished). Partial reversal of these effects by treatment with luteotrophic hormone (LTH) in a number of cases showed that the corpus luteum is capable of producing progesterone in the presence of ergo-alkaloid (Shelesnyak 1958).

It seemed logical to assume that pituitary function was disturbed either directly or possibly indirectly by an effect of the drug on the hypothalamus.

A later (unpublished) experiment* showed that the hypothalamus was not involved in the primary action of ergocornine. It has been shown that pseudopregnant rats which had had their pituitary autotransplanted from the sella into the kidney capsule on the second day of pseudopregnancy and which received ergocornine at the time of uterine traumatization two days later, developed no deciduomata.

The present study was undertaken to localize and define the primary action of the ergo-alkaloid on the hypophyseal-gonadal axis more precisely and to offer a general explanation of the findings within the framework of the functional relationship between the pituitary gland and the ovary.

The work was concerned with the effects of ergocornine methanesulphonate – one of the ergo-alkaloids which show activity in this respect (Shelesnyak 1957) – on corpus luteum function and pituitary luteotrophic function in hypophysectomized pseudopregnant rats bearing an autotransplanted pituitary gland, in intact rats bearing two isologous pituitaries and in lactating rats.

The effect of the drug in hypophysectomized pseudopregnant rats bearing an autotransplanted pituitary gland was studied since in these rats the corpus luteum function, which is dependent upon a supply of LTH, is not affected by the extra-ovarian factors, which limit the life-span of the corpus luteum in intact rats (Everett 1956).

Criteria for progesterone production by the corpus luteum were the development of deciduomata and the leucocytic vaginal smear pattern. An attempt was made to relate corpus luteum function with some aspects of its morphology.

Intact female rats bearing a pituitary fragment under the kidney capsule exhibit a predominantly leucocytic vaginal smear pattern. This is associated with the presence of functional corpora lutea. Very infrequently oestrus signs

* Performed by G. H. Z. at the Weizmann Institute of Science, Rehovoth, Israel, under the supervision of Prof. M. C. Shelesnyak.
indicate changes in ovarian function (Alloiteau 1958). The production of LTH by the additional pituitary gland is not influenced by the CNS; however, the pituitary in situ is still present and hence it was of interest to compare the effects of ergocornine in hypophysectomized and non-hypophysectomized pituitary-implanted rats.

In a following section an investigation into the effect of the drug on lactation will be presented. This is yet another condition in which LTH is formed and ergocornine administration would possibly give some information about the effect of the drug on the secretion of this hormone.

Various previous studies on the effect of ergo-alkaloids on lactation have shown a deleterious effect of these drugs on milk yield in the rat. Daily administration during the second half of pregnancy had an adverse effect on lactation after parturition (Sommer & Buchanan 1955). Grosvenor (1956) suggested that daily administration of ergo-alkaloids during lactation produced an effect on the milk ejection reflex in the rat. Reduced food intake by the mother as a cause of impaired lactation after daily administration of ergo-drugs was proposed by Tindal (1956).

MATERIALS AND METHODS

Experiments were carried out on 3–6-month-old inbred female rats (strain R, Amsterdam). Vaginal smears were taken daily and classified according to a modification of the system of Thung et al. (1956).

Pseudopregnancy was induced by electrical stimulation of the uterine cervix at prooestrus and at oestrus (Shelesnyak 1931).

Hypophysectomy was performed under bromethol (avertin) anaesthesia by the parapharyngeal approach. The pituitary gland was removed and immediately transplanted under the kidney capsule. The fate of the posterior lobe was disregarded.

Uterine traumatization was carried out by clamping one entire uterine horn with artery forceps. The uterus was examined microscopically for the presence of decidual tissue.

Weighing and inspection of the litters were performed at the same hour every day. Ergo-alkaloid treatment consisted of a single subcutaneous injection of 1 mg ergocornine methanesulphonate* dissolved in 0.2 ml 96% alcohol. The control animals received the alcohol solvent. When histological examination was necessary, the organs to be examined were fixed in Susa solution and stained with Heidenhains haematoxylin.

For the study of the deposition of lipoid materials in the corpus luteum, one ovary of the animal investigated was preserved in 4% formalin and frozen sections were stained with Sudan III; the other ovary was sectioned serially after paraffin embedding and stained with haematoxylin.

The first day on which the vaginal smear contained leucocytes following oestrus, was considered as day one of pseudopregnancy or pregnancy. The day following the day on which the litter was found was considered as day one of lactation.

* Generously supplied by Dr. A. Cerletti, Sandoz Ltd., Basle, Switzerland.
The following abbreviations are used:
LTH, luteotrophic hormone or prolactin. FTH, the folliculotrophins FSH and LH as defined by Rothchild (1960). CNS, the central nerve system.

**EXPERIMENTS AND RESULTS**

**Exp. 1.** Absence of deciduoma formation several days after ergocornine treatment in hypophysectomized rats bearing an autotransplanted pituitary gland

Eleven rats were hypophysectomized on the second day of pseudopregnancy, and the pituitary gland placed under the kidney capsule. Five of the animals were treated with ergocornine two days later and an attempt was made to induce deciduomata by traumatizing the uterus on the seventh day after the induction of pseudopregnancy. The results obtained at autopsy on the eleventh day after the induction of pseudopregnancy are presented in Table 1.

It is concluded that the continued progesterone production by the corpus luteum which can be obtained in the hypophysectomized rat bearing an autotransplanted pituitary gland was interrupted after ergocornine administration.

The appearance of blood in the vaginal smear on the second day after traumatization in the ergocornine treated animals suggested that the suppression of deciduoma development is similar to that noted in intact rats treated with the drug. Normally blood does not appear until the third day of the development of the experimentally induced deciduoma and results from a haemorrhage which occurs at that time (Krehbiel 1937).

Table 1.
Effect of ergocornine on the development of deciduomata in hypophysectomized pseudopregnant rats bearing an autotransplanted pituitary under the kidney capsule.

<table>
<thead>
<tr>
<th>No. of animals</th>
<th>Ergocornine&lt;sup&gt;1)&lt;/sup&gt;</th>
<th>Uterine weight (mg)</th>
<th>No. of animals with deciduomata&lt;sup&gt;3)&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Control horn</td>
<td>Traumatized horn&lt;sup&gt;2)&lt;/sup&gt;</td>
</tr>
<tr>
<td>6</td>
<td>−</td>
<td>93 ± 14&lt;sup&gt;4)&lt;/sup&gt;</td>
<td>335 ± 82</td>
</tr>
<tr>
<td>5</td>
<td>+</td>
<td>77 ± 10</td>
<td>84 ± 2</td>
</tr>
</tbody>
</table>

<sup>1)</sup> Injected on the fourth day after the induction of pseudopregnancy.
<sup>2)</sup> Traumatization performed on the seventh day after the induction of pseudopregnancy.
<sup>3)</sup> Confirmed histologically.
<sup>4)</sup> Mean ± S. E. M.
Exp. 2. *The induction of ovulation after ergocornine treatment in intact rats bearing two isologous pituitary glands under the kidney capsule*

In seventeen three-month-old female rats, two isologous pituitary glands were transplanted to the kidney. After ten days of continuous leucocytic vaginal smears ergocornine was given to the seventeen animals. In these rats the vaginal smear became fully cornified on the fourth day after the administration of the drug and this was followed by a new prolonged period of leucocytic vaginal smears. By putting males along with three females in prooestrus (the third day after ergocornine treatment), it was found that ovulation had occurred, since pregnancy followed the matings (Table 2). The controls were injected with alcohol and there was no change in their vaginal smear pattern.

It is concluded that the formation of a new set of corpora lutea provided a new target for LTH; subsequently a new luteal phase was observed.

**Table 2.**

Effect of ergocornine in intact female rats bearing two isologous pituitary glands under the kidney capsule.

<table>
<thead>
<tr>
<th>No. of animals</th>
<th>Treatment*</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>1 mg ergocornine s.c.</td>
<td>Appearance of oestrus three days later followed by continued leucocytic vaginal smear</td>
</tr>
<tr>
<td>4</td>
<td>Alcohol (0.25 ml)</td>
<td>No effects on vaginal smear</td>
</tr>
<tr>
<td>3</td>
<td>1 mg ergocornine s.c. Placed with male</td>
<td>Appearance of oestrus three days later followed by pregnancy</td>
</tr>
</tbody>
</table>

* Treatment started after ten days of leucocytic vaginal smear.

Exp. 3. *The demonstration of morphological changes in the corpus luteum after ergocronine treatment*

The first experiment presented evidence of a change in corpus luteum function after ergocornine treatment. The following experiment was undertaken to detect any possible morphological changes correlated with the cessation of progesterone production in hypophysectomized rats bearing an autotransplanted pituitary gland.

Nineteen female rats were hypophysectomized and in each, the pituitary gland was autotransplanted under the kidney capsule on the second day of
Table 3.
Autopsy data of rats which were hypophysectomized and which had had their pituitary gland autotransplanted to the kidney capsule on the second day of pseudopregnancy. Treatment two days later and autopsy on the 23rd day after the induction of pseudopregnancy.

<table>
<thead>
<tr>
<th>No. of animals</th>
<th>Body weight at operation (g)</th>
<th>Treatment</th>
<th>Body weight at autopsy (g)</th>
<th>Ovarium mg</th>
<th>Uterus mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>179 ± 13*</td>
<td>Alcohol s. c. (0.25 ml)</td>
<td>159 ± 8</td>
<td>44 ± 3</td>
<td>199 ± 26</td>
</tr>
<tr>
<td>7</td>
<td>187 ± 6</td>
<td>1 mg ergocornine s. c.</td>
<td>167 ± 5</td>
<td>30 ± 6</td>
<td>142 ± 21</td>
</tr>
<tr>
<td>5</td>
<td>179 ± 16</td>
<td>Pituitary extirpation from kidney</td>
<td>148 ± 13</td>
<td>28 ± 3</td>
<td>133 ± 20</td>
</tr>
</tbody>
</table>

* Mean ± S. E. M.

pseudopregnancy. On the fourth day after the induction of pseudopregnancy ergocornine treatment was given to seven animals. The pituitary implant was removed from the kidney in five rats and in seven rats, alcohol was injected at the same time. At autopsy 19 days later, the ovaries and the uterus were dissected and weighed. From two rats of each experimental group whole mount preparations of the second right thoracic mammary gland were prepared. The sella turcica was inspected macroscopically for the presence of residual hypophysial tissue. The data obtained at autopsy are presented in Table 3.

From the Table it can be seen that the ovarian and uterine weights of both the ergocornine treated group and the group which underwent pituitary extirpation from the kidney were lower than those of the alcohol-injected animals. The microscopical appearance of the corpora lutea in these groups – as observed in the sections stained with Sudan III – differed from the structure of the normal functional corpora lutea in the alcohol injected control group. In the control animals the sudanophilic substance was evenly distributed in the corpus luteum. In the corpora lutea of the ergocornine treated rats and of the animals which had had their pituitary gland extirpated from the kidney, heavily stained material occurred within the corpus luteum.

It was also noted that the corpora lutea in the experimental groups were much smaller than in the controls (Figs. 1, 2, 3).

The luteal cells in the ergocornine treated group showed extensive vacuolization as compared with those in the hypophysectomized animals, in which a decrease in cell size was noticed. This difference in morphological appearance
Fig. 1.
Frozen section of ovary, stained with Sudan III, showing 23-day-old corpus luteum from a rat hypophysectomized on the second day of pseudopregnancy and bearing its pituitary gland under the kidney capsule. 80 X.

Fig. 2.
A 23-day-old corpus luteum of the same type of rat 19 days after ergocornine treatment. Note the decrease in size. 80 X.

Fig. 3.
A 23-day-old corpus luteum of the same type of rat after pituitary extirpation 19 days previously. As in Fig. 2 the corpus luteum has shrunk and there is an uneven distribution of fatty material. 80 X.
of the luteal cells is probably due to the fact that in the ergocornine treated animals the secretion of LTH is continued and hence can exert an effect on the non-functional corpus luteum. The specimens stained with Sudan III showed that some vacuoles were sudanophilic, but that most of the sudanophilic material appeared as minute droplets in the cytoplasm (Figs. 4, 5, 6).

The mammary gland was well developed in the control rats and showed a proliferation of the lobule-alveolar system. The animals treated with ergocornine showed an equally well developed duct system with much less developed glandular parts, an effect which may be explained by the cessation of corpus luteum function. In the animals in which the pituitary gland was extirpated from the kidney, an almost complete regression of the glandular system was observed (Figs. 7, 8, 9).

Exp. 4. The effect of ergocornine methanesulphonate on lactation

The effect of a single injection of 1 mg ergocornine on lactation was studied under various conditions by measuring the milk ingested by the litter. Six groups of lactating mothers were studied:

A. Intact lactating rats.
B. The same treated with ergocornine.
C. The same treated with ergocornine and LTH.
D. Ovariectomized lactating rats.
E. The same treated with ergocornine.
F. The same treated with ergocornine and LTH.

Ergocornine was injected on the sixth or seventh day of lactation after the litter had been examined and weighed.

The administration of ergocornine to intact mothers and mothers ovariectomized on the second day of lactation, resulted in a failure to produce milkspots in the babies on the following day, although vigorous suckling had occurred. Milk production was resumed on the second and third day after treatment. During these days one or two of the litter were occasionally lost.

In the intact and ovariectomized animals it was possible to reverse the effect

---

Fig. 4. Detail of a 23-day-old corpus luteum from a rat hypophysectomized on the second day of pseudopregnancy and bearing its pituitary under the kidney capsule. In the corpus luteum cells, slightly sudanophilic material is evenly distributed. Sudan III, 1000 ×.

Fig. 5. A 23-day-old corpus luteum of the same type of rat 19 days after ergocornine treatment. Note the granular and vacuolated aspect of the cytoplasm. Sudan III, 1000 ×.

Fig. 6. A 23-day-old corpus luteum of the same type of rat after pituitary extirpation 19 days previously. Note the shrunken appearance of the luteal cells. Sudan III, 1000 ×.
Table 4.
Effect of ergocornine on the milk consumption in 6-day-old rats. The number of young with milkspots/total number of young.

<table>
<thead>
<tr>
<th>Mother</th>
<th>On day of injection</th>
<th>On 1st day after injection</th>
<th>On 2nd day after injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Intact</td>
<td>48/50</td>
<td>49/50</td>
<td>46/49</td>
</tr>
<tr>
<td>B. Intact + ergocornine</td>
<td>42/45</td>
<td>4/44</td>
<td>24/43</td>
</tr>
<tr>
<td>C. Intact + ergocornine + LTH</td>
<td>43/43</td>
<td>40/43</td>
<td>43/43</td>
</tr>
<tr>
<td>D. Ovariectomized</td>
<td>47/47</td>
<td>46/47</td>
<td>41/45</td>
</tr>
<tr>
<td>E. Ovariectomized + ergocornine</td>
<td>53/54</td>
<td>6/53</td>
<td>44/48</td>
</tr>
<tr>
<td>F. Ovariectomized + ergocornine + LTH</td>
<td>40/40</td>
<td>37/40</td>
<td>37/40</td>
</tr>
</tbody>
</table>

of ergocornine on milk ingestion by giving 15 IU luteotrophic hormone sup \( ^{\circ} \) i.m. three times daily on the day of drug treatment and also on the following day. The results of daily inspection and weighing of the litters are shown in Tables 4 and 5.

The variation in the results presented in the Tables may be explained by the fact that the littersize was not kept constant and that ergocornine was given either on day six or seven of lactation.

In a following experiment one uterine horn was traumatized in two groups of six lactating rats on the seventh day of lactation. One group served as a control while the other received ergocornine treatment on the day of traumatization. Inspection four days later, revealed that all the controls showed decidualomata whereas the traumatized horns of the ergocornine treated mothers were devoid of any decidual tissue.

It should be noted that no oestrus signs were found in the vaginal smear after ergocornine treatment in intact lactating animals (except in one case of a mother with only three suckling babies, not included in the tables).

\( ^{\circ} \) Panlitar, Armour’s Ovine Lactogenic Hormone; kindly supplied by the Endocrinology Study Section, National Institutes of Health.

Fig. 7. Mammary gland of a rat hypophysectomized on the second day of pseudopregnancy and bearing its pituitary under the kidney capsule. Autopsy 23 days after the induction of pseudopregnancy. Extensive lobule-alveolar development. 35 X.

Fig. 8. Mammary gland of the same type of rat after ergocornine treatment 19 days previously. Slightly developed glandular system. 35 X.

Fig. 9. Mammary gland of the same type of rat after pituitary extirpation 19 days previously. Note the atrophic glandular system. 35 X.
Table 5.
Effect of ergocornine on daily increment of litterweight when given on the 6th or 7th day of lactation.

<table>
<thead>
<tr>
<th>Mother</th>
<th>Number of litters examined</th>
<th>On day of injection</th>
<th>On 1st day after injection</th>
<th>On 2nd day after injection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Litter size</td>
<td>Increase in weight (g) from previous day</td>
<td>Litter size</td>
</tr>
<tr>
<td>A. Intact</td>
<td>6</td>
<td>6.2 ± 2.2*</td>
<td>6.8 ± 2.0</td>
<td>6.2 ± 2.2</td>
</tr>
<tr>
<td>B. Intact + ergocornine</td>
<td>6</td>
<td>7.5 ± 2.2</td>
<td>8.3 ± 2.9</td>
<td>7.4 ± 2.3</td>
</tr>
<tr>
<td>C. Intact + ergocornine + LTH</td>
<td>5</td>
<td>8.6 ± 1.9</td>
<td>9.0 ± 2.0</td>
<td>8.6 ± 1.9</td>
</tr>
<tr>
<td>D. Ovariectomized</td>
<td>6</td>
<td>7.8 ± 2.1</td>
<td>6.0 ± 1.5</td>
<td>7.8 ± 2.1</td>
</tr>
<tr>
<td>E. Ovariectomized + ergocornine</td>
<td>8</td>
<td>6.7 ± 2.6</td>
<td>6.5 ± 1.4</td>
<td>6.6 ± 2.5</td>
</tr>
<tr>
<td>F. Ovariectomized + ergocornine + LTH</td>
<td>5</td>
<td>8.0 ± 0.6</td>
<td>7.4 ± 1.8</td>
<td>8.0 ± 0.6</td>
</tr>
</tbody>
</table>

*S. E. M.*
DISCUSSION

The effects of a single ergocornine administration in pregnant or pseudopregnant rats, such as termination of pregnancy or pseudopregnancy and the reappearance of oestrus signs in the vaginal smear (Shelesnyak 1957) may be explained by a direct effect of the drug on the pituitary luteotrophic function, resulting in termination of corpus luteum function and a release of ovulation-inducing gonadotrophins.

Experiments in hypophysectomized pseudopregnant rats bearing an autotransplanted pituitary gland revealed that the corpus luteum function was irreversibly terminated after drug treatment since deciduomata could not be induced several days after injection. The morphological changes in the corpus luteum present 23 days after ergocornine injection are probably related to the cessation of progesterone formation. More evidence for luteal regression was provided by the decrease in weight of the uterus and ovaries in these animals.

The experiments with intact rats bearing two isologous pituitaries showed that a new set of corpora lutea was formed after ergocornine treatment. The formation of progesterone by these corpora lutea indicated that the irreversible effect of ergocornine on the functional corpus luteum observed in the hypophysectomized pituitary implanted rats was not the result of an irreversible effect on LTH production.

It is likely that ergocornine treatment also produces an effect on the corpus luteum in the intact pregnant and pseudopregnant rat. However, the subsequent oestrus makes it very difficult to evaluate any possible morphological changes in the corpus luteum caused by ergocornine since it is known that associated with ovulation, degenerative changes occur in the corpus luteum, probably due to a direct action of the pituitary hormones on this structure (Everett 1947).

A possible local effect of the drug on the corpus luteum was unlikely, in view of the results obtained in the experiments with lactating rats. The inhibiting effect on lactation which was only temporary, suggested that there was an effect on pituitary function. Similar observations in ovariectomized rats showed that the inhibition was not mediated by a primary effect on the ovary. The failure to induce deciduomata in the treated rats and the fact that the lactation deficiency could be restored by administration of exogenous LTH make it likely that ergocornine causes a temporary inhibition of the secretion of LTH (and possibly other pituitary hormones).

When the results from these experiments are combined it is tempting to conclude that the inhibition of LTH secretion by both the pituitary in situ and the transplanted pituitary gland brings about the irreversible change in the corpus luteum and subsequently abolishes progesterone formation.
Such an irreversible change is not unlikely to occur after a short interruption of LTH supply. It was shown by Astwood (1941) that after hypophysectomy on the first day of dioestrus in the rat, luteotrophic substances had to be given continuously in order to ensure continued luteal function. The same requirements were observed by Boot (personal communication) in a study of the vaginal smear pattern in mice receiving daily injections of LTH. The vaginal dioestrus was interrupted by oestrus signs if the LTH injections were omitted for one day.

The progesterone deficiency due to the change in corpus luteum function results in an inability to prevent FTH release, which in turn effects an ovulation three days later in the animals in which the pituitary gland is left in situ.

Similar observations have been made by Rotchild (1960), Rotchild & Dickey (1960) in a study of the corpus luteum - pituitary relationship. These authors have shown that during pseudopregnancy, progesterone inhibits the release but not the formation of FTH (Rotchild 1962).

During lactation, however, the suckling stimulus appears to suppress the FTH secretion of the pituitary gland by acting on a specific centre controlling its formation. In this condition, the FTH content of the pituitary is low (Rotchild 1960). This is in agreement with our observation that ergocornine administration during lactation causes a LTH deficiency and cessation of progesterone formation but not a release of FTH; subsequently no oestrus signs in the vaginal smear are found (except in the case of the 3-pup litter). A restoration of LTH secretion is »allowed« by the continued suckling stimulus.

An interruption of luteotrophic function followed by a recurrence of oestrus was also observed by Bruce (1959), when she exposed a recently mated female mouse with a male mouse from another strain. It was demonstrated that the olfactory lobe mediated the stimulus which presumably effected a temporary inhibition of LTH secretion. The effect could be reversed by exogenous LTH supply and by current lactation (Bruce & Parkes 1960 a, b).

The findings in these studies bear a resemblance to our results. The observation that concurrent lactation prevents the »Bruce-effect« indicates a difference from the »ergocornine-effect«. If we may extrapolate the findings concerning the regulation of pituitary luteotrophic function from the rat to the mouse, it appears that the pituitary gland of the mouse is able to secrete LTH in the presence of a strange male and that the »Bruce-effect« could be due to the action of factors which indirectly prevent LTH secretion (stimulation of FTH centre in the CNS). In our study ergocornine administration is followed by an inability to secrete LTH (and possibly other pituitary hormones) into the blood. This response is not prevented by lactation.
ACKNOWLEDGEMENTS

Sincere thanks are due to Prof. O. Mühlbock and Dr. L. M. Boot for their constructive criticism during the preparation of this paper and to Dr. P. J. Thung for his help with the histological part of this study.

REFERENCES

Astwood E. B.: Endocrinology 28 (1941) 309.
Bruce H. M. & Parkes A. S.: J. Endocr. 20 (1960 a) VI.
Bruce H. M. & Parkes A. S.: J. Endocr. 20 (1960 b) XXIX.

Received on February 20th, 1962.