

THE ROLE OF THE NERVOUS SYSTEM IN LACTATION

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The presence of nerve trunks servicing the mammary gland has been established by many researches; these nerves have been shown to originate from the lumbar-sacral section of the spinal cord, and their branches in the gland have been traced [3, 4, 6, 11]. Similar studies by P. Dmitrievsky [5], later confirmed by other works, proved that a mass of effector type nerve endings are present in the glandular cells of the mammary gland. Research conducted by M. Mironova (1895) and L. N. Voskresensky (1895) in I.P. Pavlov's laboratory showed first that lactation depends on the integrity of the nerve trunks and secondly that lactation is changed by stimulation of these nerve trunks. The latest studies of I. I. Grachev [3] showed the importance of the interoceptive reflexes to mammary gland activity.

However, there are certain known experimental data from which scientists have concluded that humoral factors, particularly the hypophysial hormones, play the only regulating role in lactation. The supporters of the humoral theory of lactation are W. Petersen, F. Goltz, O. Riddle and others. They discount the role of the nervous system in the lactation process.

EXPERIMENTAL METHODS

In this work, we investigated the effect on lactation of stimulating and inhibiting the autonomic nervous system by means of pharmacological substances.

The pharmacological method makes it possible to avoid the negative influence of operative intervention, which may damage nerves and vessels, and provides conditions for observation which are maximally proximate to normal conditions. Changes in the tonicity of the autonomic system may be estimated according to the operation of glands known to be regulated by the central nervous system, for example, the salivary glands, and by then comparing these data with the effect on the mammary gland. The substances we used for this purpose were:

1. Pilocarpine and carbocholine (Merck's "Lentin"), as substances stimulating the parasympathetic part of the autonomic nervous system, especially its secretory fibers. We used the following doses: 1.5-2 ml of 1% pilocarpine and 0.4-1.5 ml of a 0.1% solution of carbocholine.

2. Atropine, as an agent inhibiting the nervous elements, in a dose of 1-1.5 ml of a 1% solution.

3. Adrenalin, as a stimulator of the sympathetic part of the autonomic nervous system. It was injected in doses of 1.5-2 ml of a 0.1% solution.

4. Thyroidin, which was fed with bread in a daily dose of 2 grams. The sympathicotropic action of thyroidin was the principal effect we had in mind, and we therefore used thyroidin in several experiments in combination with adrenalin in order to intensify thyroidin's effect on the sympathetic division.

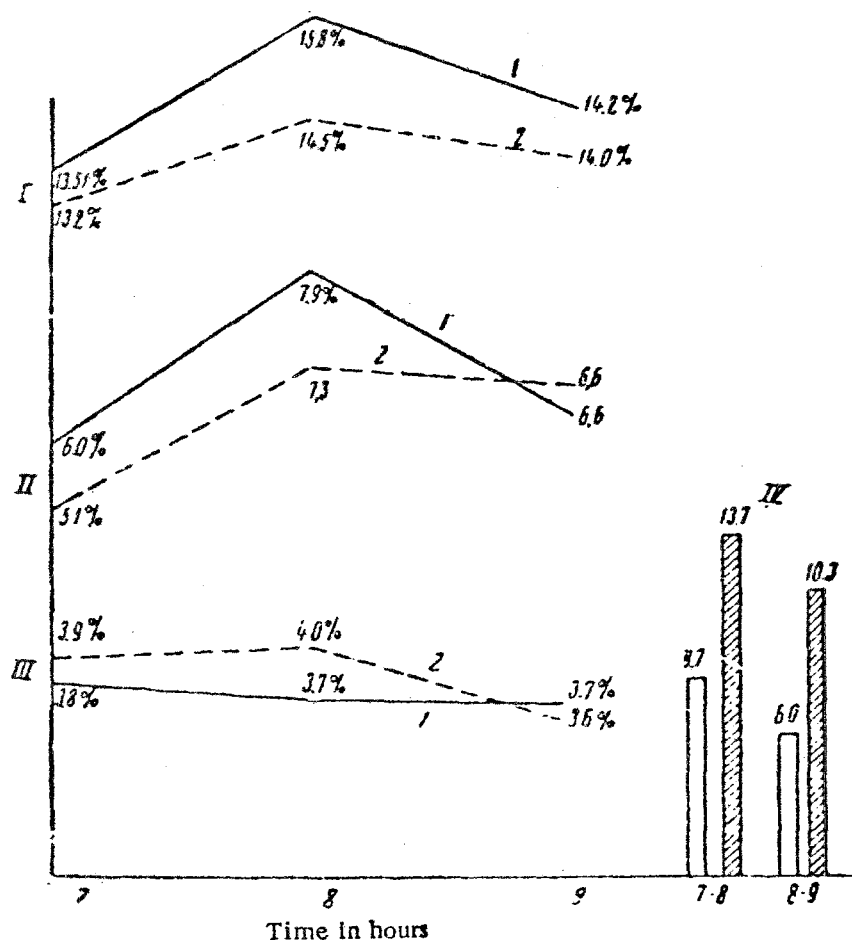
The experiments were conducted on 7 animals — 5 female goats and 2 cows. After a control period, the substance was injected daily for 4-7 days; a week elapsed between each series of experiments. The injections of the experimental substance were done in the morning. The udder was completely stripped to eliminate all

accumulated milk before the injection. The subsequent batches of milk were obtained by careful milking 1 and 2 hours after the injection. The changes in the composition of the milk were also studied, which made it possible to estimate the effect of the experimental preparation on the corresponding portion of the nervous system and also to ascertain the character of the secretion. For this purpose, we studied the changes in the dry matter content and in certain of its components – fat, lactose and ash.

To observe the effects of the substances and the change in the tonicity of the autonomic nervous system, fistulas of the parotid gland ducts were induced in 3 goats. This enabled us to calculate the intensity of saliva secretion.

EXPERIMENTAL RESULTS

1. The effect of the substances stimulating the parasympathetic part of the autonomic nervous system – pilocarpine and carbocholine – on the lactation process was expressed by an increase in the volume secreted the first hour after the injection. With pilocarpine, this increase was an average of 15% in relation to the control experiments for the first hour after the injection, and reached 56% in individual cases. With the carbocholine injection, there was a greater increase in the milk yield, which consisted of an average of 145% in relation to the control experiments the first hour after the injection, and in individual cases was more than 200%.



The effect of carbocholine on change in milk composition and on the intensity of the synthesizing work of the gland (average from 5 goats).

I) dry matter; II) percentage of fat in milk; III) lactose; IV) yield of dry matter in g per hour; 1) carbocholine; 2) control; shaded column – carbocholine; white column – control.

The effect of carbocholine was more lasting; it was still clearly evident in the second hour when the milk yield had increased by 93% in separate animals, with an average increase of 64% in relation to the control experiments. An increase in the dry matter content of the milk was also characteristic of the effect of these poisons, especially of carbocholine: when we computed the absolute dry matter content of the whole milk from the hour's yield, we found that the injection of these preparations had increased the gland's production of dry matter both absolutely and relatively, i. e. had stimulated the glandular activity. Thus, with the carbocholine injection, the amount of dry matter in the milk obtained after an hour consisted of 13.7 g, as compared with 8.7 g in the control experiments.

Therefore, the parasympathicotropic substances used also affected the secretory activity of the gland. This was also indicated by some change in the fat content of the milk. Although the usual dynamics of fat content changes (increase in fat content with repeated milking) were maintained, in separate animals during the experimental period the carbocholine injection caused the amount of fat in the milk to increase by 0.7-2%; the fat content was sometimes as high as 10%. On the average of all the experimental goats, however, no substantial increase in the fat content of the milk was observed during the first 2 hours, although the morning milk was fatter by 0.9% during the period of the carbocholine injection. Consequently, in this respect the effect of carbocholine was rather lasting. The sugar and ash content did not change; the protein content (see Figure) possibly increased.

Carbocholine also caused saliva secretion to be almost doubled. Thus, the normal saliva secretion for a 3-minute period being 3-5 drops of saliva; 10 drops were secreted during the same 3-minute period 24 minutes after the injection. These data confirm the effectiveness of the poison dose, establish the increased tonicity of the parasympathetic section of the nervous system as a whole and also show that this substance affects both glands in the same way.

| | In the control experiments | After the atropine injection | % in relation to the control exp. |
|--------------------------------|----------------------------|------------------------------|-----------------------------------|
| Average morning milk yield | 490 | 447 | 91.3 |
| Milk yield for the first hour | 59.8 | 32 | 53.5 |
| Milk yield for the second hour | 43 | 23 | 54.2 |
| Daily yield | 1147.6 | 1095 | 95.5 |

From our observations of salivary gland operation, we could establish the very important fact of the reflex interaction between the mammary and salivary glands. We found that either milking or udder massage alone caused saliva secretion to increase from 1-2 drops to 3-7 drops in a 3-minute period. The carbocholine injection, which raised the tonicity of the parasympathetic elements of the nervous system, sharply intensified this reflex reaction of the salivary glands, so much so that, during milking, the saliva was secreted in a continuous stream.

| | In the control experiments | After the atropine injection |
|--|----------------------------|------------------------------|
| Average milk yield from the 5 goats | 5.1 | 4.3 |
| Average milk yield for the first hour | 7.3 | 6.9 |
| Average milk yield for the second hour | 6.7 | 5.9 |

2. Atropine had an effect opposite from and more strongly and clearly expressed than that of carbocholine and pilocarpine. Atropinization of the animals caused a sharp reduction of lactation both the 1st and 2nd hours; the amount of lactation was 47-85% in relation to the control experiments.

Atropine's effect on the size of the milk yield (in millimeters) is shown in the averages taken from the five goats.

The inhibitory effect of atropine on secretion lasted a long time, causing the day's milk yield to decrease by 20-30%. The morning milk yield on the day after the drug injection was also reduced.

The fat content of the milk was characterized by the following data (in percent).

The decreased percentage of fat in the milk of the morning yield was evidently the result of the action of the atropine on the preceding day.

Atropine's effect on the salivary gland was typical and reduced not only the "spontaneous" saliva secretion, but also the reflex saliva secretion effected by milking. Before the atropine injection, the goats secreted 4-5 drops of saliva every 3 minutes. Fifteen minutes after the atropine injection, no saliva drops were secreted, and 1-2 drops of saliva appeared during milking, although there was no milk. An hour after the atropine injection, milking produced 15 ml of milk, and 2-3 drops of saliva were secreted in 3 minutes; there was no saliva 2 hours after the atropine injection, but 5-7 drops of saliva were secreted during a 3-minute period during milking, which produced 30 g of milk.

Therefore, there is a similarity between the activities of the mammary and salivary glands, which indicates the proximity of their regulator mechanisms.

3. The effect of the sympathicotrophic substances was manifested as follows. The adrenalin injection caused the secretion volume to increase considerably both for the first 2 hours and for the whole day: there was an increase of 86% in the yield of the first hour and of 26-36% in the 24-hour milk yield, although the effect of adrenalin is usually short-lived and the adrenalin itself quickly disintegrates. It is possible that the nervous system stimulation caused by the adrenalin lasted considerably longer than the adrenalin itself. Thus, in the experiments on goats, adrenalin affected the volume of milk (in milliliters) as follows.

| | In the control experiments | After the adrenalin injection | % in relation to the control experiments |
|---------------------------|----------------------------|-------------------------------|--|
| Average morning yield | 490 | 528 | 107.7 |
| Yield for the first hour | 59.8 | 111.2 | 186 |
| Yield for the second hour | 43 | 59.8 | 139 |
| 24-hour milk yield | 1147 | 1446 | 126 |

Still more characteristic was the considerable increase in the dry matter content of the milk, which is shown by the following data (in percent).

| | In the control experiments | After the adrenalin injection |
|----------------------------------|----------------------------|-------------------------------|
| In the morning yield | 13.18 | 13.20 |
| In the yield for the first hour | 14.5 | 16.3 |
| In the yield for the second hour | 14.0 | 15.27 |

Of the dry matter components studied, only the amount of fat and, to a lesser degree, the amount of ash changed; the sugar content remained the same. Since the increase in the dry matter seemed more than the increase of the fat, sugar and ash, one can propose that the protein content also increased rather considerably. Therefore, the sympathicotrophic substances obviously affect the intensity of the synthesizing processes in the gland, i. e., milk secretion.

Increase of Dry Matter Content of the Milk in Grams

| | In the control experiments | after the adrenalin injection | % in relation to control experiments |
|---------------|----------------------------|-------------------------------|--------------------------------------|
| * second * | 8.67 | 18.15 | 209 |
| * second hour | 6.02 | 9.13 | 151 |

The thyroidin feeding caused an increase in both the hourly and daily milk yield. This indicates that thyroidin, which raises the metabolism of the body, at the same time intensifies the excitability of the nervous system. The use of thyroidin combined with adrenalin led to the further increase of secretion volume or to stimulation caused by this combination of substances if they had had no effect individually.

| Indices | Control experiments | After injection of | | |
|---|---------------------|--------------------|-----------|-----------------------|
| | | thyroidin | adrenalin | thyroidin + adrenalin |
| Percentage of dry matter (average) in milk of morning yield | 14.1 | 16.6 | 18.4 | 14.2 |
| Average yield for a day (in ml) | 1860 | 2264 | 1851 | 2020 |
| Morning yield, ml | 752.3 | 980 | 810 | 777 |
| Yield for first hour, ml | 186 | 175 | 143 | 200 |
| Yield for second hour, ml | 73 | 95 | 51 | 130 |
| 24-hour yield, in % of control experiments | 100 | 122 | 99 | 109 |
| Yield for first hour in % of control experiments | 100 | 94.1 | 76.8 | 103.2 |
| Loss of dry matter, g: | | | | |
| a) in the first hour milk yield | 32.3 | 31.0 | 28.0 | 30.0 |
| b) in the second hour milk yield | 10.6 | 16.7 | 10.8 | 19.8 |
| c) total, without "a" and "b" | 219.4 | 321.7 | 238.6 | 221.8 |
| Total in 24 hours, g | 262.2 | 372.3 | 277.5 | 273.9 |
| Total in 24 hours (in % of control experiments) | 100 | 142 | 106 | 104 |

The table gives data concerning the changes in the amount of milk yield and in the dry matter content of the goat milk after the injection of the sympathicotrophic substances. Evidently, the metabolism intensification caused by thyroidin is conducive to the manifestation of the effect of the adrenalin.

The experiments with atropine and carbocholine were repeated on the two cows, with results similar to those obtained in the experiments on the goats.

In the first place, the material obtained amends data concerned with the effect of autonomic substances on the lactation process which are quoted in certain abstracts (in D. Espe [8], for example). In the second place, the material obtained shows that, in principle, the autonomic substances have the same effect on the mammary gland as on other glands in which nervous regulation of secretion is irrefutably established. This similarity of effect evidently indicates that the regulator mechanisms directing the activity of these glands are similar, and leads to the conclusion that not only the udder blood-supplying and milk discharge processes are regulated by the central nervous system, but also the actual secretion of milk.

The sharp changes in lactation caused by atropine refute the opinion expressed by American scientists that the hypophysial hormones play the leading role in the secretion and discharge of milk. These authors established that atropine cannot neutralize the effect of oxytocin and pitressin (V. Petersen [9]). An experiment blocking the

central nervous system by alcohol anesthesia was conducted on 2 goats. Milk was not secreted for 3 hours. As the effect of the anesthesia began to wear off, the mammary gland began to function.

This study confirms the possibility of direct nervous system influence on mammary gland activity and also the reflex effect of mammary gland stimulation on other organs, which facts help to strengthen and develop I. P. Pavlov's theories of neurism in a region where they have heretofore been criticized.

SUMMARY

The influence of changes in the condition of the nervous system due to the effect of autonomic agents (pilocarpine, carbocholine, atropine and adrenalin) and thyroidin on the secretion and content of milk in goats and cows was investigated. The above research was carried out together with the study of the secretion of salivary glands, as well as of the tone of the autonomic part of the central nervous system. This gave the opportunity for better understanding of the relationship between the organism as a whole and the mammary gland. It was established by this work that the introduction of pilocarpine and carbocholine into the organism, as well as of the sympathicotropic substances — adrenalin and thyroidin — causes increased secretion and the change of content of milk. Increased quantity of dry residue in milk is the result of increased synthetic activity of the cells of the mammary gland under the influence of excitation of the nervous system by the above substances. Block of the parasympathetic nerve endings by atropine causes pronounced decrease of milk secretion. However, it is not completely arrested. The process of milking and massage of the udder causes excitation of the central nervous system resulting in reflex increase of salivary secretion. The mammary gland receives impulses which appear due to stimulating effect of milking, sucking and massage. Nervous and nervous humoral mechanisms take part in it under the control of the central nervous system.

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