SELECTIVE ACTION OF SOME CHEMICAL AGENTS ON REFLEXES FROM CHEMOCEPTORS

PART III. EFFECT OF STREPTOMYCIN ON REFLEXES FROM INTEROCEPTORS CAUSING CHANGE IN THE WHITE CELL COUNT OF PERIPHERAL BLOOD

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It has been shown in an earlier paper [3] describing the results of acute experiments on cats that parenteral administration of streptomycin selectively inhibits reflexes from chemoceptors for respiration and blood pressure. It was, in connection with these observations, of interest to repeat the experiments, using some other effector, and under the conditions of a chronic experiment (in order to exclude the action of the narcotic).

It is known from the literature that stimulation of both mechanoceptors [4,7] and chemoceptors [1,2,7] causes definite and regular changes in the white cell count of peripheral blood.

We studied the effect of streptomycin on reflexes from interoceptors causing change in the white cell count of peripheral blood. Fifty-four experiments were performed on 9 cats, involving 340 hematological studies.

In the first series we studied the effect of streptomycin on reflexes from gastric mechanoceptors. For this purpose, we first established a gastric fistula, through which a thin-walled rubber balloon was inserted into the lumen of the stomach, and inflated to a pressure of 30-40 mm; the duration of stimulation of the gastric mechanoceptors was 2 hours. The white cell count was performed before stimulation of gastric mechanoceptors, and at various times after inflation of the balloon ($^1/_2$, 1, 2, 3, and 4 hours), taking blood from the ear.

In the control experiments stimulation of the gastric mechanoceptors led to a fall in the white cell count, followed by a return to the initial value, and then by a further rise, reaching its maximum by the end of the first or second hour of observation; a second rise then ensued, giving maximum values towards the fourth hour.

Experiments involving administration of streptomycin were carried out on the same animals. Forty minutes before distension of the stomach we gave an intramuscular injection of 200,000 units of streptomycin.

As in the control experiments, the first phase of the reaction was one of fall in leucocyte count, and this was followed by one or two waves of leucocytosis; the preliminary injection of streptomycin did not, therefore, qualitatively affect the response to distension. A comparison of the quantitative responses shows, however, that the response is greater after injection of streptomycin (the rise in leucocyte count in the first phase exceeded the control by 8%, and in the second phase by 17%). These effects are clearly seen in Fig. 1, which illustrates the results of control and streptomycin experiments (the maximum changes are taken for the comparison).

In the second series of experiments we studied the effect of streptomycin on leucocytary responses to stimulation of chemoceptors, effected by injection into the thigh muscles of 3 ml of defatted boiled milk; the reflex nature of this reaction has been demonstrated by a number of workers [2,4,5,7], and the presence of chemoceptors in the hind limb muscles, where we made the injection, may also be taken as proven [6,7].

The experimental procedure was the same as in the first series and, as before, the same cat was used for experiments with and without streptomycin.

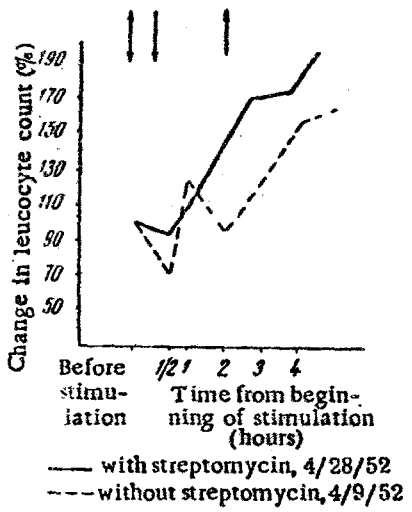

Fig. 1. Effect of streptomycin (200,000 units) on the change in white cell count caused by stimulation of gastric mechanoceptors.
Chronic experiment on Cat No. 8.
(↓) Injection of streptomycin; (↓↓) beginning and end of distension of the stomach.

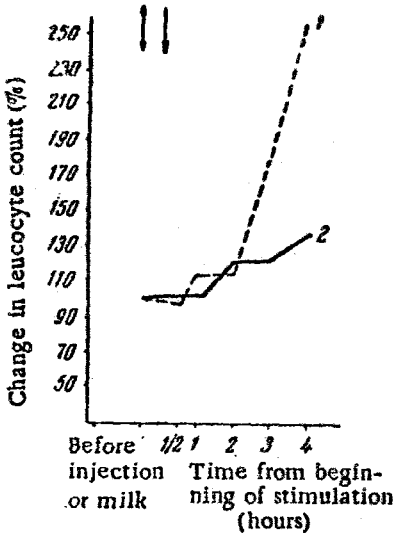

Fig. 2. Effect of streptomycin (200,000 units) on change in leucocyte count following intramuscular injection of milk.
1) Control; 2) with streptomycin.
Chronic experiment on Cat No. 3.
(↓) Injection of streptomycin; (↓) injection of milk.

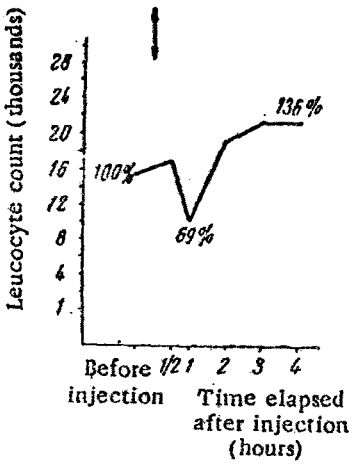

Fig. 3. Effect of intramuscular injection of streptomycin (↓) on the leucocyte count of peripheral blood.
Chronic experiment on Cat No. 4, March 5, 1953.

In the control experiments we found a brief and slight fall in leucocyte count following injection of milk into the muscle, followed after 1-2 hours by a steep rise in white cell count, which persisted during the whole time of observation (4 hours), and was accompanied by a shift to the left of the Arneth differential count.

A leucocytosis also developed in cats which had previously been given streptomycin, attaining a maximum towards the end of the observation period; it was, however, less pronounced than in the control experiments (Fig. 2). The average rise in leucocyte count in response to injection of milk was 34% less than in control animals at the end of the 2nd, 3rd, and 4th hours (the data for the first hour are not considered, in view of the fall in white cell count during this period). If we take the maximum leucocytosis found in the control experiments as 100, then that found for streptomycin-injected cats would be 40%.

Two hours after injection of milk the leucocyte count was 128% of the initial value for control cats, as compared with changes of not more than 6% for those previously given streptomycin; this does not exceed the normal range of fluctuations, without any injections. The leucocyte count only rises during the third hour after injection of milk, although to a much smaller extent than in controls (127% of initial, as compared with 162% for controls). The leucocyte count rises further during the 4th hour, to 140% of initial, as compared with 185% for the control experiment.

It may be concluded from the results of the second series of experiments that streptomycin considerably depresses the leucocytary reflex reaction to stimulation of chemoceptors; the reaction is retarded, and is much weaker.

In the third, control series of experiments we studied the effect of injection of 200,000 units of streptomycin on the leucocyte count of peripheral blood. The count fell by 6-10% during $^1/_2$ - 1 hour after the injection, and then began to rise, to a maximum at the 3rd-4th hour after injection (128% of initial value). The mean rise over the 2nd, 3rd, and 4th hours following injection of streptomycin amounted to 18% (Fig. 3).

It may be concluded from the results of the second and third series of experiments that the leucocytosis observed when milk was injected after streptomycin was due much more to the action of streptomycin itself than to that of the milk. Streptomycin profoundly depresses the leucocytary reflex reaction to stimulation of the chemoceptors of the muscles of the hind limbs. This effect may be partially masked by the leucocytosis evoked by the action of streptomycin alone.

Our experiments show that, under comparable experimental conditions, streptomycin suppresses the leucocytic reflex response to stimulation of chemoceptors, but not to stimulation of mechanoceptors. Thus the same regularities are found for the action of streptomycin under conditions of chronic experiment as were found earlier under conditions of acute experiment.

LITERATURE CITED

[1] M. L. Belenky and Yu. N. Stroikov, Byull. exptl. Biol. i Med. 1950, No. 11, pp. 358-360.

[2] R. I. Volynskaya, Mechanisms of Pathological Reactions* (Leningrad, 1941), No. 3, pp. 25-33.

[3] G. S. Kan, Byull. exptl. Biol. i Med. 1953, No. 9, pp. 56-70.

[4] E. L. Kan, Byull. exptl. Biol. i Med. 38, No. 8, pp. 12-18 (1954).

[5] M. G. Malysheva, Mechanisms of Pathological Reactions* (Leningrad, 1950), No. 16-20, pp. 138-149.

[6] V. M. Khayutin, Byull. exptl. Biol. i Med. 1952, No. 10, pp. 1-5.

[7] A. Ya. Yaroshevsky, Problems of the Physiology of Interoception* (Leningrad, 1952), No. 1, pp. 596-614.

*In Russian.