

# THE EFFECT OF INTRAVENOUS INJECTIONS OF NOVOCAIN ON THE BLOOD SYSTEM

## COMMUNICATION I. CHANGES IN THE COMPOSITION OF THE BLOOD RESULTING FROM REPEATED INJECTIONS OF NOVOCAIN

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In spite of the comparatively wide use of novocain in clinical practice and for experimental purposes, the changes in the blood system resulting from repeated injections of novocain have received quite inadequate study.\*\* According to A. Aslan, addressing the Bucharest congress in 1957, the systematic injection of novocain causes a significant increase in the red and white cell counts of the blood. G.N. Penn [6] proved that after recovery from novocain convulsions the leucocytic reactions were greatly modified.

For two years we have systematically investigated the effect of single and repeated injections of 1% novocain solution on the composition of the blood and bone marrow.

Our findings were obtained from experiments on thirty rabbits and two dogs. In the present paper we give those which relate to the effect of repeated intravenous injections of novocain on the composition of the blood.

All the experimental animals may be divided into three groups. The first contains five rabbits which every day for five to six months received an intravenous injection of 4-5 ml of a 1% solution of novocain (this dose did not usually cause convulsions). The second group contains 14 rabbits and two dogs which were injected every five days for one month, after which the animals underwent a two-stage operation of denervation of the carotid sinuses by a method previously described [7]. After restoration of the composition of the blood the animals were again given novocain in the same doses as before. The third group consists of 11 rabbits in which the changes in the composition of the blood resulting from novocain were studied before and after hemorrhage (the volume of blood withdrawn from the femoral vein varied between 20 and 35 ml). In all cases, control observations on the composition of the blood were made for a period of two to four weeks before the experiment. The bone marrow hemopoiesis was investigated twice (before the start of the novocain injections and one month after them) by means of puncture of the distal epiphysis of the femur. Blood films were stained by Pappenheim's method.

\*Deceased.

\*\*We omit here a number of investigations on the effect on the blood system of novocain block [2].

## EXPERIMENTAL RESULTS

The results obtained show that injection of novocain may cause, in a portion of the animals, certain ill-defined changes in the composition of the blood. The most characteristic finding was an increase in the hemoglobin content by 11-18 units in 16 out of 30 animals (Figure 1). A reduction in the hemoglobin was observed in one case only, while in the remaining 13 cases the increase in the hemoglobin content was not more than ten units, which is not significant. It began after three to four weeks (but in four rabbits after two weeks), and greatly exceeded the spontaneous variations and changes arising in consequence of injections of physiological saline. In four out of five animals the hemoglobin content remained elevated for three to five months. In rabbit No. 26, for instance, between December 1, 1955 and January 28, 1956 the hemoglobin level varied between 59 and 64 units. On January 29, the novocain injections began. On February 28, the hemoglobin was 78 units and on June 23, 78 units.

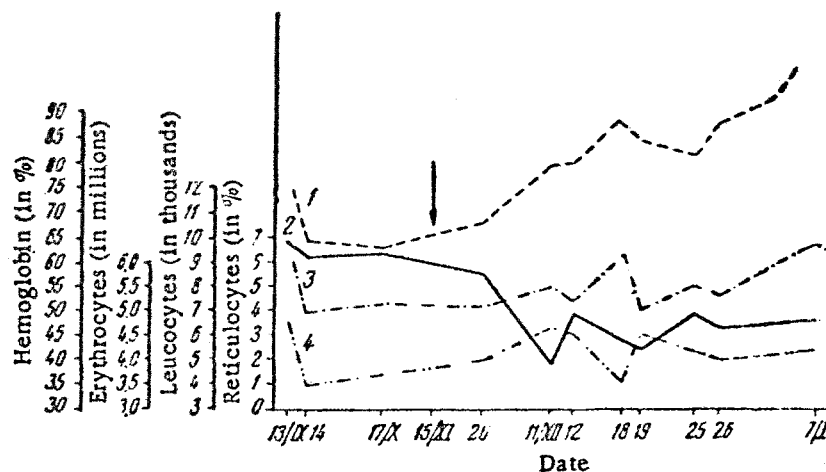


Fig. 1. Changes in the composition of the blood in a rabbit as a result of repeated intravenous injections of 4 ml of a 1% solution of novocain. ↓ - beginning of the novocain injections; 1) hemoglobin content; 2) leucocyte content; 3) erythrocyte count; 4) reticulocyte content.

The mean values of the variations in the hemoglobin content in all 30 rabbits for the month preceding the novocain injections were from +5.2 to -13.8 units, and for the first month of the injections, from +12.2 to -2 units, which undoubtedly shows a tendency for the hemoglobin content of the peripheral blood to rise. In the majority of the animals the erythrocyte count also rose slightly: the mean increase was 580,000 per  $\text{mm}^3$  with variations between 300,000 and 1,000,000 per  $\text{mm}^3$ . In only three out of 30 rabbits was the erythrocyte count lowered by 100,000 to 300,000.

Can it be concluded from these findings that novocain stimulates erythropoiesis? In order to answer this question we studied the reticulocyte content of the peripheral blood of the rabbits. It was found that out of 16 rabbits with a marked increase in the hemoglobin content, in only eight animals was the reticulocyte count raised by more than 1% above its original level. In all the remaining animals it did not vary more than in control animals (Figure 1).

In the bone marrow we counted the cell content of the erythroblastic and leucoblastic series and calculated their ratio. In only nine animals was there observed a slight increase in the number of erythroblasts, mainly orthochromatic. The ratio of leucoblastic to erythroblastic cells before the injections of novocain varied from 2.1:1 to 1.5:1. One month after the first injection of novocain it varied in the same animals from 1.6:1 to 1.1:1. In 21 rabbits, including the seven rabbits with an abnormally high erythrocyte count, no appreciable changes were present in the bone marrow.

Following the novocain injections the leucocyte count rose in 21 out of 30 rabbits, starting on the third week after the first injection. The absolute numbers did not exceed 7000 per  $\text{mm}^3$ , or 101.3% of the original level. No changes were seen in the leucocytic formula.

The results of the action of novocain on the leucocyte count must be treated with great caution, since rabbits are very prone to spontaneous variations in the numbers of this section of the blood cells, in our experience extending to 103.7% (Figure 2).

In order to shed light on the problem of whether the normal innervation of the carotid sinuses is concerned in the response of the blood system to novocain, we set up special experiments, as already indicated above.

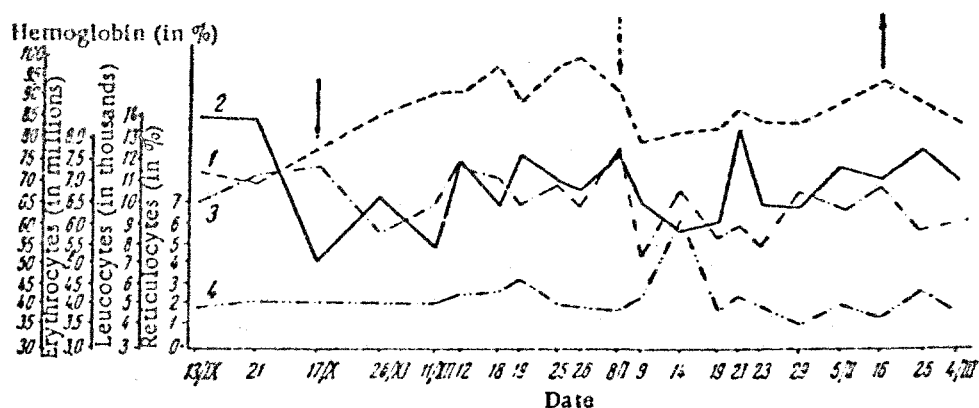


Fig. 2. Changes in the composition of the blood of a rabbit as a result of repeated intravenous injections of 5 ml of a 1% solution of novocain before and after hemorrhage (20 ml). ↓ - beginning of novocain injections; ↓ - hemorrhage; ↑ - beginning of second course of novocain injections. Remaining signs as in Figure 1.

In these experiments a two-stage denervation of the carotid sinuses was performed on 14 rabbits and two dogs, and when the normal composition of the blood had been restored - usually after 25 to 40 days - a further series of novocain injections was given. In these circumstances we were unable to detect any increase in the hemoglobin and erythrocyte content in one single animal, even after injections lasting for five months, while in two cases a moderate anemia developed.

According to reports by K.V. Maslovskaja [5], N.N. Beller [1], R.A. Durinian [3], denervation of the carotid sinuses leads to a prolonged anemia with a cyclic course. In our experiments 14 of the 16 rabbits did not develop anemia, which must be due to the systematic injection of novocain. These findings are in agreement with those of G.S. Kan and K.A. Poletaeva [4].

Novocain injections were instituted in 11 rabbits after hemorrhage and subsequent restoration of their hemoglobin and erythrocyte levels.

As may be seen in Figure 2, novocain administration in these cases not only did not lead to stimulation of erythropoiesis but in three animals it actually caused a fall in the erythrocyte count, on the average by 640,000 per  $\text{mm}^3$ , and in the hemoglobin, by 19 units. Consequently, the reaction of the blood system in response to injection of novocain after hemorrhage is essentially modified.

Thus, in our experiments repeated intravenous injections of 4-5 ml of a 1% solution of novocain into rabbits and dogs led to an increase in the erythrocyte count by 540,000 per  $\text{mm}^3$  and in the hemoglobin by 11-18 units after two to three weeks in half the animals.

Injection of novocain into animals after hemorrhage and subsequent restoration of the composition of the blood either had no effect on the erythrocyte and hemoglobin values or caused them to be reduced.

## SUMMARY

Repeated injection of 4 to 5 ml of 1% novocain solution (once a week) to 30 rabbits resulted in the increase of hemoglobin concentration and the number of erythrocytes. Leucocytosis, without the shift of the leucocytic formula, was also present. No change in the hemopoiesis or in the number of reticulocytes was noted in animals. Injection of novocain to animals with denervated carotid sinuses one month after the operation prevents the development of the first and second wave of anemia in the majority of animals.

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\*In Russian.

\*\*Original Russian pagination. See C.B. translation.