

PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

CHANGES IN ERYTHROCYTE COUNT AND HEMOGLOBIN CONTENT IN THE PERIPHERAL BLOOD UNDER PROLONGED NOCICEPTIVE IRRITATION

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Short-term nociceptive irritation produces in rats, rabbits and dogs an increase in the erythrocyte count and hemoglobin content in the peripheral blood [1, 7, 8, 12]. L. B. Nice and H. L. Katz [8] noted in addition that polycythemia is detected also in blood from the internal organs of rabbits, while N. S. Dzhavadyan [4, 5] made similar observations in blood from the femoral arteries of dogs.

The question of the influence of prolonged nociceptive irritation on the erythrocyte count and hemoglobin content in the peripheral blood has not attracted the attention of researchers, although the influence of just such irritation should of course, be of primary interest to the clinic.

Our task was to study the influence of prolonged (chronic) nociceptive irritation on the erythrocyte count and hemoglobin content in the peripheral blood of animals.

EXPERIMENTAL METHODS

The research was carried out on 7 dogs and 5 rabbits. For a period of 4-7 weeks determinations were made of the erythrocyte count and hemoglobin content in the peripheral blood of the intact animals. Blood was taken from a marginal vein of the ear of the animal, always from the same side, by the usual, universally adopted hematological methods. The erythrocytes in 2 drops of blood were counted, and a hemoglobin determination was made in 2 hemometers of the GS-2 type. After obtaining a steady initial erythrocyte count and hemoglobin content, the animals underwent operations for the purpose of creating a focus of prolonged (chronic) nociceptive irritation. A description of the operations is given in previous work [6].

Before and after the operation the quantity of reticulocytes in the blood was determined; changes in the reticulocyte formula according to Heilmäier's system were taken into account.

RESULTS

In a previous report [6], we showed that the number of erythrocytes among all of the dogs during the first 4-6 days after the operation increased by 500,000 per mm^3 of blood; during the first month their number increased by 2,000,000, and toward the third month was 2,500,000-3,000,000 higher than the initial level. In the subsequent months the number of erythrocytes, with certain fluctuations, exceeded the initial level by 1,500,000-2,000,000.

During the first 10-20 days after the operation the hemoglobin content increased by 28%; it remained on this level for a duration of 3 months, fluctuating sharply, but not falling to the initial value.

After 3-4 months following the operation the hemoglobin content began to decrease gradually, but remained however, 10-15% higher than the initial level; this level, occasionally with sharp fluctuations, was preserved during the subsequent months of the research.

Analogous changes were observed among the rabbits, but their onset was detected at later dates after the operations, and their expression was less distinct.

Beginning from the 25th-30th day after the operation the number of reticulocytes in the peripheral blood of the animals increased significantly: from 0.7-0.8% to 3.4-4.5% among the dogs, and from 5-8% to 16-21% among the rabbits. A shift to the left was noted in the reticulocyte formula in consequence of the appearance in the peripheral blood of reticulocytes of the 1st, 2nd and 3rd groups.

How is one to explain the significant increase in erythrocyte count and hemoglobin content in the peripheral blood under the indicated conditions?

In the opinion of some authors [3, 10, 12], the cause of the increase in erythrocyte count during acute nociceptive irritation is the constriction of the spleen; others [1, 4, 5, 7] have shown experimentally that an increase in erythrocyte count, although a less significant one, is observed even among animals upon which splenectomies have been performed. V. N. Chernigovsky and A. Ya. Yaroshevsky [11] consider that the very removal of the spleen results among cats in an increase in erythrocyte count and hemoglobin content for a period of one month. Assuming it to be possible that the increase in erythrocyte count and hemoglobin content in our experiments occurred as a result of contraction of the spleen as the fundamental blood depot, we set out to prove the significance of the spleen in the changes in the composition of the blood during prolonged nociceptive irritation.

Two series of experiments were conducted. In the first the spleen was removed prior to the infliction of prolonged nociceptive irritation; in the other it was removed at the time of greatest change in erythrocyte count and hemoglobin content in the peripheral blood, produced by prolonged nociceptive irritation.

The results of the experiment were very much of the same type and can be illustrated by the following data.

In the dog Pika, prior to removal of the spleen, the erythrocyte count for a month amounted to from 4,800,000 to 5,200,000 per mm^3 of blood, while the hemoglobin content was 69-73 Sahli units.

After removal of the spleen we also observed, as did V. N. Chernigovsky and A. Ya. Yaroshevsky [11], an increase in erythrocyte count and hemoglobin content for 28 days after the splenectomy; after that the composition of the blood approached normal. Examination of the blood following splenectomy was continued for 2 months, after which an operation was performed which produced prolonged nociceptive irritation. On the very following day the erythrocyte count had increased by 3,300,000 per mm^3 of blood, and for a period of three months it remained higher than normal by, on the average, 1,500,000 per mm^3 with individual sharp fluctuations. From the first days of infliction of the physical irritation, the hemoglobin content increased by 30 Sahli units and remained on this level with slight fluctuations for a period of $2\frac{1}{2}$ months, after which it increased by an additional 10 units. Then after 15 days the hemoglobin content, parallel with the reduction in erythrocyte count, began gradually to decrease but remained 10-15 Sahli units above normal. Simultaneously with the increase in erythrocyte count and hemoglobin content in the peripheral blood, distinct reticulocytosis was observed; the number of reticulocytes increased from 0.65% to 4-6%. During the 6th month of postoperative examination, the number of reticulocytes fell off to 0.1%, i.e., it became less than normal (Fig. 1).

The spleen was removed from the dog Naida at the time of the significant increase in erythrocyte count and hemoglobin content produced by prolonged nociceptive irritation. The initial erythrocyte count was 5,100,000-5,500,000 per mm^3 of blood, and the initial hemoglobin content was 82 Sahli units. After the operation producing prolonged nociceptive irritation the number of erythrocytes increased by, on the average, 2,800,000, and remained on this level until removal of the spleen. On the third day following the splenectomy the erythrocyte count not only did not fall off, but even increased by 1,200,000 per mm^3 of blood; however, it quickly returned to the level prevailing before the splenectomy.

Prior to removal of the spleen the hemoglobin content was 15 Sahli units above normal, and after the splenectomy it increased by an additional 8-10 units; it remained on this level for an extended time with sharp fluctuations.

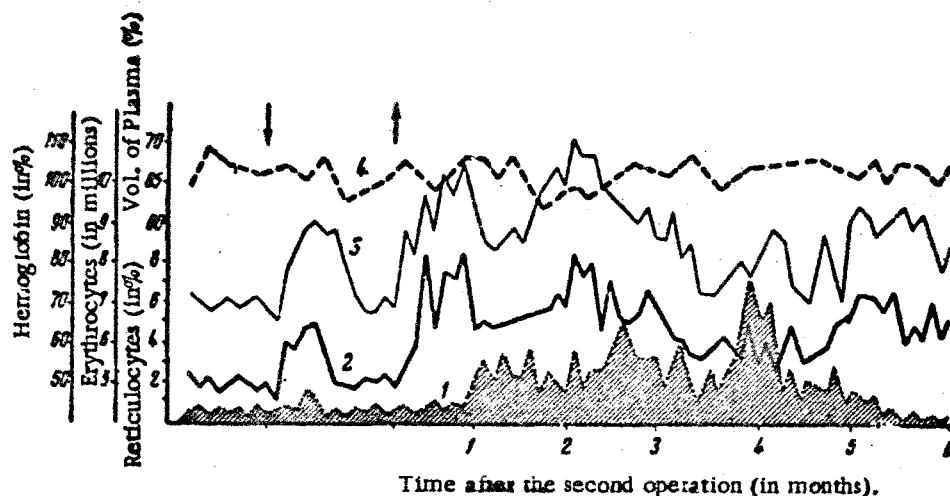


Fig. 1. The dynamics of the blood changes in the dog Pika during prolonged nociceptive irritation against a background of a removed spleen.

1) reticulocytes; 2) erythrocytes; 3) hemoglobin; 4) volume of plasma; ↓ —the operation removing the spleen; ↑ —the operation producing prolonged nociceptive irritation.

In order to check whether the increase in erythrocyte count and hemoglobin content was caused by blood clotting, we systematically examined the relative volume of the plasma with a hematocrit. It turned out that the relative volume of the plasma fluctuated within the normal limits. It can be supposed in this connection that the volume of each erythrocyte is reduced, although we have not, as yet carried out special measurements.

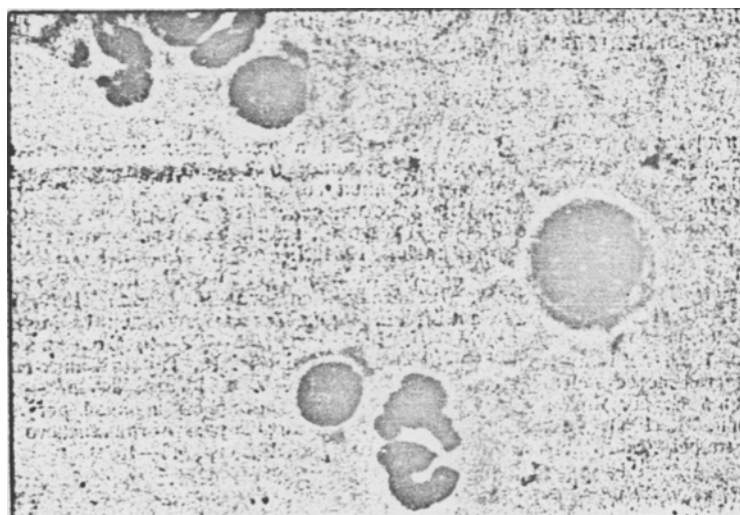


Fig. 2. The peripheral blood of the dog Sharik during the second month after the operation producing prolonged nociceptive irritation. In the field of vision are 1 proerythroblast, 1 basophilic and 1 polychromatophilic erythroblast and polymorphonuclear leucocytes. Ocular 8, objective 100.

Thus the removal of the spleen before or after infliction or prolonged nociceptive irritation did not eliminate the increase in both the erythrocyte count and the hemoglobin content in the peripheral blood of the animals.

How are the changes in the peripheral blood to be explained?

In order to answer this question, aside from peripheral blood smears, we examined samples of bone marrow from normal and splenectomized dogs. From the sternum and the ilium 0.1-0.2 mg of bone marrow were withdrawn with Kassirsky's needle.

After 15-20 days following the operation producing the prolonged nociceptive irritation, there appeared in the peripheral blood, young forms of erythrocytes—erythroblasts with basophilic and polychromatophilic protoplasm. In one case (the dog Sharik) a proerythroblast was encountered (Fig. 2). From time to time erythroblasts were found with nuclei in a state of disintegration, a fact which attests to degenerative changes in the nuclear erythrocytes in the peripheral blood. Up to 6-7 erythroblasts on the average were encountered among 600 nucleate cells. Significant reticulocytosis was noted with a shift of the reticulocyte formula to the left; erythrocytes were encountered with Jolly bodies, in especially large amounts among splenectomized dogs.

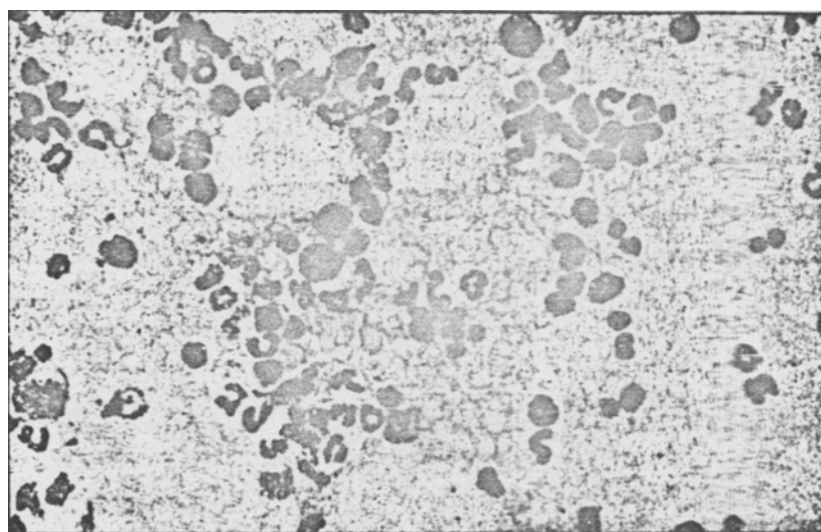


Fig. 3. Bone marrow of the dog Naida after $2\frac{1}{2}$ months following the operation producing prolonged nociceptive irritation. The proliferation of erythroblasts in the bone marrow. Ocular 8, objective 25.

In the bone marrow samples taken at different times after the operation inflicting prolonged nociceptive irritation, proliferation of erythroblasts was more or less always detected. In some cases the amount of proerythroblasts increased from 2.2 to 5.8%, the quantity of basophilic erythroblasts from 7.4 to 19.4%, and that of polychromatophilic erythroblasts from 16 to 26.6% (Fig. 3).

A relationship was also noted between the increase in the number of reticulocytes in the peripheral blood and the increase in the number of nucleate erythrocytes in the bone marrow. In this respect our data agree with the data obtained by M. I. Arinkin [2] and A. V. Solovyev [9].

The data obtained attest to the increased activity of the bone marrow, as a result of which reticulocytes of the 3rd, 2nd and 1st groups and the young forms of erythrocytes, the erythroblasts, appear in the peripheral blood of animals.

Thus it can be assumed that prolonged nociceptive irritation induces the significant generation of red

formed elements in the bone marrow, a fact which primarily explains the increase in erythrocyte count in the peripheral blood. The spleen, as the erythrocyte depot, to all appearances does not play a significant role.

SUMMARY

In rabbits and dogs prolonged nociceptive irritation causes an increase in erythrocyte count and the content of hemoglobin, the peak being reached three months after the beginning of the experiment. The number of reticulocytes is considerably increased with a shift to the left, and erythroblasts appear in the peripheral blood. The removal of the spleen either before or after the focus of prolonged nociceptive irritation has been formed, does not change the cell count. The plasma volume does not change. Increased proliferation of erythroblasts is observed in samples of the bone marrow, proving that prolonged nociceptive excitation accelerates the activity of the bone marrow.

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