THE INFLUENCE OF THE NERVOUS SYSTEM ON BONE MARROW HEMOPOIESIS

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Carrying out an idea of I. P. Pavlov's, Academician K. M. Bykov conducted research on the functional interrelations between the cerebral cortex and the internal organs [2]. Later, V. N. Chernigovskii and A. Ya. Yaroshevskii [7] established experimentally that the hemopoietic organs possess a well-developed innervation, modification of which can cause marked changes in hemopoiesis.

In explanation of this, V. N. Chernigovskii and A. Ya. Yaroshevskii [7] established that there is a direct relationship between the functional condition of the cerebral cortex and the composition of the blood. The data obtained by these authors have been confirmed by other researchers.

Data indicating central regulation of hemopoiesis have also been obtained by N. A. Grigorovich [3] experimentally and V. A. Beier [1] on clinical material.

Starting with Academician A. D. Speranskii's hypothesis that a previously existing pathologic process can be reproduced by inflicting trauma on the nervous system, A. Yu. Tilis and Kh. Z. Lyubetskii [5], using the "second stroke" method, discovered trace phenomena during the regeneration of red blood in animals with saturnine anemia. A. Yu. Tilis and G. A. Suleimanova [6] et al. demonstrated the dependency of the leukocytic reaction on the functional condition of the autonomic nervous system. The literature, then, contains sufficient data to indicate that the nervous system "is the regulator rightfully regulating the whole blood system" (K. M. Bykov [2]).

TABLE 1. Change in Peripheral Blood Composition in Healthy Animals after "Collision"

Time examined	Hemoglobin content (in %)	Number of erythrocytes	Number of leukocytes
Before collision	78	5 880 000	11 790
30 min after collision	73	5 786 000	13 616
2 hr " "	71	5 681 000	16 667
24 hr " "	76	5 408 000	14 816
48 hr " "	78	5 621 000	13 533
96 hr " "	78	5 878 000	14 883

In earlier investigations [4], we were able by means of the "towing" technique to reproduce to a certain extent a peripheral blood picture, the specific hematologic indices of which suggested the blood picture observed after phenylhydrazine poisoning.

The purpose of this work was to determine the influence of the nervous system on bone marrow hemopoiesis and on the composition of the cellular element of bone marrow in hemotoxic anemia under experimental conditions.

We wished to determine the nature of the hemopoietic changes occurring in healthy animals under conditions of higher nervous activity collapse ("collision") and to detect by this method the trace reactions of bone marrow hemopoiesis on a background of preliminary phenylhydrazine poisoning.

METHOD

Twelve dogs were used in the experiments. The initial pathologic process was induced by administering 0.5-1 ml of a 2% phenylhydrazine hydrochloride solution per kg weight to the animal until a pronounced picture of anemia had developed.

When the normal composition of the blood had been restored, higher nervous activity collapse was induced in the animal by acute intensification of the excitation processes. To this end, painful stimulation by 10 volt alternating current was applied to the animal the moment it touched food. This caused collision of the excitation process induced by the offer of food with the defense reflex associated with painful stimulation.

The composition of the formedelements in the bone marrow and peripheral blood was studied before the experiment, after phenylhydrazine poisoning, during restoration of the hematologic indices and after the "collision". Control experiments were conducted in which the painful stimulation by electric current was not administered in conjunction with food. In these experiments, either the hematologic indices showed no apparent change or some slight increase in the number of erythrocytes was observed.

RESULTS

After the "collision", we were able to establish that collapse of higher nervous activity is attended by some change in hemopoiesis in healthy dogs. In the bone marrow, for example, the young, undifferentiated cells (hemohistioblasts, hemocytoblasts, myeloblasts, et al.) increased from an average 2.23% to 13.23%.

The bone marrow neutrophil index, computed according to the formula $\frac{PRM+m+y}{s+p}$*, increased from 0.44 to 0.47, which indicates intensified hemopoiesis of the myelocytic precursors of neutrophils. Because of this shift to the left, the number of mature neutrophils diminished. There was some increase in the relative content of eosinophils and red bone marrow elements (which increased respectively from 3.16 to 3.66% and from 36.9 to 40.3%) after the "collision".

The result obtained shows that "electrocollision" causes some intensification of the regenerative processes, especially with respect to the white elements of the bone marrow.

The peripheral blood indices are given in Table 1.

Even 30 min after the collision, the number of leukocytes had increased in a majority of cases; this index continued to increase for 2 hr until it was an average of 1.5 times higher than the original. It then decreased slightly, but remained higher than the original even after two to three days.

A slight decrease in the hemoglobin content and number of erythrocytes occurred immediately after the "collision".

The data presented were compared with the results of the second, cardinal series of experiments in which the hematologic indices were studied after "collision" on a background of preliminary phenylhydrazine poisoning (Table 2).

A picture of macrocytic hemolytic anemia usually developed in the animals poisoned with phenylhydrazine. The ratio of the myeloblastic elements to the erythroblastic $(\frac{\text{leukocytes}}{\text{erythrocytes}})$, by which the erythropoietic function of the bone marrow is usually evaluated, was 2.2 : 1 in our experiments before the poisoning. This ratio changed to 1:2.5 during the development of anemia following phenylhydrazine poisoning.

If the "collision" was reproduced during the period when the original hemopoietic indices were restored, this ratio again decreased to the level typical of the anemic condition. The erythroblastic elements themselves followed a similar pattern. After phenylhydrazine poisoning, for example, the number of basophilic and polychromatophilic normoblasts was 1.85 times higher than the original level, and when "electrocollision" was induced after restoration of the hematologic indices, the number of these cellular elements increased to the same degree (1.8 times) as after phenylhydrazine poisoning. The number of orthochromic normoblasts was halved in both cases.

From the data presented, it is evident that "collision", on a background of previous phenylhydrazine poisoning, causes changes in the bone marrow hemopoiesis of animals, attended by intensification of the processes of erythroblast maturation. Finally, the changes which develop in the blood system recall the hemopoietic changes observed

* PRM - promyelocytes, m - myelocytes, y - young, s - stab, p - polymorphonuclear.

TABLE 2. Hemopoiesis in Hemolytic Anemia under Conditions of "Electrocollision"

Time examined	Reticular Cells	Hemohistioblasts	Hemocytoblasts	Myeloblasts	Promyelocytes	Neutrophils: Myelocytes	Neutrophils: Metamyelocytes	Neutrophils: Stab	Neutrophils: Polymorphonuclear	Eosinophils: Myelocytes	Eosinophils: Metamyelocytes	Eosinophils: Stab	Eosinophils: Polymorphonuclear	Basophils	Prolymphocytes	Lymphocytes	Promonocytes	Monocytes	Megakaryoblasts	Megakaryocytes	Proerythroblasts	Basophilic erythroblasts	Polychromatophilic erythroblasts	Basophilic normoblasts	Polychromatophilic normoblasts	Orthochromic normoblasts	Plasma Cells: Erythrocytic series	Plasma Cells: Myelocytic series
Before experiment	-	-	2	2.4	0.8	4.8	9.2	21	23.4	1	1.4	2.6	0.2	0.2		1	-	0.4	-	0.2	2.8	3.4	9	0.4	6	5.8	0.4	0.4
				4.4		(14.8)			(44.4)			(5.2)											(27.4)					(0.8)
After phenylhydrazine poisoning	-	-	7.4	3	2	0.2	3.4	10	16	0.4	0.6	0.8	0.4	-	-	-	-	-	-	1.2	7.6	8	12	2	18	2	1.8	3.2
			(10.4)			(5.6)			(26)			(2.2)											(49.6)					5
During restoration of hematologic indices	0.2	1.2	3.2	2.6	2.8	5.2	8	20.6	22.8	1.2	0.8	0.6	0.4	-	0.8	1.4	0.2	0.4	0.2	0.4	0.2	2.8	6	3.2	8	6	0.4	0.4
			(7.2)			(16)			(43.4)			(3)											(26.2)					(0.8)
After "electrocollision"	-	-	11.4	5	3.4	0.6	8	19.6	22	0.6	1.6	3.8	0.4	0.6	-	0.6	-	0.2	0.4	0.4	1.4	1.6	7	-	6	4.8	0.6	-
			(16.4)			(12)			(41.6)			(6.4)											(20.8)					(0.6)

in macrocytic anemia resulting from phenylhydrazine poisoning.

A similar pattern was established with regard to the peripheral blood composition. By the 30th-35th day after phenylhydrazine poisoning, a typical picture of hemotoxic anemia had developed. The hemoglobin content fell to 28-32%, and pronounced leukocytosis and reticulocytosis were observed. Collapse of higher nervous activity was induced after 35-44 days, when the hematologic indices were almost completely restored.

The results obtained showed that the "collision" acted as a stimulus which, to a certain extent, reproduced the blood picture typical of the previously existing hemotoxic anemia. This was more true in the case of the leukocyte and reticulocyte indices than in that of the erythrocyte and hemoglobin indices.

The question of the mechanism of hemotoxic anemia development has not yet been solved – it is uncertain whether hemolytic poison acts directly on the mature elements circulating in the blood or whether it acts through the nervous system.

Our investigations permit the hypothesis that trace reactions remain after the resolution of hemotoxic anemia, due to which hemopoietic changes observed during the anemia can be reproduced according to many hematologic indices by altering the functional activity of the cerebral cortex (in this case, by "electrocollision"). In the pathogenesis of certain anemia conditions, therefore, particular significance should be attached to disturbances of cortical regulation.

SUMMARY

As established by experiments, disruption of the higher nervous activity in dogs ("electrocollision") is accompanied by the change of the regeneration processes, especially of the white bone marrow series. Simultaneously there was a greater discharge of the white blood elements into peripheral blood. Functional disturbances of the higher portions of the CNS provoked by the "electrocollision" method against the background of phenylhydrazine poisoning led to some changes in the bone marrow hemopoiesis and in the peripheral blood composition, in many

ways similar to those occurring in the blood system during development of macrocytic hemolytic anemia.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
