BLOOD REGENERATION AND SERUM HEMATOPOIETIC ACTIVITY AFTER BLOOD LOSS IN SPLENECTOMIZED ANIMALS AT HIGH ALTITUDES

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The hematopoietic activity of the blood serum is considerably increased in splenectomized animals, especially at high altitudes. Meanwhile, anemia in such animals runs a longer course after blood loss, and the periods of blood regeneration are somewhat longer than in control animals.

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According to reports in the literature removal of the spleen is not accompanied by essential changes in the composition of the blood or may cause the development of some degree of anemia [1, 3, 4, 7, 8]. Cessation of the production of hematopoietins has also been reported after splenectomy [5, 6]. However, after removal of the spleen, N. A. Fedorov and co-workers [2] in some cases found an increase in the serum concentration of hematopoietins, while in some animals their concentration did not exceed the control level.

The present investigation was carried out with the aim of examining the influence of the spleen on hematopoiesis after blood loss. Since anoxia stimulates hematopoietic function, we studied the character of blood regeneration and serum hematopoietic activity in splenectomized animals exposed to a combination of anemic and anoxid anoxia.

EXPERIMENTAL METHOD

The experiments were carried out in the city of Frunze (altitude 760 m above sea level) and at the Tyuya-Ashu pass (altitude 3200 m). Altogether 40 dogs weighing 11-20 kg were investigated. Splenectomy was carried out on 8 dogs in Frunze and on 16 dogs at Tyuya-Ashu Pass (on unacclimatized dogs). Control experiments were performed in Frunze (8 experiments) and at 3200 m above sea level (8 experiments).

After blood loss equal to 2% of the body weight, the erythrocyte count, hemoglobin concentration, and reticulocyte counts in the circulating blood and bone marrow (obtained by puncture), the total blood volume, the erythroblast picture, and the concentration of hematopoietins were determined. All these tests were carried out in the initial state, 30 min and 2 h after blood loss, and on subsequent days until complete restoration of the hematologic indices. The composition of the blood was determined by the usual method. The circulating blood volume was measured by means of the dye T-1824. Quantitative estimation of hematopoietins was carried out by a biological method [2].

EXPERIMENTAL RESULTS AND DISCUSSION

The hemoglobin concentration in Frunze after blood loss fell by 4.2 g% (27% of the initial level) and the erythrocyte count by 1,070,000 cells mm^3. On the 4th day the reticulocyte count in the circulating blood was 2.4±0.1% (normal (0.5±0.03%), and in the bone marrow 6.3±0.48% (normal 2.1±0.16%). The number of hemoglobin-containing normoblasts was doubled, and the leucoerythroblastic ratio was 1.8:1-1.5:1 compared with an initial value of 2.5:1.

After blood loss a posthemorrhagic leucocytosis developed, gradually increasing in severity, but after 10-12 days the leucocyte count returned to its initial level. During the first 30-120 min after blood loss the hematopoietin concentration (in conventional units) fell significantly (8.0±4.6 compared with an initial 18±5.3). This result was evidently due to increased utilization of hematopoietins during the first few hours

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after blood loss while they were still being formed in insufficient amounts. The hematopoietin concentration 24 h after blood loss was 2.7-5.5 times above the initial value. Later the hematopoietin concentration in the blood increased still further, reaching its maximum (102±11.8) at the time of development of severe anemia. The cell composition of the blood was fully restored on the 18th day after blood loss.

Splenectomy led to the development of slight anemia: the hemoglobin concentration and erythrocyte count fell by 22-24% while the reticulocyte count rose to 1.3±0.11% from an initial level of 0.7±0.07%. The splenectomized dogs showed leucocytosis and a slight increase in the serum hematopoietic activity (46±6.2 compared with an initial 14±3.6). After 12-14 days all the hematologic indices had returned to their original values.

In response to blood loss the splenectomized animals very quickly developed the picture of acute posthemorrhagic anemia. By the 2nd day the hemoglobin concentration had fallen from 13.1±0.6 to 8.9±0.5 g%, and the erythrocyte count from 3960±865 to 3070±206 thousands/mm^3. At this period the reticulocyte count in the circulating blood had risen to 2.5±0.3% and in the bone marrow to 4.1±0.18%. The leucoerythroblastic ratio was 1.7 : 1. A further increase in serum hematopoietic activity was observed (153±9.5 conventional units after 1 day and 192±13.2 units after 2 days). As usually happens, a post hemorrhagic leucocystosis (12,100±152 cells/mm^3) and signs of hydremia developed. The plasma volume rose from an initial value of 41.7±3.6 to 48.1 ±2.7 ml/kg body weight. Complete recovery of the hematologic indices took place on the 27th day compared with the 18th in the control.

During the first 2-3 days after the animals had been taken up to an altitude of 3200 m a small decrease took place in their hemoglobin concentration (by 0.8 g%) and erythrocyte count (by 800,000). Meanwhile a tendency was observed for the reticulocyte count to increase (by 0.5-0.7%). On the 3rd day of the dogs' stay at Tyuya-Ashu Pass, the hematopoietic activity of their serum increased by 3.3 times (59±5.4 compared with an initial value of 18±3.9). Against this background blood loss did not produce such a severe anemia as in the control experiments. The hemoglobin concentration fell from 13.6±0.23 to 11.0±0.13 g% while the erythrocyte count was 3624±927 thousands compared with an original value of 4456±470 thousands/mm^3. On the 2nd-3rd day the reticulocyte count in the circulating blood was 6.3±0.4% and in the bone marrow 9.6±1.7%. The leucocyte count was high (21,800±670). Increased functional activity of the bone marrow was clearly apparent: the number of young regenerating cells was increased to 3.4-4.2% compared with an initial value of 2%. The leucoerythroblastic ratio was 0.56 : 1.

Under high altitude conditions during the first 30 min after blood loss the hematopoietin concentration rose to 175±30 compared with an initial 58±5.4 conventional units. Later (2nd-3rd day) the serum hematopoietic activity rose to 365±17.5, or even to 402±26.1, which is 6.3-6.9 times higher than the initial value.

After blood loss the circulating blood volume was reduced (48±1.7 compared with an initial 69±2.5 ml/kg body weight). However, after 24 h this index was 120±7.4 ml/kg body weight, or 74% above the initial value (on account of an increase in the plasma volume). Regeneration of the blood was complete by the 9th day, i.e., in only half the time required by the controls (18 days).

In the mountains the splenectomized animals developed less severe anemia than in the analogous experiments in the city of Frunze. At the same time, at an altitude of 3200 m there was an appreciable increase in the number of reticulocytes (1.7-1.9% in the bone marrow) and an exceptionally high increase in the serum hematopoietic activity (342±44 compared with an initial 46±19).

The increased functional activity of the hematopoietic system had not completely subsided 15 days after splenectomy. In these animals blood loss did not give rise to such severe anemia as in Frunze. The hemoglobin concentration fell by 2.2 g% and the erythrocyte count by 890,000, i.e., by less than in the control. The reticulocyte count in the circulating blood increased to 3.9±0.4% and in the bone marrow to 6.8±0.48%.

In the first 2 h after blood loss the hematopoietin concentration increased to 541±82 compared with an initial value of 142±24, reaching a maximum (621±52) after 24 h. During development of anemia the leucoerythroblastic ratio fell to 0.53-0.62 : 1. The leucocyte count increased to 10,750±740/mm^3.

Combined exposure to anemic and anoxic anoxia is thus a powerful stimulus for hematopoietin formation.

After splenectomy the serum hematopoietic activity rises, and the increase is particularly marked under high altitude conditions.

On the basis of these results a dual role of the spleen can be postulated. After its removal, when the inhibitory influence of this organ is removed, the serum hematopoietic activity increases but, at the same time, the factor increasing hematopoietin utilization disappears, and accordingly the process of regeneration of the blood is retarded.

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