DEAFFERENTATION ANEMIA IN SPLENECTOMIZED ANIMALS

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Experiments on cats have shown that the reaction of the blood and bone marrow to division of the brachial plexus is the same in intact and splenectomized animals. This reaction consists of the development of anemia and neutrophilic leukocytosis, as the result of myeloid metaplasia of the bone marrow, which regularly develops in response to a focus of deafferentation in the body. The changes described are fully developed 3–4 weeks after denervation. They are uniform in character and show no tendency toward normalization throughout the period of observation (until 6 months after denervation). The experiments also show that the spleen does not play a leading role in the mechanism of development of this type of anemia.

Despite advances in the study of regulation of the blood system (the formation of new blood cells, their distribution and destruction), much still remains to be explained especially as regards the regulation of hematopoiesis. Workers who have studied the role of particular organs in the regulation of hematopoiesis have stressed the importance of the fact that anemia develops after denervation of an organ [4, 7, 8]. Anemia of this type has been found after denervation of many organs [1-4, 7-14].

Analysis of the pathogenesis of this anemia is naturally particularly important. The view is widely held that this anemia is based on a reflex stimulation of the hemolytic function of the spleen [7, 8]. Yet in these investigations no significant changes have as a rule been reported in the hematopoietic organs which would correspond to the peripheral blood picture. In other publications [2, 3, 9, 10], including those describing the writer's previous investigations [5, 6], it is stated that considerable changes in medullary hematopoiesis take place after denervation of various organs.

The object of the present investigation was to determine whether denervation anemia develops in animals after preliminary splenectomy and to study its character and causes.

EXPERIMENTAL METHOD

Experiments were carried out on 25 young, sexually mature cats. Splenectomy was carried out on the clinically healthy animals with normal blood indices. When the clinical and hematological pictures had returned to normal, the right brachial plexus was resected in nine animals. Both operations were performed with full aseptic precautions. Special attention was paid to careful hemostasis. Six animals on which splenectomy alone was performed and 10 animals undergoing no experimental procedures were used as the controls. Periodic blood tests (hemoglobin concentration, erythrocyte and leukocyte counts, leukocyte formula, relative reticulocyte count) were carried out on the animals, and the bone marrow from the contralateral (undenervated) limb was investigated post mortem. Marrow was studied in sections and films. The myelograms were based on counts of 2000 cells in the films. The animals were sacrificed 3 weeks and 1, 2, 3, and 6 months after the second operation. The longest overall period of observation was 7.5 months.

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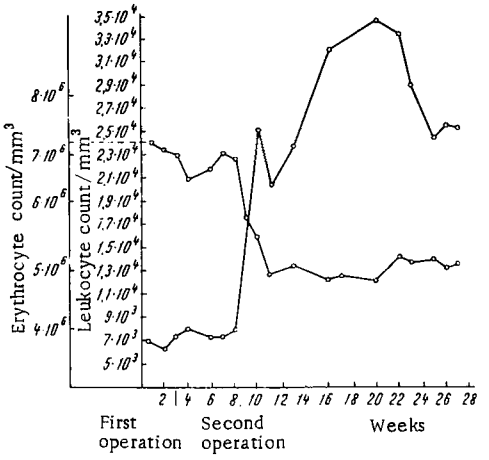

Fig. 1. Dynamics of changes in leukocyte and erythrocyte counts of blood after denervation preceded by splenectomy. Times of operations indicated by arrows.

EXPERIMENTAL RESULTS

Division of the brachial plexus in preliminarily splenectomized animals led to the development of anemia (Fig. 1). The erythrocyte count fell by approximately 2,000,000/mm^3 (with variations from 1,500,000 to 3,000,000) compared with the original level. This decrease took place rapidly, especially during the first 3–4 weeks. Later the rate of decrease as a rule slowed down, although a tendency for the erythrocyte count to be maintained at a low level persisted until the end of the longest period of observation. There was a corresponding decrease in the hemoglobin concentration, usually to 50% (lower in some cases). With an increase in the period after denervation, the blood contained a higher proportion of polychromatophilic or even basophilic erythrocytes, unsaturated with hemoglobin. During the first few days after the operation there was a marked increase in the leukocyte count. The number of neutrophils rose, and mature forms were predominant. Later in the investigation the leukocyte count showed a steady increase, in some cases to 55,000/mm^3. About 90% of the leukocytes were neutrophils (confirmed by the reaction for peroxidase). There was a steadily increasing shift to the left of the neutrophils, with appearance in some cases of myelocytes in the circulating blood. Later, especially when the leukocytosis was particularly high, a decrease in the leukocyte count began to develop. Nevertheless, a high leukocytosis was constantly observed, including at the end of the longest experiments.

In animals undergoing splenectomy only, 1 week after the operation the erythrocyte count either was normal or was slightly increased, and a slight increase was also found in the leukocyte count. After 2-3 weeks the leukocyte count was back to normal. As a rule a normal erythrocyte count was restored rather later. The blood picture thus differed significantly in the animals undergoing one and two operations.

The depth and duration of the changes arising after denervation exclude the possible role of redistributive reactions as causes of these changes. The spleen, the major focus of blood destruction, was absent in these experiments. In this case, it was natural to assess the state of the bone marrow. A study of the bone marrow in fact showed a steady increase in its content of cells of the neutrophil series and a corresponding decrease in its content of erythroid cells. This process of myeloid metaplasia of the bone marrow

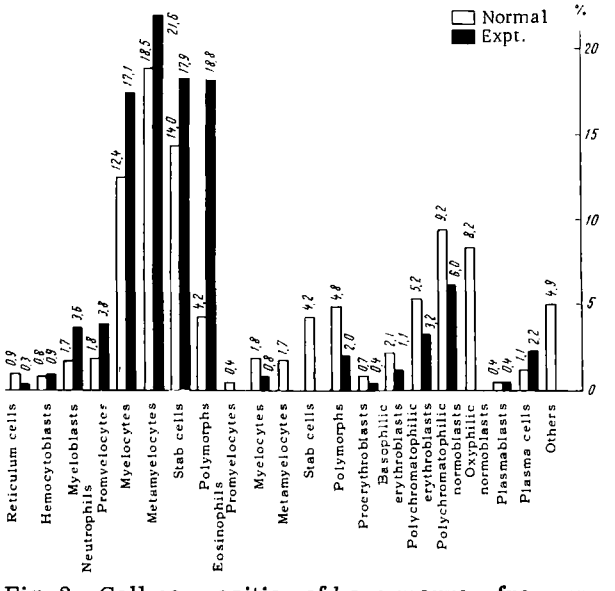

Fig. 2. Cell composition of bone marrow from undenervated limb 1 month after second operation.

began during the first days after denervation and was complete after 3–4 weeks (Fig. 2). Evidence of stimulation of neutrophilic granulopoiesis was given by the large numbers of precursor cells and mature cells counted, and also by the fact that at least half of all the dividing cells were neutrophilic granulocytes. Meanwhile, fewer erythroid cells were found and hemoglobin synthesis was disturbed. The normoblasts were predominantly polychromatophilic, or even basophilic. Some basophilic erythrocytes were seen. This picture, that of myeloid metaplasia of the bone marrow, still persisted at the end of the longest experiment, with no sign of any return to normal.

To complete the description of the hematologic changes after denervation, it should be noted that changes in the bone marrow correspond completely to the circulating blood picture. It is also important to note that the character of these changes was the same as the previously described reaction of the blood and bone marrow of animals with an intact spleen to division of sensory nerves [5, 6, 9, 10]. The results show that there is no basis for ascribing a leading role to the spleen in the pathogenesis of denervation anemia. This anemia is the result of the reorganization of medullary hematopoiesis, as expressed by an increase in neutrophilic granulopoiesis and a corresponding decrease in erythropoiesis. This reaction is specific for blocking of the sensory neuron [2, 3, 5, 6], and the developing anemia can thus be correctly described as deafferentation anemia.

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