

# PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

## QUANTITATIVE CHANGES IN THE HEMOPOIETINS OF GASTRIC JUICE FROM DOGS FOLLOWING REPEATED BLOOD LETTINGS AND TRANSFUSIONS

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Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 53, No. 5,

pp. 28-32, May, 1962

Original article submitted April 10, 1961

Experimental and clinical investigations within the last few years have established that the stomach plays a prominent role in blood production. It may be considered proven that a mucoprotein is produced in the stomach (internal factor, according to Castle [7]), which ensures the absorption of vitamin B<sub>12</sub>. The extremely important significance of the latter for normal erythropoiesis is beyond doubt.

However, there is reason to suspect that the gastric juice of healthy humans and animals possesses an independent hemopoietic activity, unrelated to vitamin B<sub>12</sub> [4, 9, 13, 20 et al]. Our previous investigations have shown that neutralized gastric juice has the capacity to stimulate erythropoiesis directly, both under tissue culture conditions [2], and with parenteral injection into animals [3].

Up until now we have not had a clear idea of the significance of the gastric hemopoietin in the general neuro-humoral system regulating blood production, or of its relation to the Carnot and Deflandre type hemopoietins [6].

The present work was devoted to studying the quantitative changes in the hemopoietins of the gastric juice following repeated blood lettings and transfusions.

### EXPERIMENTAL METHOD

The experiments were carried out on 5 dogs: 4 dogs with isolated stomachs at the fundal portion, according to I. P. Pavlov, and one dog (No. 1) with a Bassov fistula. The hematopoietic activity was determined by using the method of hemoculture [1], in gastric juice obtained over a period of 5 hours after feeding the dogs with 200 grams of raw meat (dogs Nos. 4, 10, 12), or in the juice obtained over an hour's period after injection of 0.5 ml of a 1.1% histamine solution (dogs Nos. 1, 14).

Blood lettings were carried out on the dogs once a week, taking of 23-25 ml of blood per kg of the animal's weight (dogs Nos. 10, 12, 14), or were done more often but in smaller doses (12-16 ml/kg, dogs Nos. 1, 4). In the case of the larger blood lettings, the hemopoietic activity of the gastric juice was determined twice a week: before the bleeding and 24 hours after it. For a comparative evaluation of the results obtained on the hemopoietins of the gastric juice before and after the bleeding, we simultaneously investigated them in cultures of the same leukocytic film. With the smaller blood lettings, the hemopoietic activity of the gastric juice was determined once a week.

### EXPERIMENTAL RESULTS

After bleeding, anemia gradually developed in the dogs. The hemoglobin level decreased from 17-14.4 grams% to 9.4-3.2 grams %, and the erythrocyte count fell from 8,290,000 - 5,240,000 to 5,280,000 - 1,950,000 per mm<sup>3</sup> of peripheral blood. The reticulocyte count went up correspondingly.

The level of hemopoietins in the gastric juice during development of the anemia underwent completely regular changes: in the majority of experiments it increased markedly 24 hours after the bleeding.

Thus, for example, in dog No. 12, after the seventh bleeding, the hemoglobin level fell from 16 grams % to 5 grams %, and the erythrocyte count from 7,080,000 to 2,410,000. At 24 hours after the first blood letting the level of hemopoietins rose from +30 to +111; after the second bleeding, from +14 to +30, after the fourth, from

+ 63 to + 77. Before the fifth bleeding we did not observe any hemopoietins; after it they rose to a level of + 25. The same relationships were observed after the seventh blood letting as well.

In the majority of experimental dogs, with development of anemia, the hemopoietic activity of the gastric juice fell, i.e., before each successive blood letting it was lower than the previous level. Thus, for example, in dog No. 12 the level of hemopoietins before the first bleeding was + 30, before the second, + 14, before the third, + 10, before the fifth, - 15, and before the seventh, - 35.

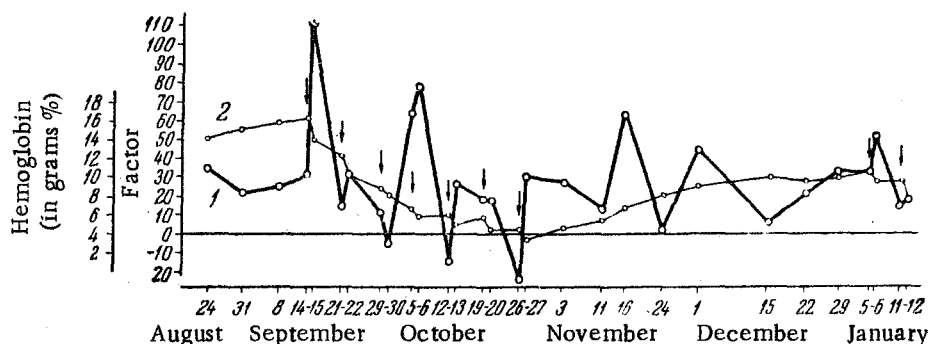


Fig. 1. Changes in the hemoglobin concentration and the hemopoietins after repeated blood lettings in dog No. 12. 1) Factor; 2) hemoglobin; arrow) blood letting.

After stopping the blood lettings, the amount of hemoglobin and the erythrocyte count rose in this dog over a period of 2 months, up to a figure close to the original. Simultaneous with normalization of the peripheral blood indices, the original hemopoietic activity of the gastric juice was restored. After 2 months, this dog was again subjected to two blood lettings over a period of 2 weeks. Each bleeding again caused a transient elevation (after 24 hours) in the concentration of hemopoietins within the gastric juice, with a subsequent fall (Fig. 1). The same changes were observed in dog No. 14 (Fig. 2).

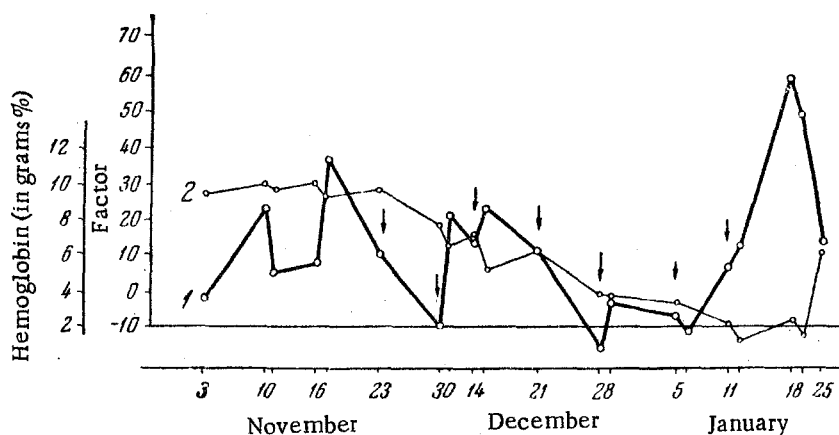


Fig. 2. Changes in the hemoglobin concentration and the hemopoietins following repeated blood lettings in dog No. 14.

In the remaining 3 dogs, in which the hemopoietic activity of the gastric juice was determined only once a week, we also observed a lowering of the hemopoietic activity in the gastric juice with development of anemia, up to its complete disappearance. Only in certain cases, with a marked degree of anemia, did we observe an elevation in the concentration of hemopoietins within the gastric juice. Thus, for example, in dog No. 14 (see Fig. 2) after the sixth blood letting, when the concentration of hemoglobin fell to 3.2 grams %, the level of hemopoietins in the gastric juice rose from - 2 to + 17, and, after the seventh bleeding, reached + 69. We observed the same picture in dog No. 10.

We felt it of interest to study the quantitative changes in the hemopoietins of the gastric juice associated with the opposite state to anemia, i.e., with artificially induced hyperemia, when the need of the organism for hemopoietins decreases. Repeated transfusions of packed erythrocytes were carried out on 2 dogs with stomachs isolated according to the method of I. P. Pavlov, which had been made anemic in the previous investigations.

Dog No. 12 received 9 transfusions of packed erythrocytes or whole blood over a period of 3 months, in amounts of 175-400 ml. In the majority of the experiments, we observed a picture opposite to the one described above: blood transfusion caused a lowering of the hemopoietic activity in the gastric juice 24 hours after transfusion; at 24 hours after the first transfusion the hemopoietic activity fell from + 60 to + 34, after the second, from + 8 to - 17, after the fourth, from + 31 to + 5, after the sixth, from + 34 to + 20, and after the seventh, from + 28 to + 24.

When the indices of the peripheral blood rose, the hemopoietic activity in the gastric juice increased, i.e., in the majority of cases, before each successive transfusion the hemopoietin level was greater than before the foregoing transfusion. Thus, for example, in this dog, before the first transfusion, the level of hemopoietins in the gastric juice was equal to + 8, before the third, + 17, before the fourth, + 31, and before the fifth, + 51. After the peripheral blood indices were restored and exceeded the normal figures (the hemoglobin level reached 20 grams %, and the erythrocyte count, 9,590,000 per mm<sup>3</sup> of blood), the concentration of hemopoietins rose sharply and held at a high level for a prolonged period of time, reaching + 100. Similar data were obtained in the other experimental dog.

Analysis of the data obtained shows that blood letting stimulates the production of hemopoietins, which leads to a rise in its level within the gastric juice; this elevation is noted 24 hours after the blood loss, appears transiently, and then quickly falls. Subsequently, with development of posthemorrhagic anemia, the concentration of hemopoietins in the gastric juice continues to fall, down to its complete disappearance. It may be postulated that hemopoietins enter the blood from the site of their formation, and the surplus appears in the gastric juice. Each blood letting stimulates the organism to increased production of hemopoietins, which apparently find access to the sites of their use, i.e., to the organs of blood formation. Under conditions of developing anemia, when the need of the organism for hemopoietins rises, its concentration in the gastric juice falls. It must be postulated that under conditions of chronic posthemorrhagic anemia, the balance of hemopoietins shifts to the side of predominance of usage over formation.

Other relationships are seen in the organism with artificially induced hyperemia, when the need to use hemopoietins decreases. Under these conditions, an increase is observed in the concentration of hemopoietins within the gastric juice. With hyperemia, the balance of hemopoietins shifts to the side of predominance of formation over usage.

Elevation of the hemopoietic activity in the gastric juice in certain cases with a marked degree of anemia, has also been noted by other authors in connection with blood hemopoietins [21, 22], possibly related to nonusage of the hemopoietins due to insufficiency of the blood forming organs. This question requires special study.

There are no data in the literature on the effect of blood letting and transfusion on the hemopoietic activity of the gastric juice; contradictory results have been obtained in regard to the blood hemopoietins. In the experiments of Carnot and Deflandre [6], with repeated blood lettings, the blood serum lost its hemopoietic activity. According to the data of other investigators, after repeated bleedings the blood was hemopoietically active [12, 16, 21]; certain authors even noted increased effectiveness from repeated blood lettings [5, 14]. After experimental blood transfusion, a lowering was noted in the concentration of blood hemopoietins [11, 15, 23]; on the other hand, an elevation in the concentration of blood hemopoietins has been established many times in patients with polycythemia [8, 10, 17, 18, 19, et al].

Our previous investigations [3] showed that the fluctuation in the concentration of hemopoietins, after blood loss, in the blood and in the gastric juice of dogs coincides. Thus, there is reason to assume that the hemopoietic activity of the blood undergoes changes analogous to those which we observed in connection with the gastric juice. In considering the discrepancies between our data and the results of different authors, an explanation should be found in the fact that the conditions of their experiments were extremely varied, both in connection with the length of time that the blood was studied after blood letting and transfusion, and in the method of determining the hemopoietins.

#### SUMMARY

A study was made of the hemopoietic activity of the gastric juice after repeated blood lettings and blood transfusions in dogs (4 dogs with the isolated pouches on the fundus according to I. P. Pavlov, 1 dog with Bassov's fistula). Blood letting was done repeatedly (23-25 ml of the blood per kg of body weight, once or several times a week, and

in lower doses). Transfusion of erythrocytic mass or blood was conducted repeatedly – once in 1-2 weeks, 175-400 ml each time. Blood letting was accompanied by a brief rise of the hemopoietin content in the gastric juice, later alternated by a reduction (with the progress of marked anemia). The hemopoietin content rises in some cases with anemia. In conditions of artificially created post-transfusional plethora there was a rise of the hemopoietin content in the gastric juice following its brief reduction directly after the transfusion.

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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.

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