MECHANISM OF CHANGES IN THE COMPOSITION OF THE BLOOD FOLLOWING STIMULATION OF GASTRIC MECHANOCEPTORS

E. L. Kan

From the Laboratory of Physiology of Receptors (Director : V. N. Chernigovsky), I. P. Pavlov Physiological Institute (Director: Academician K. M. Bykov), Acad. Sci. USSR, Leningrad

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We have shown in a previous communication that stimulation for 2 hours of the gastric mechanoceptors of a cat causes pronounced and regular changes in the white and red blood cell counts of the peripheral blood. The erythrocyte count rose by 20-30% during the first phase of the reaction, and by 40-50% in the second. The maximum rise in the number of erythrocytes was by 2,900,000 per mm^3, and in hemoglobin content by 18° Sahli. In most of the experiments the erythrocytosis, mostly in the second phase, was accompanied by a rise in the reticulocyte count of 5-10%.

Stimulation of gastric mechanoceptors also caused regular changes in the leucocyte count. Following a transient leucopenia, a leucocytosis developed in the peripheral blood, attaining its maximum 4-5 hours after commencement of stimulation of the gastric receptors; the maximum rise in leucocyte count was by 11,600 per mm^3. In two thirds of the experiments the leucocytosis was accompanied by a shift to the left of the white cell formula, a lymphopenia, and an increase in the count of oligolobate cells.

The present paper is devoted to the elucidation of the mechanism whereby these changes occur in the peripheral blood in response to stimulation of gastric mechanoceptors.

In the first place, we examined the significance of the nervous system in reactions of this type on the blood cell system.

Changes in the morphology of the blood were first followed over a period of 4-5 hours during which the experimental animals (cats) were maintained under experimental conditions (control experiment), after which the nature and magnitude of the changes in blood morphology due to stimulation of gastric receptors were studied in 2 or 3 experiments. In the next experiment on the same animal we first excluded afferent nerve endings before distending the stomach.

After taking the first peripheral blood sample, we opened a gastric fistula, and painted the gastric mucosa for 3 minutes with a 2-3% cocaine hydrochloride solution, which was freshly prepared. Stimulation of the gastric mechanoceptors was initiated 10 minutes later, lasting for 2 hours, by inflating a thin-walled rubber bag inserted into the stomach; the pressure within the bag was kept at 30-40 mm of mercury. Blood samples were taken before stimulation of the interceptors, and after ½, 1, 2, 3, and 4 and, in some experiments, 5-6 hours.

The preliminary cocainization of the gastric mucosa inhibited the development of the erythrocytic and leucocytic reactions in 10 out of 11 experiments, although these reactions appeared regularly with untreated mucosa. The variations in the erythrocyte and leucocyte counts and the hemoglobin content did not exceed those found in the control experiments (Fig. 1). However, in half the experiments the qualitative changes in the blood cells (reticulocytosis and shift to the left of the Arneth differential count) persisted, although to a smaller degree. This effect may be due to incomplete inactivation of all the receptor nerve endings in the gastric mucosa by the cocaine solution.

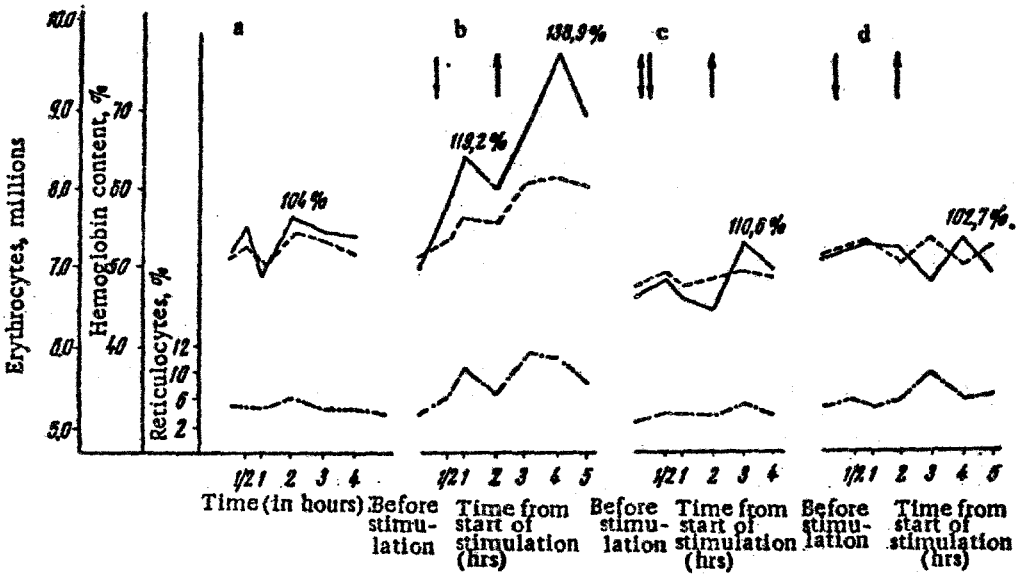

Fig. 1. Changes in erythrocyte count (—), hemoglobin content (- - -) and reticulocyte count (—·—·—·—) in the control experiment (a), after stimulating the mechanoceptors of the intact stomach (b), after stimulating the cocainized stomach (c), and after stimulating the denervated stomach (d). Cat No. 13. (↑↓) beginning and end of stimulation, (↕) cocainization of the gastric mucosa.

In a second series of 6 cats we performed partial denervation of the gastric mucosa, by transection and excision of both vagus nerves over a length of 1 cm below the diaphragm, at the point of insertion of the esophagus into the stomach. A section of the left splanchnic nerve was similarly excised, in the abdominal cavity. The cats were taken for experiment 3 weeks after the operation.

The changes taking place in blood composition following stimulation of mechanoceptors of the previously denervated stomach in many respects resembled those found with cocainized stomachs. In some of the experiments the changes were no greater than those occurring spontaneously, and in some cases erythropenia and leucopenia were found (Fig. 2), instead of the usual erythrocytosis and leucocytosis. In half of the experiments on denervated stomachs reticulocytosis and shift to the left of the Arneth differential count persisted.

It appears from our experiments on cats with cocainized and partially denervated stomachs that the changes in blood cell counts following distension of the intact stomach are of nervous origin, and are brought about by stimulation of the gastric mechanoceptors. The reflex nature of the leucocytic reaction to stimulation of the gastric mechanoceptors was demonstrated by A. Ya. Yaroshevsky [2].

Further experiments, similar to those described above, were performed on cats in nembutal narcosis. It was found that definite changes took place in the nature and the magnitude of the unconditioned reflex reaction to stimulation of the gastric mechanoceptors. The erythrocytic response reaction diminished in strength; in chronic experiments the erythrocyte count rose by 40-50%, and in acute experiments by 25-30%. The first, leucopenic, phase of the reaction was either absent or weaker than with unanesthetized cats, while the second phase of leucocytosis was more pronounced. Whereas the leucocyte count in chronic experiments on unanesthetized cats rose by 110.5%, the increase with cats under nembutal narcosis amounted in some cases to 200%. Hence, these experiments pointed to the active participation of the central nervous system in the reflex changes in blood cell counts due to stimulation of gastric mechanoceptors, and also gave evidence of the existence of different nervous mechanisms of development of the erythrocytary and leucocytary reactions. In the acute experiments on stimulation of gastric mechanoceptors, performed on anesthetized cats, blood samples were taken not only from the peripheral vessels (ear), but also from those of certain viscera (stomach, intestine, spleen); bone marrow specimens were also taken.

Examination of the myelograms taken before stimulation, and 30 minutes and 4 hours after, gave evidence of accelerated maturation of granulocytes and erythroblasts in the late stages of the reaction. At the same time, a more rapid rate of entry of mature erythroid and myeloid elements into the peripheral blood stream is observed, and this is responsible for the erythrocytosis and leucocytosis.

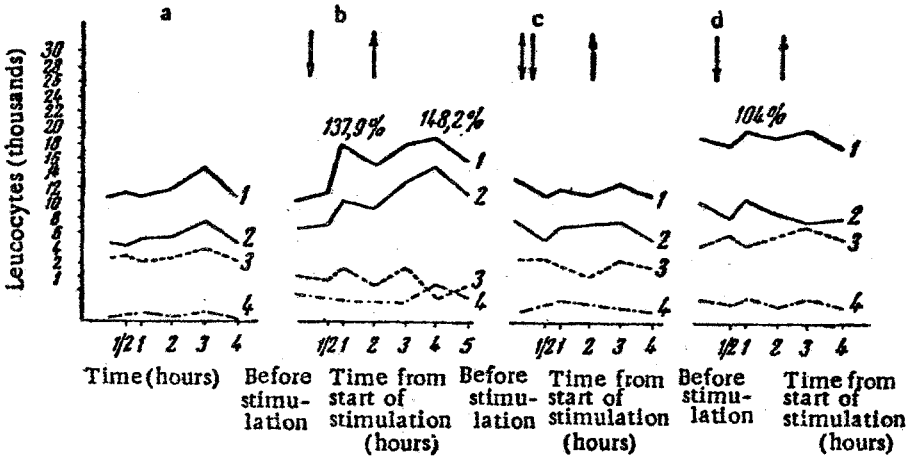

Fig. 2. Changes in the leucocyte count (1) and the differential count (2 - polymorphonuclear neutrophiles; 3 - lymphocytes; 4 - band neutrophiles) in the control experiments (a), following stimulation of the mechanoceptors of the intact stomach (b), of the stomach after painting with 3% cocaine hydrochloride solution (c), and of the denervated stomach (d). Cat No. 13. Designations as in Fig. 1.

A comparison of the cell composition of ear blood and of visceral blood following stimulation of gastric mechanoceptors shows that the red cell count and the hemoglobin show parallel variation (Fig. 3,a). Determination of the relative volumes of cells and plasma showed that the first phase of erythrocytosis is connected with hemoconcentration, which causes the rise in red cell count of peripheral and visceral blood; this phase of the erythrocytic reaction is thus one of redistribution of blood elements. Hemoconcentration appears to be absent in the second phase of erythrocytosis, as appears from hematocrit data, but there is, nevertheless, an over-all rise in erythrocyte count and hemoglobin content of blood from the ear, stomach, intestine, and spleen. Over the same period changes of a single type are observed in the bone marrow - the number of more mature erythroblasts (polychromatophilic and normoblastic) rises. The maturation curve of the erythroblasts is shifted to the right, which is firm evidence of acceleration of the process of maturation and differentiation of erythroblasts to the stage of mature erythrocytes (see table). It follows that the second phase of erythrocytosis is due to acceleration of maturation and release to the blood stream of erythrocytes. Further evidence of this is afforded by the late incidence of reticulocytosis, found in both peripheral and visceral blood.

The possibility of achieving the second phase of erythrocytosis, which sets in relatively soon after commencement of distension of the stomach, by new production of erythrocytes, is supported by Dustine's findings [3] that about 2 billion erythrocytes are produced per minute.

A comparison of the leucocyte counts of blood taken from various vascular sites before and after stimulation of gastric mechanoceptors shows the following. During the first 30-60 minutes of distension a redistribution of leucocytes in the blood stream takes place, in which they tend to be concentrated in the visceral blood vessels, thereby giving rise to the leucopenic phase of the reaction in peripheral blood, or else they tend to move from the spleen to the blood vessels of the gastrointestinal tract and of the ear, thus giving rise to the first phase of peripheral leucocytosis. During the later stages of the reaction (after 2-5 hours) the leucocyte count rises in the blood taken from peripheral vessels and from those of the viscera (Fig. 3,b).

A study of bone marrow hemopoiesis showed that during the first hours after commencement of stimulation of gastric mechanoceptors, to which belongs the first phase of the leucocytic reaction, no substantial changes take

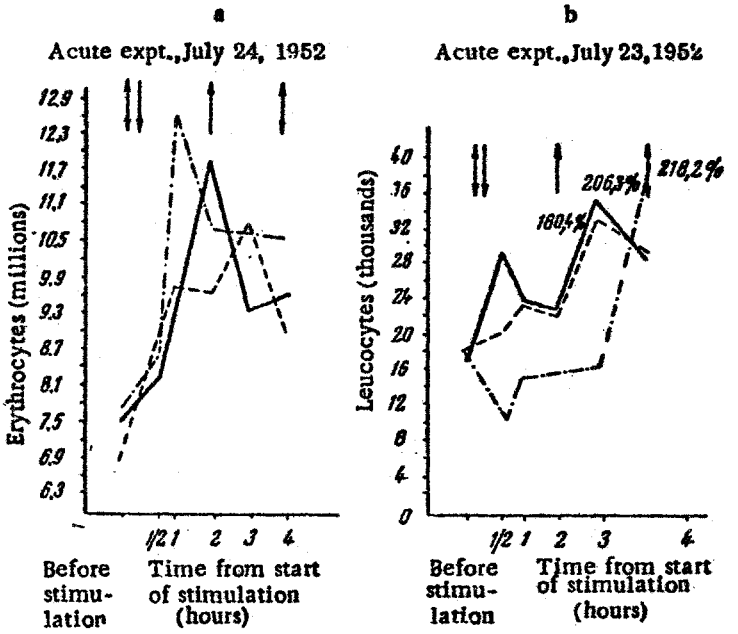

Fig. 3. Variations in the erythrocyte counts (a) and leucocyte counts (b) of ear vessel blood (—), blood from the small intestine (- - -), and from the spleen (-·- ·-).

(↓↑)- beginning and end of gastric distension; (↕)- taking of bone marrow specimen.

Changes in the Myelogram Following Stimulation of Gastric Mechanoceptors

Formed elements	4/1 1951		2/8 1952		7/23 1952	
	Before stimulation	4 hrs after start of stimulation	Before stimulation	4 hrs after start of stimulation	Before stimulation	4 hrs after start of stimulation
Myeloblasts	0.2	—	0.4	0.6	1.4	0.4
Promyelocytes	2.8	2.0	1.0	2.4	7.6	3.4
Neutrophilic myelocytes	—	—	11.6	4.0	4.8	1.4
Eosinophilic "	8.0	0.5	0.6	0.8	0.8	0.8
Neutrophilic metamyelocytes	4.2	—	10.4	8.8	7.8	3.6
Eosinophilic "	—	4.5	1.4	0.4	3.0	1.6
Band neutrophiles	6.4	4.0	7.8	7.2	9.0	12.8
Polymorphonuclear neutrophiles	26.0	33.0	20.0	34.2	21.4	33.4
Lymphocytes	15.0	7.0	16.8	2.8	11.6	4.8
Monocytes	3.0	2.5	0.8	4.2	1.2	—
Eosinophiles	0.2	—	0.4	0.4	0.8	—
Proerythroblasts	0.8	—	1.6	1.6	2.4	0.6
Erythroblasts I	3.0	6.0	3.2	1.6	5.4	2.2
" II	13.2	17.0	7.0	12.4	10.8	14.8
" III	12.6	22.5	13.8	17.0	11.6	19.6
Plasmacytes	1.8	0.5	2.0	1.0	0.4	0.4
Reticulocytes	2.8	0.5	0.6	0.4	—	—
Megakaryocytes	—	—	—	0.2	—	0.2

place in the myeloid series. In contrast to this, regular changes are found 3-4 fours after beginning the experiment; in most cases there was a fall in the number of juvenile elements of the myelocyte series, and an increase in the number of mature differentiated cells (segmented neutrophiles). The granulocyte maturation curve is shifted to the right, which is evidence of accelerated maturation of granulocytes, and of their delivery to the blood stream (see table).

Our findings show that the first phase of the leucocyte reaction is a result of a redistribution process. The second phase is a real leucocytosis, due to accelerated maturation of granulocytes and release to the circulation. This finding is confirmed by the shift of the Arneth differential count to the left in all the vascular regions examined.

Our findings confirm the possibility of interoceptive reflex action on the blood system as a whole, including both distribution of formed elements and hemopoiesis.

LITERATURE CITED

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