CHANGES IN THE ERYTHROCYTES DURING PROLONGED FASTING AND SUBSEQUENT FEEDING

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In persons fasting completely and in experimental conditions it frequently happens that the red blood indices are not lowered but, on the contrary, raised above their initial level [6, 8, 11, 13, 17, 19, 21, 22, 23]. Besides high values of the erythrocyte count and hemoglobin concentration in 1 mm^3 of blood, a reticulocytopenia may be observed, progressing as the period of fasting is prolonged [1, 4, 5, 9, 16, 20]. These facts have been attributed to hemoconcentration, i.e., to the polycythemia arising as a result of plasmorrhea.

We have investigated the morphological composition of the peripheral blood in 19 psychiatric patients treated by complete fasting by Yu. S. Nikolaev's method [10]. They fasted for periods ranging from 9 to 40 days. Water, in a volume of about 1.5 liter, was given ad lib. Observations were also made on two apparently healthy persons fasting voluntarily for 10 and 11 days.

Sternal puncture was performed on 3 subjects at various periods of the fast and subsequent feeding (on the 4th, 9th, 11th, and 26th days of fasting and 7th, 17th, and 43rd days of recovery). During the feeding period all the subjects received a salt-free diet, bland in nature, for a period roughly equal to the period of fasting.

Blood was taken at a definite time during the morning by the usual hematological methods. Because of the similar conditions of fasting and the uniformity of the results the experimental data could be analyzed statistically.

It will be seen from Table 1 that our results agreed with those in the literature. Nevertheless, they do not support the view that only plasmorrhea is concerned in the formation of hemoconcentration during fasting. The results given in Table 2 show that a direct and complete correlation between the concentration of erythrocytes and the hemoglobin indices was by no means observed in every case. On the first days of fasting the color index decreased. At the same time, in 5 cases there was a brief and ill defined increase in the reticulocyte count (a fact which we report for the first time). The reticulocytosis (from 50 to 250% above the initial value) preceded or coincided with an increase in the concentration of erythrocytes, and then changed progressively into a reticulocytopenia, whereas the erythrocyte count and hemolgobin concentration continued at a high level. In our opinion, this finding may indicate that erythrocytes (reticulocytes) were released from the blood depots into the blood stream, this mobilization taking place apparently during the first days of acute starvation. Many writers have described the emptying of depots in the early periods of complete fasting. It should be noted that in complete fasting the blood volume falls gradually, parallel to the fall in the body weight [12]. In this case it is natural to assume that the increase in the erythrocyte concentration is of the type of a polycythemia hypovolemia.

Another noteworthy feature was the tendency of the circulating erythrocytes towards microcytosis, a constant feature of the later stages of starvation. Possible causes of these changes may be variations in medullary hemopoietic function. So far as erythropoiesis is concerned, after the first few days of fasting a decrease was observed in the absolute and relative numbers of erythro-normoblasts, unattended by any significant redistribution, except, perhaps, for a relative increase in the number of polychromatophilic and oxyphilic normoblasts (a shift to the right), and for an increase in the percentage of normoblasts with nuclei in different stages of pyknosis (Table 3). The mitotic activity of the cells of this series fell slightly (to 1.5-1.0% by comparison with a normal 2%). The ratio between the numbers of reticulocytes in the marrow and in the peripheral blood tended to increase.

TABLE 1. Morphophysiological Features of the Blood at Various Periods of Complete Fasting and Subsequent Feeding

Condition of investigation	Day of investigation	Erythrocytes (in 1 mm³)	Hemoglobin (in g%)	Color index	Saturation index	Volume index	Reticulocytes (in %)	Hematocrit	Mean corpuscular volume (in μ³)	Mean erythrocyte diameter (in μ)	Mean thickness of erythrocytes (μ)	Ratio between diameter and thickness
Initial data		4 750 000 ±114 000	14,4 ±0,21	0,93 ±0,022	0,90 ±0,020	1,03 ±0,035	0,78 ±0,082	0,42 ±0,0057	91,2 ±3,081	7,3 ±0,13	2,3 ±0,10	3,1 ±0,20
Fasting	2—4 th	5 080 000 ±145 000	15,3 ±0,27	0,91 ±0,020	0,92 ±0,019	1,07 ±0,037	0,77 ±0,095	0,44 ±0,0087	89,2 ±2,642	7,2 ±0,10	2,3 ±0,16	3,1 ±0,16
	5—12 th	4 960 000 ±140 000	15,6 ±0,30	0,93 ±0,020	0,91 ±0,019	1,03 ±0,035	0,27 ±0,045	0,44 ±0,0074	90,7 ±2,737	7,0 ±0,08	2,3 ±0,08	3,0 ±0,12
	13—40-th	4 910 000 ±98 000	14,7 ±0,24	0,91 ±0,018	0,92 ±0,013	0,96 ±0,020	0,15 ±0,022	0,41 ±0,0070	84,5 ±1,700	7,0 ±0,05	2,0 ±0,07	3,3 ±0,10
Feeding	1—12 th	4 827 000 ±84 910	14,6 ±0,23	0,94 ±0,015	0,91 ±0,014	1,00 ±0,014	0,31 ±0,043	0,41 ±0,0070	88,3 ±1,342	7,1 ±0,04	2,1 ±0,02	3,1 ±0,08
	13 th and later	5 088 000 ±119 200	14,5 ±0,26	0,92 ±0,019	0,92 ±0,018	0,97 ±0,030	1,19 ±0,130	0,42 ±0,0083	87,1 ±2,166	7,1 ±0,06	2,2 ±0,02	3,1 ±0,10

It can be concluded from a comparison of the results of investigation of sternal marrow and peripheral blood that the hemoconcentration developing during the first few days of fasting is not due entirely to plasmorrhea, but also to the release of large numbers of erythrocytes from the depots. It is possible that the maturation of erythro-normoblasts may be accelerated.

The resulting hemoconcentration may, in turn, affect the functional state of medullary erythropoiesis. The presence of large numbers of erythrocytes in the blood stream (which may be regarded in this instance as a special form of depot [2]), their high hemoglobin saturation, and their relatively high resistance (as regards shape) leads to some degree of inhibition of medullary erythropoiesis. The most highly differentiated forms (polychromatophilic and oxyphilic normoblasts) are probably affected first. Inhibition in this case takes the form of a lengthening of the life span of the normoblasts, accompanied by delay in enucleation. It may also be assumed that elimination of erythrocytes is made more difficult, which leads to a relative "accumulation" of reticulocytes in the marrow.

Hence, it follows that during fasting mature erythrocytes develop mainly from oxyphilic normoblasts [3], as a result of which highly hemoglobinized normomicrocytes are formed [7].

More severe changes in erythropoiesis (destruction and degeneration of cells, marked functional disturbances) have been demonstrated experimentally in various animals, notably in stages 3 and 4 of complete starvation (loss of over 25-30% of the initial body weight) [1, 4, 9, 14]. The morphological changes observed in the recovery period should probably be regarded as a sign of more intensive self-renewal. This period is characterized by the following features.

1. All the peripheral red blood indices are lowered during the 1st-3rd days of feeding by comparison with the figures during the last days of fasting.

2. Morphological changes, which may be interpreted as a sign of the maximal development of the processes of regeneration, are not found until $1\frac{1}{2}$ - $2\frac{1}{2}$ weeks after fasting has ceased.

3. As a rule, at the height of development of regenerative processes these changes extend above the level of the original figures.

According to reports in the literature, during the first days of feeding after a period of fasting hydrophilia of the tissues, including the blood, is observed [17, 23]. We may therefore postulate that the lowering of the "red" blood indices during the first few days of the period of feeding in our investigation was a sign of oligocythemic hypervolemia. It should be remembered that "regeneration cannot take

TABLE 2. Correlation Between Concentration of Erythrocytes and Hemoglobin in the Peripheral Blood

Patient's name	Coefficient of correlation ($r \pm m_r$)	Coefficient of reliability	Patient's name	Coefficient of correlation ($r \pm m_r$)	Coefficient of reliability
Z-kov	+0,96±0,025	38,6	P-in	+0,63±0,25	2,5
T-in	+0,907±0,072	12,6	Og-ov	+0,59±0,24	2,5
Zag –	+0,85±0,084	10,0	S-nov	+0,56±0,25	2,2
Nik-ev	+0,84±0,12	7	N-ii	+0,54±0,23	2,3
Sel-ov	+0,82±0,12	7	S-f	+0,43±0,3	1,2
Kor-ii	+0,81±0,17	6,2	Moz-ev	+0,35±0,29	1,2
Gol-in	+0,78±0,13	6	Mak-ov	+0,25±0,29	0,9
Pr-ra	+0,75±0,15	4,8	Khut-v.	–0,058±0,356	0,15
Yak-ev	+0,75±0,19	3,9	G-in	–0,53±0,29	1,9
Wp-in	+0,68±0,15	4,5	S-kin	–0,59±0,204	2,9
G-an	+0,65±0,16	4			

TABLE 3. Differential Erythroblast Counts (in %) During Fasting and Feeding

Patient's name	Day of investigation	Condition of investigation	Proerythroblasts	Erythroblasts		Normoblasts		
				basophilic	polychromatophilic	basophilic	polychromatophilic	oxyphilic
G-an	4th	Fasting	1	9	8	7	28	47
B-kin	9th	Fasting	3	9	6	11	38	33
G-an	11th	Fasting	—	8	13	3	37	39
Kh-nov	26th	Fasting	4	7,5	12,5	8,5	19	48,5
G-an	7th	Feeding	4	6	10	8	12	60
G-an	17th	Feeding	3	8	9	16	27	37
G-an	43rd	Feeding	2	5	5	24	39	25

place at once" [15]: a "latent" period is required, during which intracellular synthesis can occur, without which proliferative processes are impossible [18]. It should not be forgotten that all the subjects whom we investigated had received a diet restricted in both quality and quantity for a definite period of feeding.

Besides the features we have enumerated, common to all the hematological shifts, differences were also observed; these were quantitative in character and did not upset the fundamental tendencies. It should be noted that the differences were most obvious in the first days of acute fasting, and also during the period corresponding to maximal development of regenerative processes. With an increasing duration of the period of starvation these differences became less marked and the results of the investigation were more uniform. In our opinion the uniformity of the changes in the erythrocyte composition during complete fasting and subsequent feeding should be taken to imply that these are the characteristic changes arising in this state in man.

SUMMARY

Erythrocyte blood composition was studied in 2 volunteers and in 19 patients treated with a course of complete starvation. Periods of complete alimentary starvation (without limiting the water intake) ranged from 9 to 40 days.

Concentration of erythrocytes – hemoglobin as well as hematocrit indices – proved to be increased during the first period of starvation (2-4 days) and did not drop below the initial figures even during the remote periods of starvation (13-40 days). At the same time the peripheral reticulocyte count showed a steady progressive reduction with the prolongation of starvation periods. The peripheral blood data were confirmed by the bone marrow puncture material obtained at various periods of complete starvation and subsequent nutrition. Phenomena of intensified regenerative processes were seen during the subsequent restorative period; the maximal development of the latter was observed not directly after the discontinuation of starvation, but in 1.5-2.5 weeks. The type of the shifts noted was the same in healthy individuals and in mentally ill patients, which permitted a conclusion to be drawn on the common biological character of the complete alimentary starvation effect on the human body.

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