VASCULAR AND RESPIRATORY REFLEXES IN DOGS WITH CHRONIC POSTHEMORRHAGIC AND PHENYLHYDRAZINE ANEMIAS

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There are several reports in the Soviet and foreign literature that the vascular reflexes may vary with the degree of oxygen deficiency [1-6, 9, 10, 12, 13, and others]. Although these workers cited studied the vascular reflexes in the most widely different types of oxygen deficiency (acute blood loss, asphyxia, poisoning with cyanides, sodium nitrate, and so on), the identity of the disturbances of these reflexes could not fail to be observed: distorted reflexes were found, with balancing and paradoxical phases; as the oxygen lack deepened, the magnitude of the reflexes decreased gradually, and finally they disappeared altogether.

The aim of the present investigation was to study the importance of a reduction in the hemoglobin concentration and the number of red cells in the blood in the functional disturbances of certain divisions of the central nervous system. This problem has not received its rightful attention in the literature.

METHOD

Experiments were carried out on 4 dogs: chronic posthemorrhagic anemia induced in two of them (Naida and Belka), and phenylhydrazine in two (Chernukha and Abrek). The unconditioned and conditioned vascular reflexes were studied by means of a pneumatic plethysmograph [11] from the dog's left thigh in recumbency. Respiration was recorded on an ordinary pneumograph. Before induction of anemia, a definite stereotype of orientational and unconditioned vascular reflexes to cold (0-5° and 20°), heat (42-44°), and pain in the form of a series of pricks with a needle, was studied in the dogs. A system of positive and negative conditioned reflexes was next developed to the same unconditioned stimuli in combination with various colored lamps and a bell of medium loudness, and the magnitude of the respiratory reflexes to the intravenous injection of 0.5 cm^3 of a 1% solution of lobeline was studied.

Orientational vascular reflexes in dogs to the novelty of the laboratory conditions appear on the plethysmograms as spontaneous or "third order" waves, which are recorded in addition to the pulse and respiration waves, for the origin of which the cerebral cortex is chiefly responsible [8]. As the animals become accustomed to the laboratory and experimental conditions, this fluctuation gradually diminishes, and the vascular curve becomes almost horizontal. In our experiments, we were unable to obtain horizontal (zero) plethysmograms, but were limited to 4-7 experiments only, in the course of which the fluctuation became less pronounced in three dogs, and only in one did the initial background of the plethysmogram become of zero type.

RESULTS

The results of the investigation of the unconditioned reflexes in all the dogs before anemization demonstrated that the depth of the fall in the plethysmograms during constriction of the vessels in response to the application of pain and cold stimuli, and the height of its rise during dilation of the vessels in response to the action of heat, as well as the duration of the reflexes, were dependent on the character and strength of the unconditioned stimulus. For instance, cold (0-5°) and pain caused vascular reactions of considerable magnitude, with a depth of fall of the plethysmograms of 9-20 mm and a duration of 35-60 seconds. Cold (20°) caused a correspondingly less pronounced vasoconstricting reaction. The heat stimulus (42-44°) at first caused orientational vasoconstricting reactions, and after 7-18 applications, a persistent vasodilatator effect, which raised the level of the plethysmogram by 6-18 mm for a period of 30-50 seconds. The latent period of the reflexes varied between 1 and 5 seconds.

The vasoconstrictor conditioned reactions to the combination of indifferent stimuli with cold (0-5° and 20°) and pain appeared at the sixth to twelfth combination, but were firmly consolidated only after the 18th-25th combination (see figure). If two conditioned light signals were combined with unconditioned stimuli of different strength (cold, 0-5° and 20°), then, when these

signals were applied in isolation, they were accompanied by vascular effects of different magnitude. The vasoconstrictor conditioned reflex was firmly established after 17-25 combinations with heat. A differential signal, introduced into the investigation, was converted into a negative signal after 8-15 applications in isolation. All the adequately consolidated conditioned reflexes were approximately of the same magnitude as the reactions in response to the action of the unconditioned stimuli with which the conditioned signals were combined. The latent period of the conditioned reflexes was 1-4 seconds.

In all the dogs the intravenous injection of lobeline caused reflex excitation of the respiratory center, which was shown on the pneumogram by the strengthening and the increased frequency of the respiratory reactions.

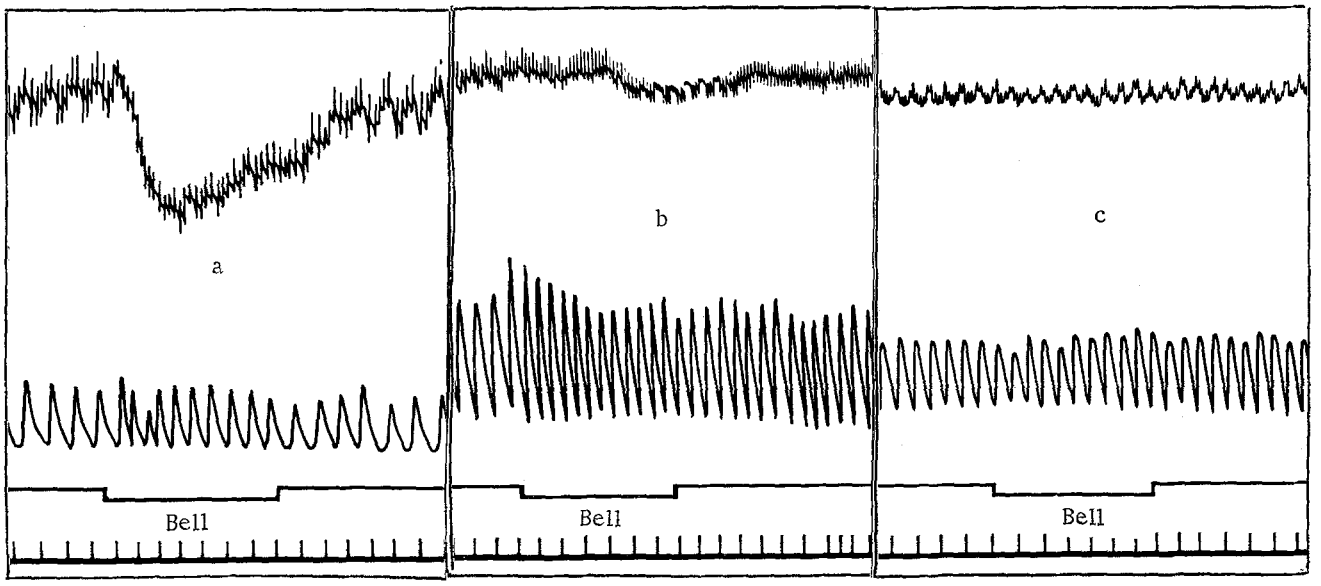
After sufficient attention had been paid to the study of the orientational, the unconditioned and conditioned vascular, and, also, the respiratory reflexes in the animals, the investigations were continued against a background of gradual anemization and the converse restoration of the hemoglobin level and the red cell count.

A fall in the hemoglobin concentration to 60-55% and a decrease in the number of red cells to approximately 3,000,000 caused a considerable disturbance of the conditioned reflexes, as shown by the disinhibition of differentiation. Under these circumstances the positive conditioned reflexes were not perceptibly affected, apart from individual reflexes which were very slightly decreased in magnitude, or distorted. The unconditioned vascular reflexes remained within normal limits. During anemization in dogs, disturbances of conditioned reflex activity thus develop significantly earlier than changes in the unconditioned reflexes.

Within the limits of this degree of anemization, the vascular orientational reflexes were characterized by a moderate, constant fluctuation of the plethysmograms.

As the degree of anemia increased (the hemoglobin level falling to below 60-55% and the red cell count to less than 3,000,000) as a rule, the magnitude of the conditioned vascular reflexes gradually decreased (see figure, b); they were produced extremely inconstantly, their latent period was considerably lengthened (to 4-8 seconds instead of a normal 1-4 seconds), and balancing, paradoxical and ultraparadoxical phases developed. The disturbances in the conditioned reflexes listed above were most marked in the period of fall in the hemoglobin concentration from 50 to 30% and decrease in the red cell count from 3,200,000 to 1,500,000. The dogs in this stage of anemization showed a characteristically rapid fatigue of the cortical cells, which was revealed as a considerable decrease in magnitude of the conditioned reflexes, or even their complete disappearance during one experiment.

At the upper levels of this degree of anemization (hemoglobin 55-45%, red cells 3,300,000 – 2,200,000) only in individual cases were the unconditioned reflexes diminished in size or distorted: heat caused constriction, and cold – dilation. Particularly severe disturbances of



Vascular reflexes during anemization. a) Conditioned vasoconstrictor reflex after 22 combinations of the bell with pain. Dog Belka, experiment no. 16, Nov. 29, 1956; b) diminished conditioned reflex (hemoglobin 32%, red cells 2,000,000). Dog Belka, experiment no. 47, Feb. 4, 1957; c) absence of conditioned vascular reflex (hemoglobin 26%, red cells 1,700,000). Dog Belka, experiment no. 48, Feb. 5, 1957. Significance of the curves (from above down): plethysmogram, pneumogram, conditioned signal marker, time marker (1 second).

the unconditioned vascular reflexes were observed during a fall in the hemoglobin concentration from 45 to 35% or below, and in the red cell count from 2,700,000 to 1,700,000 or below. These pathological changes in the reflexes took the form of a gradual decrease in their magnitude, with a lengthening of their latent period (sometimes to 9 seconds) as the degree of anemization increased, and of the appearance of balancing and paradoxical phases. In severe anemia (hemoglobin 35-30%, red cells 2,300,000 - 1,500,000) the magnitude of the unconditioned vascular reactions at the end of one investigation fell sharply so that the reflexes completely disappeared. This fact is evidence of the rapid fatigue of the cells of the vasomotor center.

At this degree of anemia, in the majority of cases, the orientational vascular reflexes were zero in type, or preserved only a trace of fluctuation.

The conditioned vascular reflexes completely disappeared in 3 dogs when the hemoglobin concentration fell to 30-28% and the red cell count to 1,800,000 - - 1,700,000 (see figure, c), and in the fourth (Abrek), when the hemoglobin level fell to 25-24% and the red cell count to 1,300,000. At this degree of anemia the unconditioned reflexes were still present. The vascular reflexes to the unconditioned stimuli disappeared with a further increase in the degree of anemization in three dogs in which the hemoglobin concentration fell to 24--22% and the red cell count to 1,500,000 - 1,300,000, and in the fourth (Abrek), when the hemoglobin concentration fell to 17% and the red cell count to 900,000.

It must be emphasized that the vasodilator unconditioned and conditioned reflexes were particularly vulnerable in anemia; they either changed to vasoconstrictor, or were completely absent. Instability of the conditioned vasodilator reflex was apparent when the hemoglobin concentration had fallen only to 60-50% and the red cell count to 3,600,000 - 2,500,000. The unconditioned vasodilator reflexes were disturbed at a more marked degree of anemia, but much earlier than the unconditioned vasodilator reflexes. When the hemoglobin level had fallen below 35-30% and the red cell count below 2,300,000 - 1,500,000, we were, in general, unable to detect dilatation of the vessels in response to the heat stimulus.

The magnitude of the respiratory reflexes to the injection of lobeline gradually decreased as the degree of anemization deepened, although their complete disappearance was not observed at levels of the hemoglobin and red cell count at which the vascular reflexes were absent. It may be assumed that this decrease in the magnitude of the respiratory reflexes to lobeline in anemia is associated with a lowering of the excitability of the respiratory center.

The dogs' behavior also changed during anemization. When the hemoglobin concentration had fallen below 45-35% and the red cell count below 2,700,000 - - 1,700,000, the animals became sluggish, lethargic, and indifferent to their surroundings, took part reluctantly in the investigation, and occasionally fell asleep during an experiment. As the state of anemia was corrected, and as a result of regeneration of the red cells, there was a gradual restoration of reflex activity and normalization of the animals' behavior.

SUMMARY

Vascular and respiratory reflexes are disturbed in anemized dogs. The first to be disturbed are the conditioned vascular reflexes; with a more considerable anemization the unconditioned also become impaired. With a gradual reduction of the amount of hemoglobin and red cells, these disturbances follow a definite sequence; they start with disinhibition of differentiation, reduction of the reflex value, and prolongation of the latent period; later, the reflexes are perverted and become phasic in character; when the hemoglobin level reaches 30-24% and 24-17%, the number of red cells being 1.8-0.9 million, the conditioned, and then the unconditioned, reflexes disappear completely. Gradual anemization is also attended with a decrease of respiratory reflexes to lobeline administration.

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