tions of a "normalized" coronary blood flow. These situations can be observed if the data in Fig. 1 are compared. Third and last, preliminary injection of ionol abolished the decrease in resistance to hypoxia compared with the control described above, and which was observed in the myocardium of animals with hemolytic anemia on normalization of their coronary blood flow. This can most likely be explained on the grounds that ionol prevented injuries to the myocardium which caused the fall in its resistance to hypoxia in hemolytic anemia. This protective effect of the LPO inhibitor is evidence in support of the important role of hyperactivation of LPO in the pathogenesis of myocardial damage in hemolytic anemias and it opens up prospects for the use of antioxidants in the combined treatment of disturbances of cardiac function in patients with anemias.

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# MECHANISMS OF DISTURBANCE OF RHEOLOGIC PROPERTIES OF THE BLOOD AFTER PROLONGED CLINICAL DEATH FROM ACUTE BLOOD LOSS


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KEY WORDS: acute blood loss; increased viscosity syndrome; clinical death.


The "increased viscosity syndrome" or "syndrome of hemorheologic disturbances" [1, 5-7, 9], observed in various pathological states, is based on increased viscosity of the blood which may be connected with changes in the hematocrit index and concentrations of protein and fibrinogen in the plasma, disturbance of hemostasis and of the acid–base balance of the blood, and also with changes in the morphological and functional state of the erythrocyte membranes. An increase in blood viscosity has also been observed in postresuscitation states [2, 4, 5], but the leading causes of this change in the early postresuscitation period are not yet sufficiently clear.

The object of this investigation was a comprehensive study of several factors affecting blood viscosity in the early period after resuscitation from prolonged clinical death from acute blood loss.

## EXPERIMENTAL METHOD

Acute and chronic experiments were carried out on 22 anesthetized (trimeperidine 6-8 mg/kg, pentobarbital 10-15 mg/kg) mongrel dogs weighing 10-17 kg. Clinical death from acute


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TABLE 1. Rheologic Properties of Blood and Acid–Base Balance in Early Postresuscitation Period after Clinical Death from Acute Blood Loss for 10 min

| Parameter studied | Initial value | Recovery period, min | | |
|---|---|---|---|---|
| | | 5 | 60 | 180 |
| Plasma viscosity, cP | 1,4±0,01 (10) | 1,1±0,02[a] (10) | 1,2±0,02[a] (10) | 1,3±0,03[a] (10) |
| Blood viscosity (in cP) at shear velocities of | 13,+±0,3 (10) | 11,5±0,5 (10) | 14,6±0,4 (10) | 17,0±0,1[a] (10) |
| 2,2—91,3 $sec^{-1}$ | 4,5±0,3 (10) | 3,9±0,2 (10) | 4,9±0,1 (10) | 4,6±0,1 (10) |
| Limit of flowability, mPa | 0,91±0,1 | 0,84±0,1 | 1,1±0,2 | 1,4±0,1[a] |
| Fibrinogen, g/liter | 3,5±0,2 (17) | 1,9±0,1[a] (17) | 2,3±0,1[a,b] (17) | 2,9±2[a,b] (17) |
| Protein, g% | 5,73±0,26 (8) | 4,47±0,3[a] (8) | 4,8±0,2[a] (8) | 4,8±0,1[a] (8) |
| Hematocrit, liter/liter | 0,50±0,02 | 0,41±0,001[a] | 0,48±0,2[b] | 0,50±0,03[b] |
| Acid-base balance: pH (arterial) | 7,25±0,01 (22) | 7,09±0,02[a] (22) | 7,19±0,01[a] (22) | 7,29±0,01 (22) |
| BE, mmoles/liter | —5,7±0,9 (22) | —19±1,5[a] (22) | 14,8±1,0[a] (22) | —10,2±1,5[a,b] (22) |
| $pCO_2$ (arterial), mm Hg | 49±1,6 | 30±3,0[a] | 33,8±2,0[a] | 32,9±2,6[a] |
| $pO_2$ (arterial), mm Hg | 94±1,5 | 344±41[a] | 178±26[a] | 113,6±10[a] |
| Electrophoretic mobility of erythrocytes | 1,23±0,029 | 1,19±0,033 | 1,21±0,033 | 1,21±0,032 |

Legend: a) $P < 0.05$ relative to initial value, b) $P < 0.05$ relative to 5th minute of recovery period. Number of observations in parentheses.

blood loss was used as model of the terminal state. Resuscitation was carried out by intra-arterial injection of the lost blood, stabilized with preservative (TsOLIPK 12b with adrenalin, 0.3-0.6 mg/kg), and artificial ventilation of the lungs with 80% oxygen (tidal volume 40 ml/kg, 20 inspirations/min). If necessary, external massage and electrical defibrillation of the heart were used. Before the experiment and for 3 h after restoration of the vital functions the viscosity of the blood and plasma was determined on a VIR-75 rotary viscometer at shearing velocities of 2-91 $sec^{-1}$, and the limit of flowability was calculated graphically [8]. The configuration of the surface membranes of the erythrocytes was studied stereoscopically by means of a scanning electron microscope. Morphological characteristics of the erythrocytes were studied using the classification of Kozinets et al. [3]. Electrophoretic mobility of the erythrocytes was determined with an Opton (West Germany) Cytoferometer. The fibrinogen concentration [10], total plasma protein (with a refractometer), hematocrit index, and parameters of the acid–base balance of the blood were measured. The blood pressure in the aorta and the central venous pressure at the mouth of the venae cavae were recorded on a polygraph.

## EXPERIMENTAL RESULTS

The duration of agony in all animals was 9.0 ± 1.5 min and clinical death lasted 10 min (clinical death for 10 min is the longest period after which recovery of the bodily functions is possible in some cases). The volume of blood lost was 50.7 ± 1.6 ml/kg. Cardiac activity, respiration, and corneal reflexes were restored 3.2 ± 0.6, 5.0 ± 1.1, and 21.0 ± 1.8 min respectively after the beginning of resuscitation. In ten chronic experiments four animals survived with incomplete neurologic recovery, as shown by disturbances of static posture and movement coordination. The remaining six animals died during the first day after revival.

At the beginning of resuscitation the viscosity of whole blood, limit of flowability, and viscosity of the plasma were reduced by 14, 8, and 22% respectively. The fibrinogen and protein concentrations in the plasma and hematocrit index were reduced, due to dilution of the blood with the solution of the TsOLIPK 12b stabilizer during resuscitation. Uncompensated metabolic acidosis (Table 1) was observed in the blood at this time. Besides the changes mentioned above, significant changes also affected the configuration of the erythrocyte membranes. For instance, the number of discoid forms of erythrocytes fell to 62.0 ± 5.0% compared with an initial level of 92.0 ± 1.0%. Intermediate forms accounted for 25.0 ± 6.0% (4.0 ± 1.0% in the original state) and nontransitional forms appeared — 13.0 ± 4.0% (Fig. 1b).

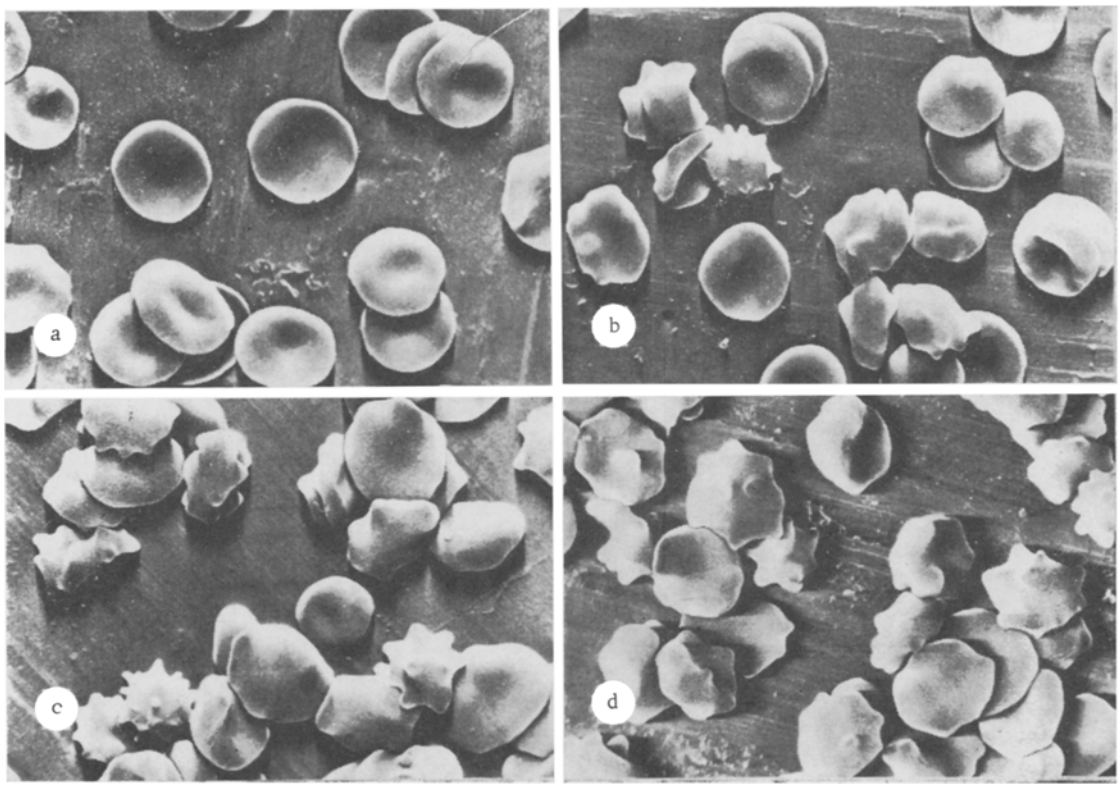


Fig. 1. Ultrastructural changes in surface architectonics of erythrocytes after clinical death for 10 min from acute blood loss. a) Control (intact dog), b) 5th minute of postresuscitation period, c) 1st hour, d) 3rd hour of postresuscitation period. Scanning electron microscopy. 3000 ×.

Later, during the first 3 h of the postresuscitation period, a progressive increase in the viscosity of the blood and the flowability limit took place compared with their values before blood loss and at the beginning of resuscitation ($P < 0.05$). The concentrations of fibrinogen and protein were increased a little but remained significantly ($P < 0.05$) below their initial level, and the hematocrit index rose to the initial level (Table 1). The viscosity of the plasma remained significantly lower than initially ($P < 0.05$) throughout the period of observation. The study of the surface architectonics of the erythrocytes revealed a further decrease in the number of normal discoid forms to 37.0 ± 3.0% of the inital value. The number of transitional forms increased to 38.0 ± 3.0% and of nontransitional forms to 25.0 ± 3.0% (Fig. 1c, d). The electrophoretic mobility of the erythrocytes remained unchanged during the first 3 h of the postresuscitation period.

The increase in the number of transitional and nontransitional forms of erythrocytes was evidently due to a hypoxic disturbance of their metabolism, and also to a change in the composition and properties of the surrounding medium: the acid–base balance, protein and fibrinogen concentrations, and activation of the proteolytic systems of the blood [7].

The increase in the viscosity of whole blood in the early postresuscitation period was thus largely connected with damage to the erythrocytes and disturbance of the surface configuration of their membranes, which begins in the period of clinical death and progresses at the initial stages of the recovery period.

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# EFFECT OF BENZODIAZEPINES ON NEUROPATHOLOGICAL SYNDROMES OF SPINAL ORIGIN

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KEY WORDS: benzodiazepines; neuropathological syndrome; hyperactivity.

Creation of a generator of pathologically enhanced excitation (GPEE) in a system of propriospinal interneurons causes generalized spinal myoclonia [5], whereas in a system of nociceptive posterior horn neurons it causes a pain syndrome of spinal origin [5]. Since benzodiazepines depress hyperactivity of structures of the CNS [16, 19, 20] and, in particular, activity of GPEE in different parts of the brain [5], it was decided to study the effects of these substances in the above-mentioned neuropathological syndromes.

To determine the effectiveness and to study the mechanisms of action of these substances it was necessary to test the effect of different benzodiazepines on the same syndrome, the action of the same preparation on different syndromes (myoclonia and the pain syndrome), and also on the same clinical syndromes but evoked by GPEE of different nature, and created by means of different substances. In this investigation diazepam (seduxen), phenazepam and clonazepam were used.

## EXPERIMENTAL METHOD

Experiments were carried out on noninbred albino rats weighing 200-220 g. A syndrome of spinal myoclonia was induced by creating a GPEE in a system of propriospinal connections with the aid of tetanus toxin (TT), which disturbs various types of inhibition [7, 9, 12, 14]. TT (40 mld for mice) was injected into the calf muscles, from which it travels along the regional neural pathway to the anterior horns of the lumbosacral segments, after which it spreads within the nearest segments of the spinal cord [4]. The vascular pathway of spread of TT was blocked by intravenous injection of antitoxin (0.025 AU). The model of the syndrome and the method of its creation were fully described previously [1, 3]. The GPEE was activated by the method adopted previously [4, 5] by stimulation (pinching the skin of the toes) of the limb into which TT was injected. To record biopotentials, bipolar needle electrodes were used. Electrical activity (EA) was recorded in the spinal and sacral muscles on both sides and the posterior group of thigh muscles of both limbs. The electromyogram (EMG) was recorded on an 8-channel RM 86M encephalogram (Nihon Kohden, Japan). In a special series of experiments the spinal cord was divided at the level T2-T3 24 h before EA was recorded.

A pain syndrome of spinal origin was induced by forming a GPEE in the system of posterior horns of the spinal cord [6] by means of substances disturbing various types of inhibition (TT, strychnine, and penicillin) and substances inducing depolarization of neuron membranes (KCl and ouabain) [2]. The substances were deposited in 1% agar, a slab of which (measuring 10 × 4 × 1.5 mm) was applied to the dorsal surface of the spinal cord on one side in region

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