Later, as the hypertension becomes stabilized (24 weeks), the leading mechanism in the increase in peripheral resistance, in the writers' opinion, is no longer a decrease in the number of arterioles, but adaptive hypertrophy of the smooth muscles of the resistive vessels. In adult SHR the structural component of resistance (by 35% compared with 17% in young SHR) and the angle of slope of the BP–dose of NA curve (by 100% compared with 40% in young SHR) increases even more in adult SHR.

The experiments thus showed that two mechanisms may evidently participate in the increase in the structural component of resistance of the resistive vessels: a decrease in the density of the network of arterioles and hypertrophy of the vessel walls; moreover these are two interconnected processes, causing an increase in the systemic resistance in SHR in the course of development of hypertension.

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TIME COURSE OF CHANGES IN THE HEPATIC MICRO- AND MACROCIRCULATION FOLLOWING ACUTE BLOOD LOSS IN RATS

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KEY WORDS: acute blood loss; hepatic micro- and macrocirculation; biomicroscopy; ultrasonic method.

Many investigations of the hepatic circulation in acute blood loss have been published [1, 3, 4, 7-9]. However, the question of what changes arise under these circumstances at the level of the terminal microvessels of the liver, how they are connected with hemodynamic disturbances in the liver and the hepatic system, and what their role is in the pathogenesis of the posthemorrhagic syndrome still remains insufficiently explained.

In the investigation described below the hepatic micro- and macrocirculation and the systemic arterial blood pressure (BP) were studied in rats after acute blood loss.

EXPERIMENTAL METHOD

Experiments were carried out on 56 male Wistar albino rats weighing 250-300 g. The microcirculation in the liver was studied by contact luminescence biomicroscopy under general urethane anesthesia [5]. Simultaneously with visual observation of the hepatic microcirculation, measurements were made of the volume

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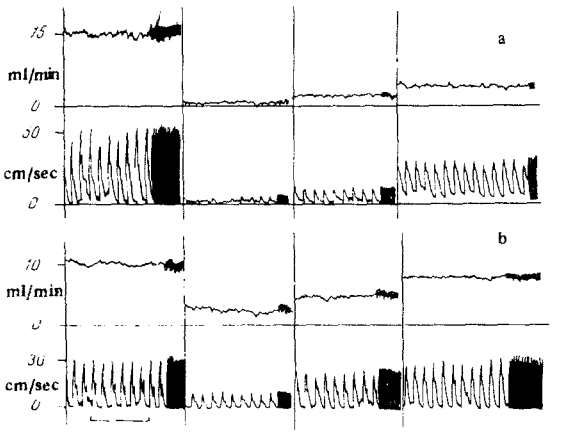

Fig. 1. Character of changes in blood flow velocity in portal vein and hepatic artery of rat liver after acute blood loss. a) Decompensated type of course of acute blood loss; b) compensated type of course of acute blood loss. Above – volume velocity of blood flow in portal vein; below – linear velocity of blood flow in hepatic artery. From left to right: before blood loss, 5, 15, and 30 min after beginning of blood loss. Time marker 1 sec. Time course of recovery of linear velocity of blood flow along hepatic artery precedes changes in blood flow in portal vein.

velocity of the blood flow in the portal vein and the linear velocity of the blood flow in the hepatic artery by the ultrasonic method described in [2]. Acute blood loss was induced by single bleeding from the carotid artery in a volume equivalent to 2.5% of body weight in 5 min. No preliminary intravenous injection of heparin was given to the animals. The parameters used to indicate the general state of the animals included the length of their survival after the beginning of blood loss, and BP in the carotid or femoral artery, measured by a mercury manometer.

EXPERIMENTAL RESULTS

Three types of course of acute blood loss were discovered in the rats: decompensated (30% of cases), compensated (50% of cases), and subcompensated (20% of cases). In the decompensated type the systemic BP of all animals fell rapidly during blood loss itself to 30-25 mm Hg, and it was not restored in the posthemorrhagic period. Two subtypes of the decompensated type of course after blood loss could be distinguished on the basis of the animal's length of survival and the character of changes in the hepatic hemodynamics and microcirculation.

1. Death during the first 10-15 min after the beginning of blood loss. The animals showed a progressive fall in the velocity of the portal and arterial blood flow down to 0. At the microcirculatory level in this case the velocity of the blood flow in all microvessels was slowed. As the total volume of portal and arterial blood entering the liver decreased, a sharp reduction was observed in the volume of blood in the microvessels and in their diameter. The microcirculatory system of the organ was emptied. In the posthemorrhagic period, a very small increase in the linear velocity of the arterial blood flow took place, but the volume velocity of the blood flow in the portal vein still remained at zero and tissue perfusion at the level of the terminal microvessels was considerably reduced.

2. Death during the first hour after the beginning of blood loss. In the animals of this group, during the period of actual removal of the blood a rapid decline was observed in the velocity of the portal and arterial blood flow. After the end of blood loss there was a tendency for these parameters of the hepatic circulation to recover. The increase in the velocity of the arterial blood flow to the liver was greater than that of the portal blood flow (Fig. 1a). Biomicroscopically, mosaic changes in the microcirculation developed in the liver in the posthermorrhagic period against the background of depressed values of the total blood volume in the organ and the velocity of the sinusoidal blood flow. In some zones all the terminal microvessels were constricted and

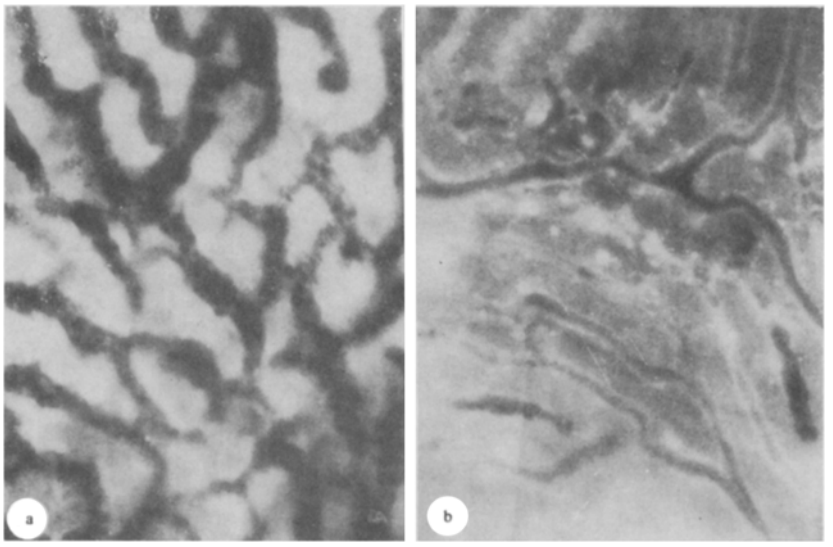

Fig. 2. Rat liver 30 min after beginning of blood loss. a) Decompensated type of course of acute blood loss. Sinusoids dilated and filled with static blood; b) compensated type of course of acute blood loss. Blood flow at microcirculatory level remains intact, zones with fragmentary dilatation of sinusoids and with microstasis can be seen. Tissue vascular permeability increased – luminescence vacuoles of FITC-labeled bovine albumin can be seen in cytoplasm of liver cells. Contact luminescence biomicroscopy, 75×.

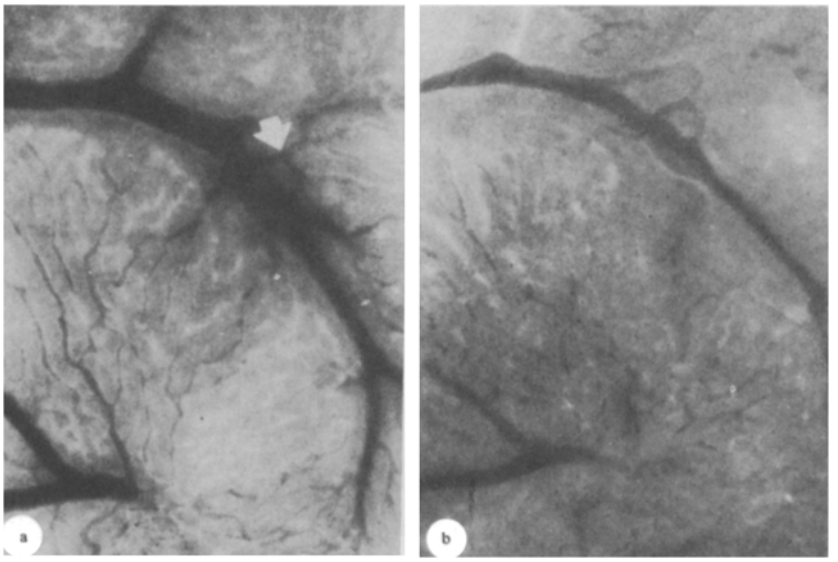

Fig. 3. Reaction of rat liver microvessels to acute compensated blood loss. a) Microcirculatory system of liver before beginning of blood loss. Portal venule and hepatic arteriole, with smaller diameter (arrow), can be seen on right, terminal hepatic venule in top left corner; b) the same place 3 min after beginning of blood loss. Reduction of blood flow in microcirculation along terminal portal venule and hepatic arteriole, emptying of sinusoidal system, reduction in diameter of terminal microvessels. Contact luminescence biomicroscopy, 30×.

empty, whereas in other, large areas, the sinusoids in the region of the afferent microvessels and of the middle part of the functional structure were dilated and filled with blood. The blood flow in them was greatly retarded and in some places stopped altogether (Fig. 2a), and the sinusoids in the region where they emptied into the terminal hepatic venules, and the draining venules themselves were anemic. The microvessels of the functional structure drained into the hepatic venules in the manner of a system of collecting sinusoids.

In the compensated type of course of acute blood loss in the period of actual removal of the blood the systemic BP fell to 30-25 mm Hg (Fig. 1b). However, as a rule changes in the hepatic macro- and microcirculation during this period were more gradual than in the decompensated type. The decrease in linear velocity of the arterial blood flow developed after the decrease in the portal vein. At the microcirculatory level a gradual decrease was observed in the blood volume in the terminal hepatic microvessels, and the velocity of the blood flow in them was slowed. The sinusoidal system was empty and difficult to focus (Fig. 3a, b). In the posthemorrhagic period a comparatively rapid improvement of the parameters of the hepatic macro- and microcirculation took place. The velocity of the arterial blood flow returned to normal more rapidly and completely than the velocity of the portal blood flow, values of which usually remained 10-30% below their initial level (Fig. 1b). The improvement in the parameters of the regional blood flow in the hepatic macro- and microcirculation in the compensated type of course took place parallel with elevation of the previously lowered systemic BP. A period of comparatively long stabilization of the systemic hemodynamics and of the hepatic macro- and microcirculation began. The length of survival of the animals was not less than 3 h. In the posthemorrhagic period, the gradual development of focal changes in the microcirculation was observed at the level of functional structures of the liver, in the form of the appearance of fragmentary foci of microthrombosis and microstasis, aggregation of erythrocytes, and disturbances of tissue vascular permeability. These changes had a clear topography and were located in zone No. 1 of the functional structure of the liver, without disturbing the microcirculation at the level of the organ as a whole, composed of its functional structures (Fig. 2b).

In the subcompensated type of blood loss the time course of changes in the hepatic macro- and microcirculation during the actual blood loss and in the posthemorrhagic period was the same as in the compensated type. However, restoration and temporary stabilization of the region of hepatic hemodynamics took place without any increase in systemic BP, which remained depressed to 30-25 mm Hg. The mean length of survival of the animals of this group was 2 h.

The severity and stability of changes in the hepatic macro- and microcirculation in rats after blood loss thus correlate with the severity of the course of the posthemorrhagic period. A rapid fall of the portal and arterial fractions of the hepatic blood flow, leading to prolonged ischemization of the functional structures of the organ, has the most unfavorable prognosis. The course of the posthemorrhagic period also is severe if, against the background of uncompensated reduction of the portal blood flow, only the arterial blood supply to the organ improves. In most functional structures microcirculatory changes leading to pathological storage of blood in the hepatic microvessels develop in response to a prolonged and stable decrease in the inflow of portal blood. Regions with congested, dilated sinusoids alternate with zones of smaller area in which all the terminal microvessels are constricted and empty, and this also increases the intravascular hepatic resistance. On the whole the microcirculatory changes developing in the liver in decompensated blood loss limit the return of blood to the right heart, make the hepatic tissue perfusion less effective, and lead to insufficiency of hepatic functions. Results of the present investigation show that the course of the posthemorrhagic period is benign only if reduction of the portal blood flow, leading to evacuation of blood from the splanchnic basin into the general circulation and to its centralization, is temporary in character. Rapid quantitative compensation of the portal fraction of the hepatic blood flow and the absence of changes in the microcirculatory system leading to an increase in the intrahepatic vascular resistance under these circumstances maintain, on the one hand, the return of blood to the right heart at the level required to support the general systemic circulation and, on the other hand, the level of the local tissue blood flow required for adequate liver function. The results confirm the views expressed by the writers previously on the leading role of the portal circulation in the physiology and pathology of the liver [6]. Attention is also drawn to the fact that the regional hepatic blood supply is relatively free from the level of the general systemic blood flow. In the posthemorragic period self-regulating regional compensation of the hepatic circulation may be possible, with preservation of shock values of the systemic BP. Self-regulating compensation of the hepatic blood flow under conditions of lasting systemic hypotension is regarded by the writers as an important compensatory mechanism aimed at maintaining life of an individual in a state of shock.

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COMPENSATORY REACTIONS OF THE RESPIRATORY CENTER AND THEIR PERIPHERAL MANIFESTATIONS IN ANIMALS WITH INJURIES OF THE RESPIRATORY TRACT AND LUNGS

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KEY WORDS: respiratory center; electrical activity; experimental inflammation of the respiratory tract.

It is generally considered that electrical activity of the respiratory muscles under normal conditions reflects the functional state of the respiratory center. In pathology, however, when the flow of efferent impulses to the respiratory muscles and also, probably, the flow of afferent impulses to the respiratory center (from receptors of the affected respiratory passages and lung) is modified, electrical activity of the respiratory muscles can no longer be the chief criterion used to evaluate the state of function of the respiratory center. In such cases only a simultaneous study of the discharge patterns of bulbar respiratory neurons and of the electrical activity of various groups of respiratory muscles in a model of experimental inflammation of the respiratory tract and lung can adequately elucidate the functional state of the respiratory center in animals in different stages of the disease.

In the investigation described below the firing pattern of respiratory neurons and electrical activity of different groups of respiratory muscles and compensatory reactions of the respiratory center were studied in cats with an experimental lesion of the respiratory tract and lungs.

EXPERIMENTAL METHOD

A model of injury to the respiratory tract and lungs was created in cats (60 animals) by injecting 0.3 ml of wood turpentine into the trachea in the direction of the lungs [5]. Experiments were carried out 24-72 h after injection of the turpentine. Under pentobarbital anesthesia (40 mg/kg) action potentials of medullary respiratory neurons were derived by microelectrode and stereotaxic techniques (using Szentagothai's atlas). The metal microelectrode had a tip 1-3 μ in diameter. Parallel recordings were made of the pneumogram, EMG of the diaphragm, intercostal muscles, and abdominal muscles, and the composition of the blood gases. Gas mixtures of 10% in N_2 and 2% CO_2 in air and O_2 were used. After the investigation the animal was autopsied to establish the extent and severity of the lesion of the trachea and lungs.

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