Intravascular Measurements of the Blood Flow in Rats

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The dynamics of the cardiac output is now being successfully studied in rats with the aid of ultrasound and electromagnetic transducers [1,4,10]. However, drastic procedure of thoracotomy, which is performed to apply the transducers to the ascending aorta, makes a number of studies difficult. Such investigations are less traumatic for catheterization, when thoracotomy is not necessary and the transducers are inserted in the relevant portion of the circulatory bed. Today, ultrasonic catheters are widely used in clinical practice for diagnostics of heart defects [2,3,13]. Their use in experimental investigations is restricted due to the size of the animals [14]. The technology of high-frequency ultrasound makes it possible to reduce the dimensions of the measuring device. On this basis, transducers were developed for registering the blood flow in the coronary vessels of rats by the contact method [8]. The aim of the present work was to study the possible use of an intravascular high-frequency ultrasonic transducer for measurements of the blood flow in the circulatory bed of rats.

MATERIALS AND METHODS

The experiments were carried out on nembutal-narcotized rats of both sexes weighing 250-300 g, in which thoracotomy was performed under conditions of artificial lung ventilation with air. Ultrasonic transducers of the bandage type, operating at a frequency of 8 and 13 MHz, were positioned on the ascending portion of the arch of the aorta. These transducers, serving as a reference, were calibrated in units of linear and volume velocity and made it possible to assess the value of the cardiac output [7,10]. For measurement of the blood flow in the vessel, an ultrasonic transducer, fixed at the end of a polyethylene tube 0.6 mm in diameter, was inserted in the circulatory bed. This transducer was the source of ultrasound with a frequency of 33 MHz; it consisted of a piezoelectric plate made of titanozirconium salt of lead 60 μ thick and of an area of 0.3 mm^2. The piezoelement picks up signals reflected by the formed elements of the blood. The device detects the differences between signals which occur due to the movement of the blood in the region of piezoelement radiation, by comparing their frequency with the ultrasound radiated. This difference is proportional to the flow rate; it is determined by the frequency of the Doppler signal and is used for comparison with the readings of the bandage transducer.

The intravascular transducer was inserted in the ascending aorta via the right carotid artery, and the shape of the flow curve registered was observed. When a signal of an irregular shape appeared (this being evidence that the transducer was in the zone of operation of the heart valves), the catheter was moved slightly back and fixed in this position.

Polyethylene catheters were inserted in the femoral artery and jugular vein in order to register the arterial pressure and to inject pharmacological preparations. Studies of the operation of the

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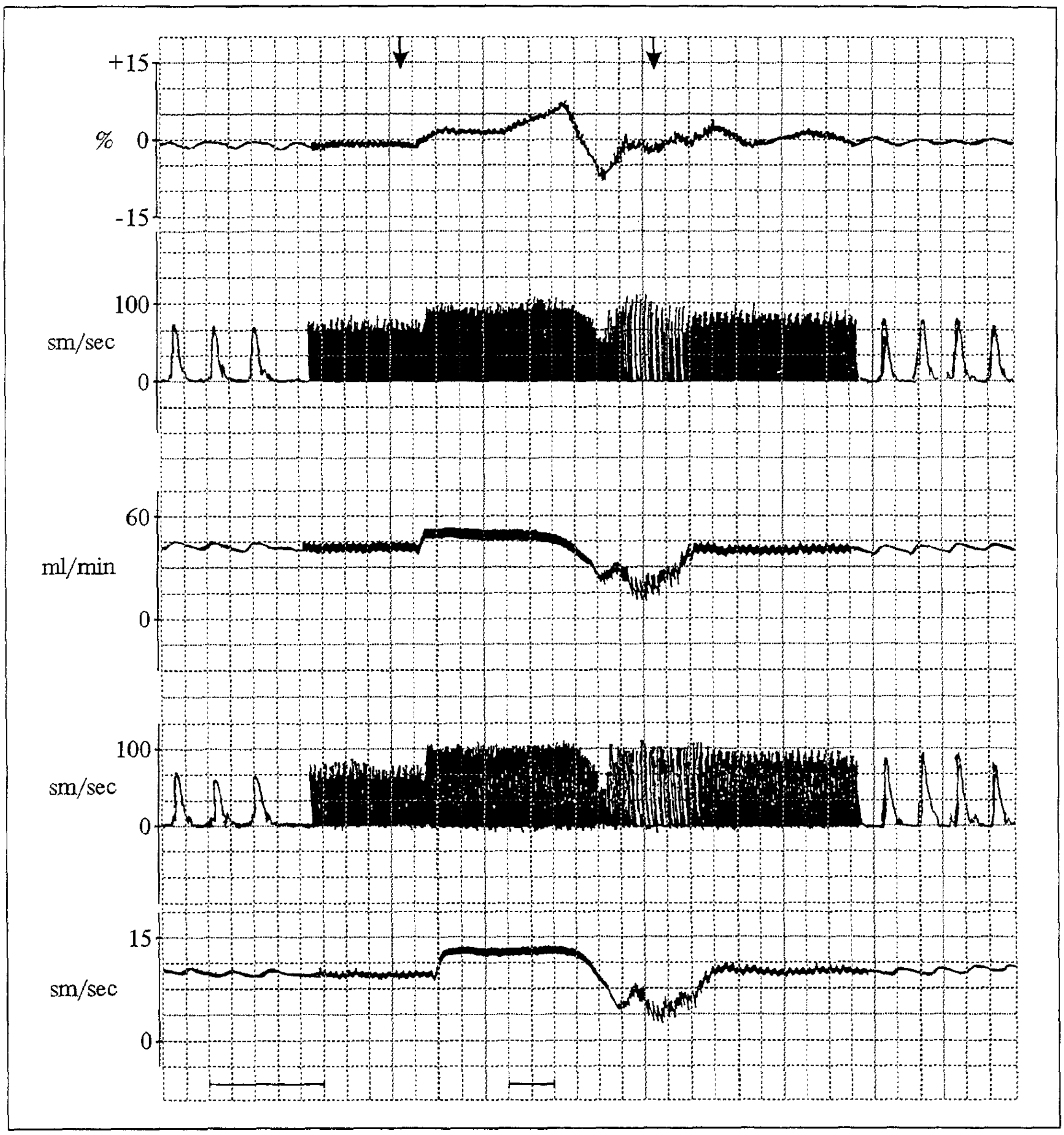

Fig. 1. Simultaneous recording of blood flow in the ascending aorta of a rat with the aid of bandage and intravascular transducers for 1-min asphyxia. From top to bottom: balance between measurements performed by bandage and intravascular transducers; minute volume according to bandage transducer; mean blood flow rate according to intravascular transducer; blood flow in the aorta according to intravascular transducer. Time scale: 1 and 10 sec. Arrows show start and end of asphyxia.

intravascular transducer and comparison of its readings with those of the bandage transducer were carried out under conditions of relative physiological repose (static tests), as well as under different influences: administration of physiologically active substances (epinephrine, norepinephrine, histamine, etc.) in different doses, asphyxia, and inhalation of various gas mixtures.

The blood flow was also measured in the descending aorta. The transducer was inserted via the left carotid artery or via the femoral artery. The measurements were performed in portions of the aorta suitable for applying bandage transducers. However, of more interest are our findings on the cardiac output in the ascending aorta, and this is the focus of the present study.

RESULTS

The signal of the intravascular transducer was calculated in units of linear flow rate. However, since the transducer might occupy an indefinite position in relation to the profile of the flow in the vessel, it was preliminarily studied on a hydrostand in Pito's tube [6], where the profile of the flow was monitored by a dynamic pressure receiver. At the same time, the readings of the intravascular transducer were compared with those of a pulse

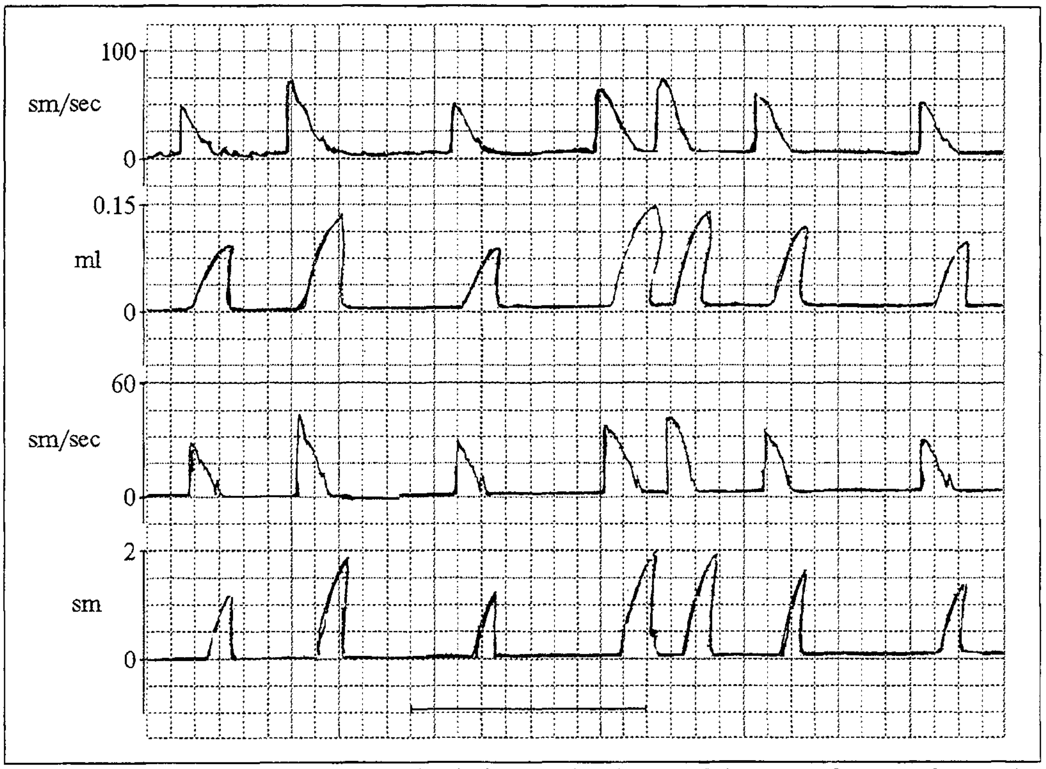

Fig. 2. Simultaneous recording of blood flow by bandage and intravascular transducers for changes of the heart rhythm. From top to bottom: blood flow rate and stroke volume measured by bandage transducer; blood flow rate and stroke volume measured intravascularly. Time scale 1 sec.

ultrasound transducer, which measured the velocity close to the mean velocity in the profile of the flow. This transducer, positioned nearby, performed measurements according to the difference in the transit time of the pulses between two piezocrystals positioned at opposite ends of the diagonal of Pito's tube, this making it possible to integrate over the velocity profile of the flow [5]. The fundamental possibility of using a miniature Doppler transducer for measuring the blood flow in the circulatory bed was established as a result of the stand tests, and its sensitivity to linear velocity (Hz/cm/sec) was roughly determined.

The rat study was aimed at the determination of the correction coefficient for operations in blood flows inside blood vessels. Transducers of the bandage type were used as a reference. The static investigations demonstrated that, in contrary to expectations, little scatter was found between the readings of these measuring systems, the correlation coefficient being 0.96. Possibly, this stability was due to the method of inserting the catheter in the ascending aorta, whereby the transducer is pressed against the inner wall of the vessel, and, thus, occupies a fixed position vis-a-vis the profile of the flow.

Another factor providing an explanation for the high correlation between its readings and those of the bandage transducer was the presence of an acoustic lens in the piezocrystal. A lens was introduced into the construction of the transducer in order to broaden the beam of ultrasound and to integrate the measurements over the profile of the flow. In addition, during the development of the design, the piezocrystal was positioned at various angles to the axis of the catheter. Our aim in this was to improve the signal/noise ratio. However, in the experiments on rats these transducers sometimes occupied a position whereby the radiation of the piezoelement was directed at the aorta wall, the flow near the wall being recorded. In this case the effect of the pulsation of the vessel, which was manifested as an intermodulation distortion of the Doppler signal, was observed.

On the above basis, the end position of the crystal was chosen, where the axis of ultrasound radiation coincided with or was parallel to the axis of the flow; such a design, in combination with the presence of an acoustic lens, proved to be the most effective.

In the present work we also studied intravascular transducers operating at frequencies of 13.4 and 26.8 MHz. However, the end position of the piezoelement, chosen in order to stabilize the readings of the transducer at work in the circulatory bed, led to a reduction of the dimensions of the

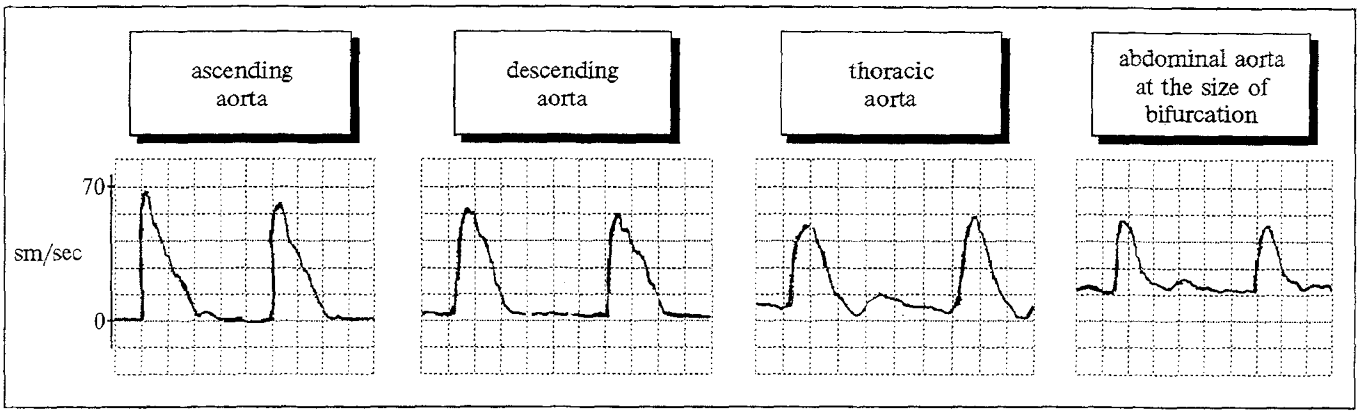

Fig. 3. Examples of blood flow curves recorded in portions of aorta. *1*) ascending aorta; *2*) descending aorta; *3*) thoracic aorta; *4*) abdominal aorta at the site of bifurcation.

piezoelement, and, as a result, worsened its performance. An increase of the frequency of ultrasound to 33 MHz enabled us to raise the signal due to a significant increase of the reflecting properties of the formed elements of the blood and, thereby, to compensate for the loss of sensitivity. At the same time, the signal/noise ratio for the transducer operating at a frequency of 33 MHz constituted no less than 38 dB, this providing for a reliable recording of the shape of the curve of the cardiac output.

For a study of the work of intravascular transducers in dynamics, the cardiovascular system was exposed to different influences. The doses of epinephrine, norepinephrine, and other physiologically active substances, as well as the duration of asphyxia were chosen in such a way as to cause strong responses in the circulatory system. In such cases, the blood flow in the ascending aorta of a rat changed by 50-80%, and fluctuations of the arterial pressure constituted 30 to 150 mm Hg; this enabled us to study the performance of the transducer in a wide range. Comparison of the bandage and intravascular systems was performed using three major parameters: the maximal velocity of the cardiac output, the mean blood flow rate (or the value of the minute volume in the case of the bandage transducer), and the value of the stroke volume determined by electronic integration of the area beneath the cardiac output curve [9]. To determine the value of the differences between the readings obtained in the dynamics of the process, the data on the mean velocity obtained from the bandage and intravascular transducers were entered into an analog computer [12], which calculated the percentage disruption of the balance between these measuring systems (Fig. 1). In our studies the value of these discrepancies for exposure to different influences usually constituted 5-7% and did not exceed 11%. The difference for the measurements of the maximal velocity constituted 6-9%, the normal values of this parameter being 60-90 cm/sec. The difference between the readings for the stroke volume was less marked (4-6%) (Fig. 2).

In the series of experiments where the transducer was inserted via the femoral artery, the blood flow was recorded over the whole length of the aorta, including the bifurcation. Various shapes of the blood flow curves registered in certain portions of the aorta are presented in Fig. 3. The difference between the readings for the blood flow rate recorded in the regions of the thoracic and abdominal aorta with the aid of intravascular and bandage transducers was 9-12%.

In this study an attempt was made to use a transducer for intravascular measurements in alert rats. The data on implantation of bandage transducers of different types in rats are widely known [7,11]. However, the trauma of thoracotomy, as mentioned above, does not allow the experiments to be started earlier than on days 4-6 postoperation, by which time the hemodynamic parameters usually normalize. In experiments with preliminarily trained or exercised animals such intervals are undesirable. In studies of the cardiac output in alert rats, E. Yu. Bychkova used intravascular transducers. The transducers were inserted in the ascending aorta via the right carotid artery. In all 10 experiments carried out on preliminarily trained rats weighing 300-350 g, recovery of the heart rate, of the arterial pressure, and of the blood flow rate occurred on the day following the operation. These parameters virtually did not change subsequently, enabling us to start the experiments.

Thus, the method described makes it possible to measure with sufficient accuracy the blood flow rate in rats over the whole length of the aorta, including the portions hardly accessible for transducers of other systems. High sensitivity was achieved by using high-frequency ultrasound, yielding a reliable determination of the shape of the blood flow curve. Under conditions of acute experiment the intravascular transducer makes it possible to investigate the hemodynamics in alert animals. The duration of the operating period of intravascular transducers under these conditions has not yet been established, and depends on the quality of the materials used. However, the relative benign procedure of implantation, greatly reduces the time before postoperative studies can be begun, which is an important plus for physiological investigations.

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Role of the Liver in the Regulation of Sideremia Biorhythms in Rabbits with Acute Alcoholic Intoxication

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One mechanism through which alcohol exerts its hepatotoxic effect is the activation of lipid peroxidation (LPO) [12,15], which is initiated by a rise in the concentration of variable valency metals, in particular iron and copper, and their transition from the bound to a free state [2,10,11]. The liver, as a depot of iron, is involved in regulating the circadian rhythmicity of sideremia, which is dependent on the activity of free-radical LPO [1]. It is therefore important to know what role this organ plays in the regulation of diurnal variations in sideremia, LPO, and antioxidants in acute alcoholic intoxication.

The purpose of this study was to examine the impact of acute alcoholic intoxication (AAI) on the temporal organization of iron metabolism, LPO, and antioxidants by considering diurnal variations in the concentrations of serum iron, LPO products, and α-tocopherol in blood from the portal and hepatic veins.

MATERIALS AND METHODS

For the experiments, which were conducted in winter, 80 male brush rabbits (*Sylvilagus bachmani*)

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