MEASUREMENTS OF THE CORONARY BLOOD FLOW BY A RADIOISOTOPE DILUTION METHOD IN CHRONIC EXPERIMENTS ON MONKEYS

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An original modification of the radioisotope dilution method is suggested. The indicator (the animals' own erythrocytes labeled with P^{32}) is injected by puncture of the left ventricle, and the dilution curve is determined from the radioactivity of drops of blood flowing from a catheter introduced into the right ventricle. The first clearly defined wave is the coronary wave. The coronary blood flow of monkeys was 15.83 ± 0.56% of the minute volume.

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Several authors [1, 2, 4-7, 9-11] have used radiocardiography, one variant of the radioisotope dilution method, for clinical measurement of the coronary blood flow. However, because of difficulty in identifying the coronary waves on the ordinary radiocardiogram, because it merges with the ventricular wave, different methods have been used for assessing the results and significantly different values have been obtained for the coronary blood flow in healthy persons even when the same method and the same measuring apparatus have been used [1, 2].

In an attempt to overcome difficulties of identification and measurement of the coronary wave on the indicator dilution curve and thus to increase the accuracy of calculation of the coronary blood flow, we have developed and tested our own modification of the radioisotope dilution method in experiments on monkeys.

The essence of the suggested method of measuring the total coronary blood flow without opening the chest is recording of the radioactive isotope dilution curve in the right ventricle after injection of the indicator into the left ventricle. The basic assumption was that part of the indicator entering the coronary system from the aortic orifice would reach the right ventricle much more quickly than the main part of the indicator entering the systemic circulation. Consequently, during its passage through the right ventricle, the front of the coronary wave will be separated from the front of the ventricular wave by a certain time interval which must evidently be adequate for precise identification of the wave on the dilution curve.

Measurements were carried out on sexually mature clinically healthy monkeys (five rhesus monkeys and two brown macaques) of approximately the same age and weight. Before and during the investigation the arterial pressure and ECG of all the animals remained within normal limits. Under superficial Nembutal anesthesia a polyvinyl chloride catheter with an internal diameter of 1.5 mm, filled with heparin solution, was introduced into the right ventricle through the right external jugular vein. The outer end of the catheter was held in a clamp fixed above the tape of an ink-writing electrocardiograph. The indicator used consisted of autologous erythrocytes labeled with P^{32} and suspended in physiological saline (1:1). Indicator in a volume of 0.01-0.02 ml, with an activity of about 20 μCi, was injected rapidly into the left ventricle by puncture through the anterior chest wall. The clamp was simultaneously opened and blood from the right ventricle flowed out continuously in drops to one of the tracks of the moving tape of the electrocardiograph at a frequency of 2-3 drops/sec, the winding speed of the tape being 25 mm/sec. The drops must not spread nor join together. Blood was taken for 1 min. A parallel recording was made of the ECG. The catheter was then filled with heparin, closed by special stopper, and its free end was fixed under the skin in the occipital region. The monkey with the catheter was placed in a special armchair limiting its movement. Every day the catheter was washed out with physiological saline. The tape was dried in an extraction cupboard and the radioactivity determined in each drop in pulses/min by means of an end-type counter on a type B apparatus. The results were plotted on a semilogarithmic scale. The time in seconds and the cardiac contractions at the moment of taking the drops of blood were plotted along the horizontal axis super-

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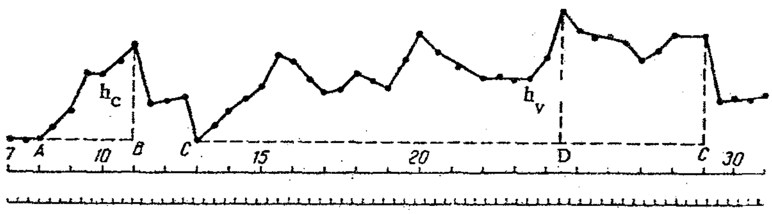

Fig. 1. Indicator dilution curve in right ventricle. Monkey No. 7115. Semilogarithmic scale. CBF 13.95% of MV. Time marker and marker of cardiac contractions given below.

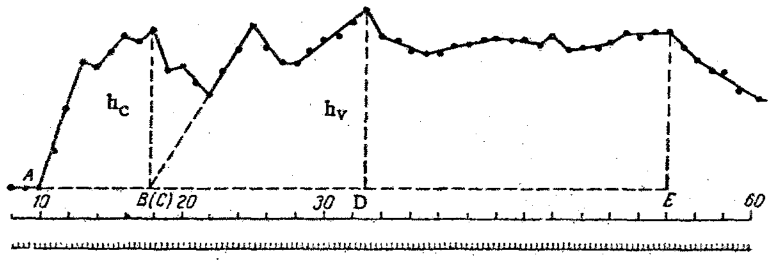

Fig. 2. Indicator dilution curve in right ventricle. Monkey No. 7038. CBF 18.66% of MV.

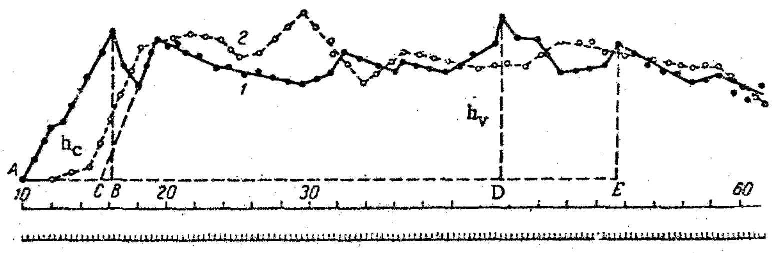

Fig. 3. Indicator dilution curve in right ventricle when measured in the usual way (1) and during clamping of main trunks of coronary arteries (2). In the second case no coronary wave can be detected.

TABLE 1. Coronary Blood Flow (in % of minute volume)

No. and species of animal	Coronary blood flow
7155; Rhesus monkey	13,95
2921; Rhesus monkey	14,74
6945; Rhesus monkey	14,86
7299; Rhesus monkey	14,98
7295; Rhesus monkey	16.09
6953; Brown macaque	16,62 after 12 days 16,4)
7038; Brown macaque	18,66 after 6 days 16,2)
	$M \pm m = 15{,}83 \pm \pm 0{,}56$

posed on the tape of the electrocardiograph, and the radioactivity of each drop along the vertical axis. A typical dilution curve showed clear separation into two waves: a coronary wave with a steep rise and an acute maximum, and the ventricular wave, several times longer and with several maxima (Figs. 1 and 2). The trough between the waves may fall to the background level if a minimal volume of indicator is injected very quickly, completely separating one wave from the other (Fig. 1). On the dilution curve obtained from a monkey in which, simultaneously with injection of the indicator, the main trunks of the coronary arteries were clamped for 5-7 sec (acute experiment), no coronary wave could be detected (Fig. 3).

The ratio between the area of the coronary wave and the area of the ventricular wave, according to the dilution equations, reflects the ratio between the coronary blood flow and the minute volume of heart. We used a simplified formula for the leading triangles for the calculations [3, 8]:

$$\frac{h_c \times AB}{h_v \times CE} = \frac{CBF}{100}, \text{ whence } CBF = \frac{h_c \times AB \times 100}{h_c \times CE} \text{ (in \% of MV)},$$

where h_c represents the height of the coronary wave, h_v the height of the ventricular wave, AB the base of the coronary "triangle" CE the base of the ventricular "triangle" (point E corresponds to the beginning of the exponential fall of the curve), CBF the coronary blood flow, and MV the minute volume.

In two monkeys kept in the special armchairs with catheters in the right ventricle the coronary blood flow was measured again 6-12 days after the first measurement. To calculate the curve, the radioactivity of the blood, which was slightly increased as a result of the first measurement, was taken as the initial background. The results of measurement of the coronary blood flow are given in Table 1.

The method described differs from other methods of measurement of the coronary blood flow using radioisotopes in the clearer separation of the waves, the absence of difficulties connected with measurements of radioactivity of the tissues surrounding the heart and escape of the indicator outside the capillary circulation, and also by the fact that the radioactivity of each sample can be determined with maximal accuracy. Yet at the same time, the method requires no expensive apparatus.

We found no data in the literature for the coronary blood flow of monkeys. If, like many other indices of the hemodynamics (in relative units of measurement), it does not differ significantly from the coronary blood flow in man, which in our results do not correspond to those given in the literature (5-10% of the min volume), but approximate more closely to those given by S. S. Vysokii [1] (12.8%), obtained by investigation of healthy persons by the method of inhalation radiocardiography.

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