STUDY OF METABOLISM OF PHOSPHORUS COMPOUNDS IN THE HEART, USING RADIOACTIVE PHOSPHORUS

COMMUNICATION I. LEVEL OF PHOSPHORUS METABOLISM OF THE MYOCARDIUM OF DOGS

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In most studies, the basic criterion for assessing the metabolism of phosphorus compounds in the heart muscle was the determination of their content at a given moment. This content, however, is the resultant of the reactions of synthesis and breakdown of the given compound, and may remain unchanged if the rates of these two reactions increase to the same degree, even when the metabolic rate is increased. In such a case it is evident that determination of the content of a given compound at any moment tells us nothing about the activity of its metabolism.

In the present paper we describe experiments involving the use of radioactive phosphorus as an indicator of the rate of phosphorus metabolism in the heart muscle. Labelled phosphate was introduced into the blood stream, and the rate of uptake into the heart muscle was determined.

The rate of uptake can be deduced either from the radioactivity of tissue phosphorus at different times after its introduction, or from the difference between P^{32} content of coronary arterial and venous blood. The published data on this subject have been obtained by the former method.

Hevesy [2], who studied the distribution of radioactive phosphorus in various organs of rats 4 hours after its subcutaneous injection, found 6.3% of the amount injected in the heart and lungs, and 22.6% in the bones.

Jones et al. [3], found that accumulation of P^{32} in the organs of mice was at maximum 5-10 hours after introduction, and that it amounted to 4.7% of the initial dose per gram of fresh heart tissue. Freerksen and Meissner [1] determined the P^{32} content of the heart after intravenous administration of $Na_2HP^{32}O_4$ and found that its activity amounted to 0.34% of the dose given after 1 hour, falling to 0.08% after 18.2 days.

Findings of this sort have only a relative value, however, since they are obtained from different animals. Apart from this, an analysis of the results shows that excretion of active phosphate during the hour after its introduction exceeds its uptake (total activity of the heart falls, instead of rising). Hence the figures obtained do not relate to the rate of uptake of phosphate by the heart; they express the difference between the rates of the opposed processes of uptake and elimination of phosphate.

It appeared to us that the most trustworthy prodecure for determining the rate of uptake of P^{32} by heart muscle would be that based on determining the differences in P^{32} content of venous and arterial coronary blood. It was accordingly applied in the present research, for determining the rate of uptake of P^{32} in a single animal. For this purpose we determined the activity of the blood entering the heart muscle through the coronary arteries, and leaving it by the coronary veins.

Dogs weighing about 10 kg were taken for the experiments. Food was withdrawn on the day of the experiment, the thorax was opened, under morphine-hexonal anesthesia and artificial respiration was started. Blood entered the coronary arteries through a cannula from the left subclavian artery, inserted at its point of origin from the aorta. Blood leaving the heart was taken from the coronary sinus, into which a long cannula, with an expanded tip, was inserted via the right auricle. The blood flowing through this cannula was returned to the right jugular vein, into which a L-shaped cannula had been inserted for this purpose.

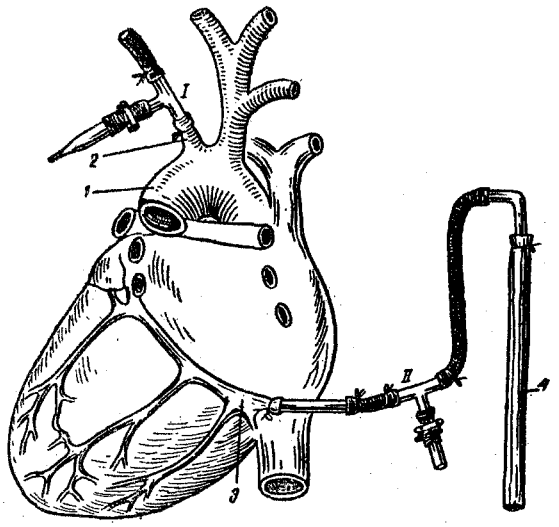

Fig. 1. Schema of attachment of cannulae for sampling of arterial and venous coronary blood. 1) aorta, 2) left subclavian artery, 3) coronary sinus, 4) right jugular vein, I) T-piece for sampling arterial coronary blood, II) T-piece for sampling venous coronary blood.

Fig. 1 illustrates how the cannulae are placed. Blood entered the coronary arteries through cannula I, and left the heart through cannula II.

15 minutes after insertion of the cannulae an intravenous injection of $Na_2HP^{32}O_4$ was given, at a dosage level of 3000 impulses per gram body weight. Blood samples were taken at set intervals, from 15 seconds to 30 minutes after injection, simultaneously from T-piceces I and II, which were opened for the same length of time (20-30 sec.). In order that the size of the sample should be approximately the same from both cannulae, the opening of the T-piece was broad for cannula II, and capillary for cannula I.

Arterial pressure was noted at the times of sampling, in order to check the functional state of the heart.

Two 0.1 ml portions of blood from each sample were placed in glass dishes and dried at room temperature, and the activity was determined and calculated per ml of blood.

EXPERIMENTAL RESULTS

Six experiments were done, and the results of two representative ones are shown in Fig. 2. The slope of the curves is due to gradual fall in the activity of the blood, as a result of uptake of the phosphorus by the body. The difference between the activities of arterial and venous blood at any given moment is determined by the relation between the rates of uptake of P^{32} from the blood by the heart muscle and of release of P^{32} from the heart muscle to the blood.

Our first experiments gave an unexpected result; the activity of venous blood was at first greater, instead of smaller, than that of arterial blood, as was expected, and the difference between the two gradually disappeared (Fig. 2, A).

Since this result pointed to the possibility that when we took the first samples, 3 minutes after injection of P^{32}, maximum uptake had already been achieved by the heart muscle, and liberation to the blood stream was already in progress, we took our samples earlier in subsequent experiments. We found, in Exp. 50, that the P^{32} content of arterial exceeded that of venous coronary blood up to the third minute, when it became equal to, and finally less than, in venous blood. In Exp. 49 (Fig. 2, B) equilibrium was only achieved at the 8th minute, i. e., up till then uptake of P^{32} by the heart muscle exceeded its release to the blood, and for this reason the P^{32} content of blood from the coronary sinus was less than that of arterial blood. The two processes were in equilibrium at the 8th minute, after which release of P^{32} predominated, giving a higher venous than arterial P^{32} content.

It appears from our results that the rates of uptake of P^{32} by the heart muscle and of release from it vary in different experiments, evidently because of different levels of phosphorus metabolism in the heart of different animals.

The very high rate of uptake of phosphorus from the blood stream by the heart muscle is evidence of its very active phosphorus metabolism.

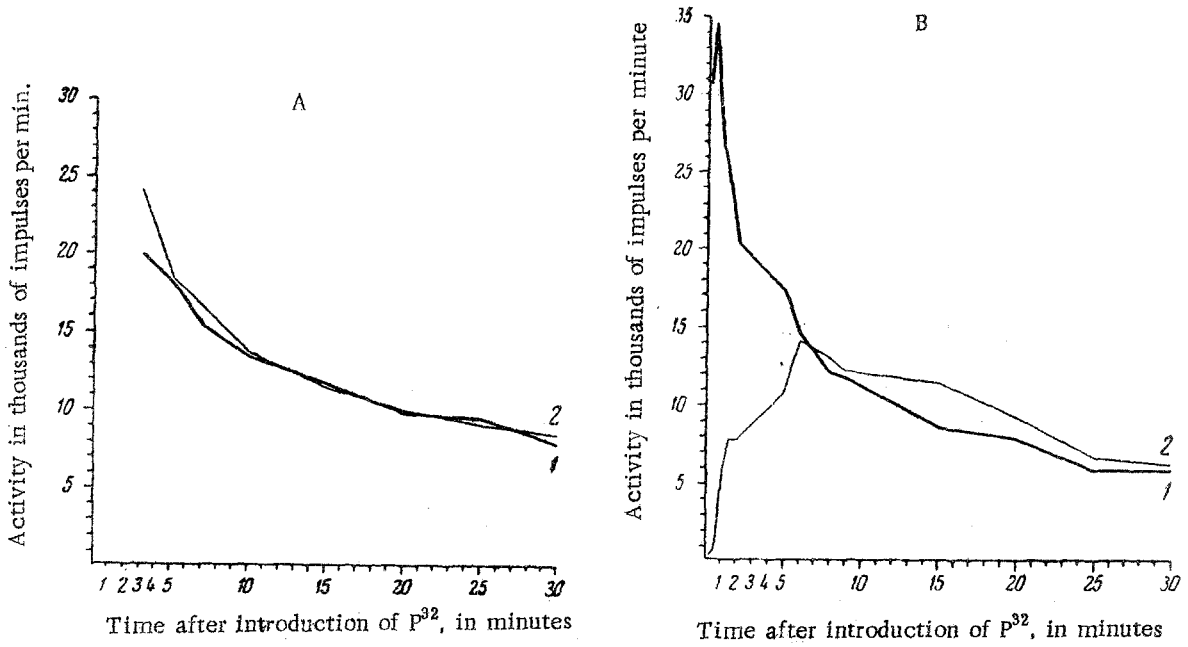

Fig. 2. Activity of 1 ml of arterial (1) and venous (2) coronary blood at various times after administration of P^{32} at a dosage of 3000 impulses per kg body weight. Exp. 46 (A). Exp. 49 (B).

LITERATURE CITED

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