AGE CHANGES IN RESPIRATION AND GLYCOLYSIS IN HEART MUSCLE

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The study of the age changes in cardiac metabolism is of essential importance to an understanding of the structural and functional changes in the myocardium in normal and pathological conditions. So far, however, little systematic investigation has been made of the changes in the metabolism of heart muscle at various age periods.

The functional activity of the heart is associated with the presence of high-energy phosphorus compounds (ATP, creatine phosphate). Their formation in the myocardium takes place in two ways: primarily as a result of respiration, and also by glycolysis. There are reports in the literature of a decrease with age of the oxygen consumption of various tissues and, in particular, of heart muscle [1, 2, 5, 6, 7, 8, 9].

No investigation of the changes in the course of glycolysis in the myocardium and its relationship with respiration at different age periods has yet been undertaken. The object of the present research was to study the age differences in the course of two processes: the intensity of oxygen utilization and of glycolysis in heart muscle.

EXPERIMENTAL METHOD

Experiments were conducted on animals of different age groups: rabbits aged from 1-2 days to 3-3½ years and rats aged from 3-4 weeks to 2-2½ years.

After decapitation of the animal the heart was extracted and washed free from blood, the fat and connective tissue were removed, and the organ was dried between sheets of filter paper and minced.

Because of the heart of an animal during the first days or weeks after birth is too small to allow the necessary material to be taken for all the investigations, the hearts of several animals (usually of the same litter) were used in these investigations and a homogeneous mince was prepared. This was used for studying the oxygen consumption of the myocardium, the intensity of glycolysis, and the lactic acid content. To determine the glycogen content pieces of heart muscle weighing 250-300 mg were excised immediately after death of the animal.

The oxygen absorption of the heart muscle was determined in a Warburg's apparatus over a period of 45 min at 37° in a phosphate-saline buffer mixture (pH 7.4) and expressed in the form of Q_{O_2}. The intensity of anaerobic glycolysis was judged by the increase in lactic acid and by the decrease in inorganic phosphorus during incubation of minced tissue in a phosphate-saline buffer mixture (pH 7.4) containing glycogen, in Thunberg's tubes. The lactic acid content was determined colorimetrically using p-hydroxydiphenyl [3] and the phosphorus content by the ordinary method of Fiske and Subbarow. The glycogen content in the heart tissue was determined by a slightly modified Pflüger's method [7]. All the quantities were calculated in terms of fresh tissue and dry weight of tissue, for according to reports in the literature [2] and personal observations the water content (and, hence, the quantity of dry residue) in the heart muscle of animals changes significantly during growth.

The experimental results were analyzed by the method of variance analysis, with determination of the standard error of the mean ($\pm$ m) and the degree of significance of the series ($t \geq 3$).

TABLE 1. Age Changes in Intensity of Oxygen Consumption (Q_{O_2}) of Heart Muscle

Q_{O_2}	Rabbits				Rats			
	Newborn	2 weeks	4-5 weeks	½-2 years	3-3½ years	3-4 weeks	9-12 months	2-2½ years
M ± m	4.18 ± 0	7.15 ± 0.31	6.95 ± 1.3	3.36 ± 0.36	2.61 ± 0.196	5.65 ± 0.13	4.76 ± 0.44	3.23 ± 0.33
t	∞	23.0	5.35	9.22	13.3	43.4	10.8	9.8

TABLE 2. Lactic Acid Formation in Heart Muscle During Glycolysis at Various Age Periods

Lactic acid content (in mg %)	Rabbits				Rats			
	Newborn	2 weeks	4-5 weeks	½-2 years	3-3½ years	3-4 weeks	9-12 months	2-2½ years
Weight of fresh tissue (M ± m)	72.0 ± 0	82.0 ± 9.7	80.0 ± 9.7	108.6 ± 2.6	126.0 ± 7.7	49.5 ± 10.4	55.6 ± 3.3	64.8 ± 5.3
Dry weight	379.0	430.0	388.0	476.0	553	235.6	278.0	324.0
t	∞	16.4	8.2	41.8	16.3	4.7	16.8	12.2

TABLE 3. Age Changes in Lactic Acid Content in Heart Muscle

Lactic acid content (in mg %)	Rabbits				Rats			
	Newborn	2 weeks	4-5 weeks	1½-2 years	3-3½ years	3-4 weeks	9-12 months	2-2½ years
Weight of fresh tissue (M ± m)	40.0 ± 0	111.0 ± 14.4	99.0 ± 32.0	123.6 ± 7.9	162.1 ± 13.2	64.0 ± 9.82	109.5 ± 12.0	152.5 ± 11.7
Dry weight	210.0	539.0	480.0	542.0	711.0	305.0	548.0	763.0
t	∞	7.9	3.1	15.6	12.3	6.5	9.1	13.0

TABLE 4. Age Changes in Glycogen Content in Heart Muscle of Rabbits

Glycogen content (in mg % glucose)	Age	
	1½-2 years	3-3½ years
Weight of fresh tissue (M ± m)	584.1 ± 36.5	378.5 ± 33.0
Dry weight	2607.6	1352.0
t	16.0	11.5

EXPERIMENTAL RESULTS

The results given in Table 1 show that in rabbits between birth and the age of 4-5 weeks a considerable increase in oxygen absorption by the heart muscle took place. Subsequently the intensity of the tissue respiration of the mycardium fell gradually, reaching its lowest values in the old animals ($Q_{O_2} = 2.61 \pm 0.19$). The same pattern of results, in principle, was observed in the rats.

Meanwhile in the rats and rabbits the intensity of glycolysis increased with age. This was shown by an increase in the accumulation of lactic acid during glycolysis as the animals grew older (Table 2). At the same time the loss of inorganic phosphorus also increased: from 96.8 ± 10.5 mg % in rabbits 2 weeks old to 136.6 ± 8.5 mg % at the age of 3-3½ years. When calculated in terms of dry weight the corresponding figures were 509 and 600 mg %. A similar pattern was observed in the rats.

Further evidence of the more intensive glycolysis during aging was also given by the lactic acid content of the myocardium of the rabbits and rats (Table 3). Our figures for the lactic acid content were slightly greater than those given in the literature. This was presumably attributable to the fact that our investigations were made without fixation of the heart in liquid air. However, since the results we obtained in all the series of experiments were needed for comparative evaluation of the processes under investigation, we consider that they may be used.

It will be clear from the results cited above that the lactic acid content in the heart muscle attained its highest values in the old animals.

Hence the relationship between the intensity of tissue respiration and the lactic acid content in heart muscle changes with age. During aging the intensity of the tissue respiration falls and the lactic acid content in the myocardial tissue rises. In other words, during aging the relative part played by oxidative processes in the metabolism of the myocardium falls and the relative intensity of anaerobic reactions increases.

This was also demonstrated by the fact that, along with the accumulation of lactic acid in the old animals, the glycogen content in their myocardium also fell (Table 4). These results were particularly demonstrative when expresed in terms of dry weight. They indicated a fall in the glycogen reserves of the myocardium in the old animals, and this also could be the result of intensified glycolysis.

Hence, during aging of animals the metabolism of their heart muscle undergoes changes in the form of a decrease in their oxygen consumption and an increase in the intensity of glycolysis. This trend in the metabolism of older animals may be regarded as a unique compensatory mechanism arising as the intensity of respiration of the heart muscle falls.

Heart muscle is characterized by a well marked oxidative metabolism. The decline in this energetically more efficient process in the myocardium of older animals leads to intensification of glycolysis, a decrease in the reserves of glycogen, and accumulation of the principal product of anaerobic breakdown of carbohydrates—lactic acid. The fall in the intensity of tissue respiration and the simultaneous increase in the intensity of glycolysis are evidence of a definite modification of myocardial metabolism in old age, and this may be of significance when explaining the differences observed in the onset and course of certain pathological conditions of the heart at this age period.

SUMMARY

A study of metabolis peculiarities in the cardiac muscle, characteristic of different ages, is of considerable importance for the understanding of structural and functional changes in the myocardium, both in normal and pathological conditions. However, current biochemistry possesses almost no systematic information on the metabolic peculiarities of cardiac muscle at different age periods.

As known, the functional activity of the heart was connected with the presence in it of phosphorus compounds, rich in energy. The formation of these compounds in the myocardium occurs in two ways: chiefly as a result of respiration and also during glycolysis.

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