PHYSIOLOGICAL NEONATAL HYPERTROPHY OF THE MYOCARDIUM

O. Ya. Kaufman

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In the fetuses of certain mammals (sheep, dogs, pigs, cows, man, etc.) the small branches of the pulmonary artery have a narrow lumen and create a high resistance to the blood flow [4]. After extrauterine respiration begins these vessels dilate, so that the resistance to the blood flow in the pulmonary circulation falls sharply [5]. In the intrauterine period the pressure within the pulmonary trunk is higher than in the aorta, i.e., the right ventricle performs relatively more work than in the definitive state; after the beginning of extrauterine respiration the situation is reversed: the load on the right ventricle diminishes while that on the left ventricle increases [9]. Structural changes in the pulmonary circulation, together with functional closure of the foramen ovale and the ductus arteriosus take place during the first 3-5 days of life. In this period changes in the weight and structure of the right and left ventricles may be expected. In fact, whereas in the intrauterine period the right ventricle is relatively heavier, after 11 days of life, conversely, the weight of the left ventricle exceeds that of the right [7].

The mechanism of such a rapid increase in weight of the left ventricle, which may conventionally be termed physiological hypertrophy, is not clear. It may possibly take place on account of proliferation of muscle fibers by amitosis [8]. Other investigators have described mitotic division of muscle cells in the myocardium of neonatal rats [2], and are dubious of the amitotic origin of contiguous nuclear pairs [3].

In the present investigation the morphology of the myocardium of animals and infants in the first days of life was studied.

EXPERIMENTAL METHOD

The myocardium of 68 newborn rats and 27 newborn puppies aged from a few hours to seven days was studied. The animals were sacrificed in the morning (about 11 a.m.). The free parts of the right and left ventricles and septum were weighed, the afferent and efferent tracts were measured, and the ratio between the weights of the right and left ventricles was calculated. The heart of 50 newborn infants was studied in the same way. The material was fixed in neutral formalin and in Shabadash's fixing fluid and embedded in paraffin wax. Sections were stained with fuchselin and counter-stained by van Gieson's method, with Heidenhain's iron hematoxylin, with cresyl violet, with toluidine blue at pH 4.5, and by the methods of Brachet and Feulgen, impregnated with silver by Gomori's method, and subjected to the PAS reaction. The succinate dehydrogenase activity was determined in frozen sections from the heart of the experimental animals. Micrometry of the thickness of the muscle fibers in the right and left ventricles and of the diameters of the nuclei was carried out, and from the results their volume was then calculated. The number of mitoses per field of vision was also counted (in each case 100 fields of vision were examined).

EXPERIMENTAL RESULTS

At birth the ventricular index (ratio between weight of the right ventricle and weight of the left) in newborn infants is 1.22-1.47, and in puppies 1.2-1.57, i.e., the right ventricle weighs more than the left. Only in young rats is this ratio equal to 1.

In the first 3-5 days of life the proportions are reversed. In infants after the 5th day of life the index becomes 0.9, in young rats 0.6-0.7, and in puppies 0.8-0.6, i.e., the left ventricle has begun to exceed the right in weight. Hence, in the first 5-7 days of life the left ventricle grows more intensively: in rats and puppies the left ventricle almost doubles in weight in this period, whereas the right ventricle increases in

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weight by only 50%. In infants the weight ratios are less clear because the larger infants died on the first day, whereas if the premature infants with a lower weight when the number of mitoses in the right and left ventricles was counted separately, then it was found that in rats and puppies during the first hours after birth the number of mitoses in the right ventricle was much higher than the number in the left [1]. By the 4th day of life the number of mitoses in the right ventricle had fallen while that in the left had risen and was now almost twice the corresponding level in the right ventricle. For instance, in newly born puppies on the first day the number of mitoses per 100 fields of vision in the myocardium of the right ventricle was 23 ± 2.2 compared with 13 ± 1.06 in the myocardium of the left ventricle; on the 4th day the number of mitoses in the right and left ventricles was 10 ± 1.13 and 22 ± 1.64 respectively, and on the 6th day 10 ± 1.4 and 17 ± 3.6 respectively. No mitoses could be found in the human myocardium; this may be due to morphological differences in the human myocardium and also to differences in the method of obtaining the myocardium. No mitoses likewise were found in the myocardium of human embryos in early stages (12-14 weeks). However, in the myocardium of infants, and also of rats and puppies, no increase was found in the thickness of the muscle fibers or the volume of their nuclei after birth. The increase of the muscle mass could have taken place therefore only by an increase in the number of muscle cells.

The author's observations show that the changing weight patterns of the myocardium were not accompanied by changes in the distribution and content of glycogen or of succinate dehydrogenase activity. Changes in the argyrophilic skeleton were dependent only on the age of the newly born animal, and no differences were found between the right and left ventricles. So far as RNA and DNA in the muscle cells of the myocardium are concerned, zonal differences could be seen in both the right and left myocardium (focal perinuclear accumulations of pyronine-positive substance, focal intensification of pyroninophilia of nucleoli); however, the mean content of RNA and DNA per unit muscle mass of the myocardium was not calculated. Nevertheless, it has been reported that on the first day of life the RNA and DNA concentrations in the myocardium of the left ventricle in rats increase relative to their concentrations in the right ventricle [6].

In connection with the increased flow of blood into the chambers of the ventricles, the ratio between the afferent and efferent tracts changed as the result of lengthening of the former. This was particularly noticeable in the right ventricle. For instance, in stillborn mature human fetuses the difference between them was 1 cm, decreasing by the 5th day to 0.7-0.6 cm. The ratio between the perimeters of the bicuspid and tricuspid valves also changed. In mature fetuses the perimeters were equal, and only after 5 days did the perimeter of the tricuspid valve begin to exceed that of the bicuspid.

Hence, in the first seven days after birth, the mass of the left ventricle in newborn infants, puppies, and rats increases rapidly and considerably. This increase is associated with processes of hyperplasia and is not accompanied by significant histochemical changes in mucopolysaccharides, succinate dehydrogenase activity, nuclear volume, thickness of muscle fibers, or in the state of the argyrophilic skeleton.

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