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Creatine Content of the Heart in Experimental Cardiac Hypertrophy.

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It was shown[1] that the concentration of creatine in the human myocardium parallels the heart's ability to maintain an adequate circulation. It follows that if, as is commonly supposed, hypertrophy increases the power of cardiac muscle to do work, the total amount of creatine in a hypertrophied heart should exceed the amount found in one of normal size.

Cardiac hypertrophy was produced in growing rats by the production of nutritional anemia as described by Forman and Daniels.[2] A litter mate of each diet rat was maintained on a standard ration of rat biscuits and water. Occasional bleeding of the diet rats (for hemoglobin estimation) doubtlessly hastened the production of anemia in these animals.

At the end of from 66 to 75 days the anemic rats, together with their litter mate controls, were killed by a blow on the head followed by section of the neck vessels. Hemoglobin estimations were done with a Sahli hemoglobinometer on samples of blood thus collected. Each rat was opened immediately after death, and the ventricles severed from the body by careful section through the atrioventricular ring. The ventricles were then opened, blotted between filters to remove all free blood, weighed, and analyzed for creatine by the method of Rose, Helmer, and Chanutin.[3] A second group of controls was picked from stock, each animal of this series weighing within 5 gm. of the anemic rat with which he was compared. This size control group was necessary since the anemic rats did not maintain normal growth curves. This group also allowed comparison of creatine concentration at different ages, since they were younger animals. There were 11 anemic rats, 10 litter mate controls, and 11 size controls. The results are shown in Table I.

The marked hypertrophy produced by the diet is shown by the fact that the actual ventricular weight averaged 36% higher in the anemic rats than in the litter mate controls, although the former

[1] Cowan, D. W., *Am. Heart J.*, in press.

[2] Forman, M. B., and Daniels, A. L., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 479.

[3] Rose, W. C., Helmer, O. M., and Chanutin, A., *J. Biol. Chem.*, 1927, **75**, 543.

TABLE I.
Data comparison of anemic rats with litter mate controls and with size controls. Each value is followed by its standard deviation.

	Litter mate controls	Anemic rats	Size controls
Hemoglobin, %	17.9 ± 1.	3.7 ± 1.7	
Ventricular wt., mg.	665.7 ± 87.2	904.8 ± 120.3	423.5 ± 95.
Body wt., gm.	228. ± 33.	120. ± 37.	122. ± 34.
Ventricular wt./body wt. ratio	2.93 ± 0.22	8.27 ± 2.60	3.51 ± 0.25
Creatine in ventricles, mg. %	192. ± 17.	141. ± 17.	206. ± 11.
Total creatine in ventricles, mg.	1.27 ± 0.15	1.27 ± 0.17	0.87 ± 0.19
Total creatine in ventricles, mg./100 gm. of body wt.	0.56 ± 0.04	1.13 ± 0.28	0.72 ± 0.05

had body weights which averaged 47% below normal. It will be noted that the ratio of ventricular weight (mg.) to body weight (gm.) is normally larger in smaller rats, so that when using this ratio as an index to the degree of hypertrophy, the size factor must be taken into consideration.

The average creatine concentration of the hypertrophied ventricles was 26.6% lower than that of the litter mate controls. However, the total amount of creatine in the ventricles was the same for these 2 series. The data show that normal growth hypertrophy is accompanied by a proportionate addition of creatine; the total amount of cardiac creatine increases with increased muscle mass, thus keeping the concentration approximately constant. On the other hand, in the anemic rats the creatine was added to the heart at the normal growth rate, while the muscle mass increased much more rapidly. Therefore, there seems to be a chemical difference between normal growth hypertrophy and hypertrophy caused by the anemia producing diet. It may be concluded that there is no more creatine in the hypertrophied ventricles of an anemic growing rat than there is in those of a normal rat of the same age.

It is to be admitted that dietary factors other than those concerned with the production of anemia may have had something to do with the lack of creatine in the excess tissue. It is also probable that this hypertrophy is not comparable in all respects to other types of so-called "compensatory" hypertrophy.