STUDIES IN CONGESTIVE HEART FAILURE

VI. The Effect of Overwork and Other Factors on the Potassium Content of the Cardiac Muscle[1]

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In one of the previous studies of this series it was shown that the cardiac and skeletal muscles of patients dying of congestive heart failure were abnormally poor in potassium, Harrison, Pilcher and Ewing (1930). The loss of potassium from skeletal muscle appeared to be related to edema, as muscles which were not edematous contained normal amounts of potassium. Pieces of skeletal muscles removed during life contained less potassium when the patients were edematous than when they were edema free. It appears therefore that the presence of edema is an important cause of the loss of potassium in skeletal muscle. The present study was undertaken in an attempt to determine the cause of the loss of potassium from the cardiac muscle.

METHOD

Tissues were obtained at the postmortem table. Pieces of ventricular muscle weighing 5 to 20 grams were freed of fat, weighed and dried to constant weight at 105 to 110°C. One to two decigrams of the dried muscle were digested with nitric acid as described by Van Slyke (1924) for chloride determinations. The nitric acid was then driven off by evaporation, and the residue was freed of ammonia by boiling with excess sodium hydroxide. The mixture was then neutralized with sulphuric acid. Potassium was precipitated as the cobalti-

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nitrate and determined in the Van Slyke-Neill apparatus as described by Kramer and Gittleman (1926). A detailed description of the technique was given by Harrison, Pilcher and Ewing.

Duplicate analyses were always made and in many instances quadruplicate determinations were done. The values in the tables are averages of these duplicate and quadruplicate determinations. The tissues were obtained from patients dying of cardiac failure and, to serve as controls, from patients dying of various other disorders. Tissues of normal individuals were of course not available as controls, and we have even been unable to obtain tissues from individuals dying accidentally who were in good health previously. Hence, subjects having no disease of the thoracic organs have been designated as controls. (One individual with severe anemia, and one patient with morphinism have been omitted from the "control" group for reasons which will be mentioned later.)

As the study progressed it was found that patients with acute pulmonary disorders showed similar changes and these were consequently grouped together.

The subjects with cardiac disease were classified according to the type of congestive failure which they presented. Most of them had both systemic and pulmonary congestion but one patient had congestion of the lungs only, two patients had systemic without pulmonary congestion and one subject had cardiac disease without congestive failure. All except one of the subjects with cardiac disease had cardiac hypertrophy and dilatation of varying degree. The chief etiological factors were (*a*) rheumatic endocarditis, one case; (*b*) syphilitic aortitis, one case; (*c*) syphilitic myocarditis, one case; (*d*) hypertension, four cases; (*e*) coronary arteriosclerosis and angina pectoris, two cases; (*f*) asthmatic bronchitis, one case; and (*g*) tuberculous pericarditis, one case.

RESULTS

The data for the "control" subjects are shown in table 1. These values are in fairly close agreement with those obtained for human subjects by Lematte, Boinot and Kahane (1928), and by Norn (1929). The three "control" subjects all died of chronic diseases and it is therefore possible that the normal values for man are slightly higher.

TABLE 1

The potassium content of cardiac muscle of subjects without cardiac or pulmonary disease

Initials	Autopsy number	Chief diagnosis	Right ventricle			Left ventricle			Congestion of lung	Congestion of liver	Edema	Chief pathological findings	Remarks
			Solids	Potassium in dry muscle	Potassium in wet muscle	Solids	Potassium in dry muscle	Potassium in wet muscle					
			per cent	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*					
E. A.	V-30-5	Lymphosarcoma	18.6	1.41	0.262	22.4	1.29	0.289	0	0	±	Enlarged glands	Edema of right leg from lymphatic obstruction. None elsewhere
R. O.	V-29-17	Brain tumor	20.5	1.30	0.267	23.0	1.19	0.274	0	0	0	Spongioblastoma	
J. S.	V-30-32	Carcinoma of esophagus	21.0	1.21	0.254	19.9	1.47	0.292	0	0	0	Perforation of esophagus	

Normal dogs usually have about 1.4 per cent potassium in the dried cardiac muscle and 0.3 per cent potassium in the wet cardiac muscle, (Calhoun, Cullen and Harrison (1930)). In any case it is safe to conclude that the normal potassium content of wet cardiac muscle is 0.3 per cent or slightly less and that the normal solids content is 19 to 23 per cent.

The term "normal potassium content" when employed in the remainder of this paper is used to designate the average (table 4) values in the "control" subjects. It is of some interest to note that in each instance the right ventricle contained a little less potassium in the wet muscle than did the left.

In table 2 are shown the values in four patients with acute and more or less extensive disease of the lungs. One of them had pneumonia; three had massive pulmonary collapse—one unilateral and two bilateral. Their left ventricles contained amounts of potassium comparable to those found in the "controls." Their right ventricles, however, were extremely low in potassium. As compared with the average (table 4) value for the "controls" the potassium content of the dry right ventricular muscle of the patient with unilateral pulmonary collapse was minus 18 per cent. A similar comparison reveals minus 39 per cent and minus 40 per cent for the two patients with bilateral collapse and minus 32 per cent for the patient with lobar pneumonia. It is interesting that the degree of diminution was least in the patient who had the least extensive pulmonary involvement. All of these subjects had normal hearts at autopsy except for slight dilatation of the right ventricle.

Values for subjects with cardiac disease are shown in table 3. In only one subject (S. C.) was there disease of the heart without any systemic or pulmonary congestion. This subject, who had hypertension and angina pectoris, died suddenly of coronary occlusion. A fresh infarct of the left ventricle and old infarcts of the interventricular septum were found. The left ventricle was somewhat hypertrophied, the right ventricle slightly dilated. The tissues taken for analysis were from the normal portions of the myocardium. Each ventricle contained a little less than the normal amount of potassium in the dry muscle.

TABLE 2

The potassium content of cardiac muscle of subjects with acute diseases of lungs (and with no cardiac disease)

Initials	Autopsy number	Chief diagnosis	Right ventricle			Left ventricle			Congestion of lung	Congestion of liver	Edema	Chief pathological findings	Remarks
			Solids	Potassium in dry muscle	Potassium in wet muscle	Solids	Potassium in dry muscle	Potassium in wet muscle					
			per cent	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*					
E. H.	V-29-111	Eclampsia	17.5	0.80	0.140	19.7	1.67	0.328	0	0	0	Massive collapse both lungs. Bronchopneumonia. Focal necrosis of liver	Hypertrophy of left ventricle. Right ventricle dilated
J. D.	V-30-24	Carcinoma of gallbladder	20.4	0.78	0.159	20.6	1.23	0.254	0	0	0	Massive collapse both lungs. Carcinoma of gall bladder and liver	Postoperative. Right ventricle dilated
W. S.	V-29-119	Ruptured appendix	18.6	1.07	0.198	19.6	1.52	0.298	0	0	0	Massive collapse left lung. Peritonitis	Postoperative. Questionable slight dilatation of left ventricle
R. J.	V-30-33	Lobar pneumonia	22.4	0.89	0.199	19.1	1.37	0.262	0	0	0	Lobar pneumonia bilateral. Acute pericarditis	Right ventricle dilated

TABLE 3

The potassium content of cardiac muscle of subjects with cardiac disease

Initials	Autopsy number	Chief diagnosis	Right ventricle			Left ventricle			Congestion of lung	Congestion of liver	Edema	Chief pathological findings	Remarks
			Solids	Potassium in dry muscle	Potassium in wet muscle	Solids	Potassium in dry muscle	Potassium in wet muscle					
			per cent	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*					
S. C.	V-29-115	Coronary occlusion	26.2	1.10	0.288	20.5	1.21	0.249	0	0	0	Hypertrophy left ventricle, dilatation right ventricle, occlusion left descending artery	Never had congestive failure. Sudden death
W. H.	V-29-112	Asthmatic bronchitis	21.4	1.09	0.233	19.4	1.60	0.310	0	++	++	Chronic bronchitis, tuberculosis, emphysema, hypertrophy and dilatation of right ventricle only	Right ventricular failure
J. M.	V-30-31	Pleurisy with effusion, hypertension	17.6	0.92	0.161	21.3	1.07	0.227	0	±	+	Pleural effusion, adhesive pericarditis, hypertrophy both ventricles, dilatation right ventricle, collapse of both lungs	Right ventricular failure (slight)
A. McC.	V-30-20	Angina pectoris. Hypertension	19.9	1.03	0.206	20.3	0.91	0.184	++	0	0	Coronary arteriosclerosis, myocardial fibrosis, hypertrophy and dilatation both ventricles	Left ventricular failure
J. B.	V-30-21	Chronic glomerulonephritis, hypertension	18.5	0.94	0.174	19.9	1.02	0.203	++	++	+++	Chronic glomerulonephritis, hypertrophy and dilatation both ventricles	Failure of both ventricles
J. F.	V-30-17	Syphilis	19.6	1.10	0.216	19.5	1.02	0.200	---	---	---	Hypertrophy and dilatation of both ventricles, syphilitic myocarditis and aortitis	Failure of both ventricles
J. J.	V-29-125	Syphilitic aortic insufficiency	18.7	0.95	0.177	20.4	0.98	0.199	---	--	--	Hypertrophy and dilatation of both ventricles, syphilitic aortitis	Failure of both ventricles
F. H.	V-29-10	Hypertension	18.6	0.95	0.177	19.4	0.83	0.162	--	--	--	Hypertrophy and dilatation of both ventricles	Failure of both ventricles
J. R.	V-29-7	Hypertension	19.9	0.85	0.148	19.9	1.10	0.221	--	--	-	Hypertrophy and dilatation of both ventricles, myocardial fibrosis	Failure of both ventricles
E. R.	V-30-35	Cardiac hypertrophy	17.5	0.97	0.170	18.6	1.07	0.199	--	-	---	Hypertrophy and dilatation both ventricles, thrombophlebitis, septicemia.	Failure of both ventricles
D. McK.	V-30-36	Rheumatic endocarditis	16.1	0.79	0.127	18.6	1.07	0.180	--	--	---	Aortic stenosis and insufficiency, hypertrophy, and dilatation both ventricles, pericardial effusion, ascites.	Failure of both ventricles
C. W.		*Concretio cordis*	22.2	1.17	0.260	22.1	1.64	0.361	0	--	-	Obliterative pericarditis without mediastinitis, pericardium ½ cm. thick	Atrophy of myocardium, massive collapse, bilateral-postoperative

Two subjects in this group were classified as having only right ventricular failure. (For the sake of clarity it should be stated here that the term "failure of a ventricle" as used in this paper, denotes a condition in which that ventricle is dilated and the tissues from which it receives blood are congested or edematous.) In neither of them were the lungs congested at autopsy. Both had some edema and some congestion of the liver. One of these subjects (W. H.) had hypertrophy and dilatation of the right ventricle only. His right ventricle was abnormally poor in potassium and his normal-sized left ventricle contained more than did those of the "control" subjects. J. M. (table 3) had hypertension, pleural effusion, partial collapse of both lungs and adhesive pericarditis. His left ventricle was hypertrophied but not dilated. It contained in the dry muscle 18 per cent less than the average amount of potassium. His right ventricle was hypertrophied and dilated at autopsy and it contained 30 per cent less than the average normal amount of potassium. As has been stated, he had right but not left ventricular failure, i.e., systemic without pulmonary congestion.

Seven individuals had failure of both sides of the heart. In all of them (table 3) the potassium content of both ventricles was much decreased in both the wet and dry tissues. The etiology of the cardiac disease seemed to be of no particular importance. The changes found in the patient with rheumatic endocarditis (D. McK.) and in the two subjects with syphilitic disease (J. F. and J. J.) were of the same order of magnitude as those observed in the two patients with "essential" hypertension (F. H. and J. R.), in the subject with hypertension secondary to chronic glomerulonephritis (J. B.), and in the individual who had hypertrophy and dilatation without obvious etiology (E. R.). The type of rhythm also made no difference, and no correlation with electrocardiographic changes was found. Consequently, data concerning the cardiac rhythm are omitted from the tables.

The findings in C. W. are of especial interest. This man had *concretio cordis* with a pericardium more than one half centimeter thick. The heart seemed only slightly enlarged by physical examination and x-ray. He had congestion of the liver and some edema.

The heart sounds were very faint, the pulse weak and the pulse pressure low. The cardiac pulsations as viewed by the fluoroscope were very small. Following an operation at which an unsuccessful attempt to resect the pericardium was made he developed pulmonary collapse and died. At autopsy the myocardium was thin and atrophic. This man suffered from pericardial insufficiency, not from myocardial failure. His difficulties were due to inability of the heart to dilate. His atrophic left ventricle was unusually rich in potassium, his right ventricle contained a little less than the normal amount in the dry muscle. It is possible that his right ventricle would also have contained increased amounts of potassium had he not developed pulmonary collapse, which, as has been shown above, is often followed by loss of potassium from the right ventricle. (Further clinical data and hemodynamic studies on this man are being reported elsewhere by Burwell and Strayhorn (1930).)

TABLE 4

Average values for potassium and solids content of cardiac muscle

Group number	Type of case	Number of cases	Right ventricle			Left ventricle		
			Solids	Potassium in dry muscle	Potassium in wet muscle	Solids	Potassium in dry muscle	Potassium in wet muscle
			per cent	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*
1	No cardiac or pulmonary disease	3	20.0	1.31	0.261	21.8	1.32	0.285
2	No cardiac disease. Acute pulmonary disease	4	19.7	0.89	0.174	19.8	1.45	0.286
3	Cardiac hypertrophy without congestive failure	1	26.2	1.10	0.288	20.5	1.21	0.249
4	Right ventricular failure only	2	19.5	1.00	0.197	20.3	1.34	0.269
5	Left ventricular failure only	1	19.9	1.03	0.206	20.3	0.91	0.184
6	Failure of both ventricles	7	18.4	0.94	0.171	19.5	0.99	0.195
7	Myocardial atrophy	1	22.2	1.17	0.260	22.1	1.64	0.361

For convenience in comparison the average values in the various groups are presented in table 4. Despite the relatively small number of cases, it is believed that these values are significant because of the uniformity of the changes observed.

DISCUSSION

The average values for the content of solids of the heart muscle of the subjects with cardiac failure were slightly lower than those of the control individuals but the difference was small and the two groups overlap in this respect. It, of course, follows that the water content of the heart muscle in the two groups is not dissimilar, and therefore, that the variation in potassium content cannot be explained on the basis of edema. It is clear that cardiac muscle, unlike skeletal muscle, does not become markedly edematous.

From the data in tables 3 and 4 it appears that when myocardial insufficiency results in pulmonary congestion the potassium content of the left ventricle is diminished and that when myocardial insufficiency results in hepatic congestion and systemic edema the potassium content of the right ventricle is decreased. The question immediately arises as to which is cause and which is effect. Does the loss of potassium precede or follow failure of the corresponding ventricle?

An answer to this question is probably to be found in Table 2. There is reason to believe that the flow of blood through atelectatic lung tissue is diminished whether the atelectasis be due to collapse or consolidation. Consequently, in such conditions the vascular channel through which the right ventricle pumps blood is narrowed with a corresponding rise in the pressure against which this chamber must work. Accentuation of the pulmonic second sound and slight dilatation of the right ventricle in such cases are well recognized phenomena. There can be little doubt that in such extensive and sudden disease of the lungs the right ventricle is overworked.

The fact that our patients with acute pulmonary disorders showed such a marked diminution in the potassium of their right ventricles seems to indicate that overwork or "strain" can cause loss of potassium from the cardiac muscle. The patients did not have any of the peripheral signs of right ventricular failure and hence loss of potassium is not due to congestive failure. Therefore, since diminished potassium content was invariably present in failing ventricles it is likely that this chemical change may have been a contributing cause of such failure. A ventricle which has failed is always low in potassium but a ventricle which is low in potassium need not necessarily have failed.

Dilatation of a ventricle was associated in every instance with a diminution in the potassium content and every ventricle which had a decreased potassium content was more or less dilated. The studies of Starling and his co-workers have shown that the normal immediate response to increase in work is dilatation. It seems probable, therefore, that loss of potassium and dilatation occur coincidentally and that both are due to overwork.

Most of the hypertrophied ventricles were also dilated and all ventricles showing both phenomena had diminished potassium content. In three subjects, however, hypertrophy of the left ventricle was present without dilatation or failure. In two of these (S. C. and J. M. (table 3)) there was a slight diminution in the potassium content of the dry muscle. The third subject, E. H., (table 2) had eclampsia and increased blood pressure. The left ventricle was unusually rich in potassium, containing about fifteen per cent more than those of the "normal" controls. Hypertrophy of a ventricle, therefore, may be associated with decreased potassium content, but not necessarily so.

Atrophy of the myocardium was associated with a tendency toward a high potassium content in one case, (C. W., table 3). Although this man had systemic congestion he did not have myocardial failure. His heart muscle was atrophic and the cavities were abnormally small. He suffered from pericardial failure, his heart was unable to dilate because of its dense fibrous coating.

In a previous study (Harrison, Pilcher and Ewing (1930)) it has been pointed out that diminished potassium content may be related in some way to "cardiac fatigue." From the results of the present study it appears that overwork is the cause of loss of potassium, and that this loss may be one of the causes of cardiac fatigue and eventual congestive failure. We do not believe that potassium is the so element concerned. It is likely that the composition of the heart in patients with cardiac failure is altered in other respects. Investigations are in progress along these lines.

SUMMARY OF RESULTS

1. The water content of the ventricular muscles of subjects dying of congestive heart failure was not significantly increased.

2. Patients dying with acute and extensive disease of the lungs

(i.e., pneumonia and massive collapse) had diminished potassium content of the right ventricle, but not of the left ventricle.

3. When myocardial insufficiency results in pulmonary congestion the potassium content of the left ventricle is diminished.

4. When myocardial insufficiency results in hepatic and systemic edema the potassium content of the right ventricle is decreased.

5. If both systemic and pulmonary congestion were present both ventricles were poor in potassium.

6. The cardiac potassium was not diminished in a subject with *concretio cordis* and myocardial atrophy.

7. The dilated ventricles were poor in potassium; the ventricles which were hypertrophied but not dilated showed variable results.

CONCLUSIONS

1. Edema is not the cause of the loss of cardiac potassium.

2. It is believed that overwork causes loss of potassium from heart muscle and that this loss is one of the predisposing factors to cardiac fatigue and failure.

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