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Determinations of intracellular potassium concentrations in normal patients and acute congestive heart failure patients

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DETERMINATIONS OF INTRACELLULAR POTASSIUM CONCENTRATIONS IN NORMAL PATIENTS AND ACUTE CONGESTIVE HEART FAILURE PATIENTS

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I. Introduction:

The purpose of this paper is to determine the potassium concentration in red blood cells both in normal persons and in patients with acute congestive heart failure in an effort to understand more fully what changes take place, if any, to the electrolyte concentrations in the various body compartments in the syndrome of congestive heart failure. The study of potassium concentrations in the red blood cells in congestive heart failure has been made only recently but no information was presented stating what treatment was given or whether the heart failure was acute or chronic (1). These factors are of importance since present theories of electrolyte distribution would make the findings of questionable value if diuretics or quinidine had been given or if the patient was in chronic congestive heart failure. Present theories postulate an increase of intracellular osmolarity during the acute stages of heart failure. A cellular uptake of water and concomitant transfer of base into the interstitial space then according to theory accounts for the development of an elevated plasma potassium level as well as the marked increase of interstitial water. The findings of elevated plasma potassium levels as well as data derived from balance experiments during recovery

from congestive failure have suggested that intracellular electrolyte content is decreased during the development of heart failure (2) (3). Since the theories presented are unsubstantiated and the direct analysis of intracellular potassium content has not been determined during acute congestive failure, the method and results are hereby presented.

First the determinations of normal potassium concentrations both in the plasma and intracellularly was required. These results were then checked with the findings of other workers. The accuracy of the method was not only checked by the comparison with other reports but also by repeat examinations on the same specimen of blood. Then patients in acute congestive heart failure were sought so that their blood could be studied and compared with the normal plasma and intracellular potassium concentrations. A few patients in chronic congestive failure were studied but the continued use of diuretics and chronicity of their conditions made them unsuitable for this study. Only patients who were in acute failure would show the shift that was theorized in other reports.

This subject was chosen not only because of an interest in congestive heart failure, but also because of an interest in electrolytes and body water. Congestive heart failure

was selected because it offers a good study of body water and electrolytes and presents an age old clinical picture that is still not solved to the satisfaction of all.

II. History:

The history of congestive heart failure is as old as medicine itself so a brief but pertinent review is presented in this paper. The fact that some knowledge of the clinical entity was known even in biblical times is illustrated in the book of Luke wherein a cure was effected with a dropsy patient. Inevitably the name of the Roman anatomist Galen (131-201 A.D.) comes into the story to show the extent of the knowledge of the circulatory system. It was Galen who showed that blood flowed to the liver via the portal veins and to the lungs via the right heart. So it can be seen that at this stage of history little was known about the circulatory system anatomy however; the clinical symptoms were at least recognizable under the name of "dropsy" (4). For the next thousand years or more the history of medicine lay dormant under the shadow of the Dark Ages and little or no advances were made until Vesalius and Servetus made more accurate observations of all anatomy and especially the circulatory system. In 1628 William Harvey concluded

from his experiments that the heart expelled its blood during systole. Also he showed that the blood flowed in a cycle from the right heart to the left and subsequently to the body (5). In the early 18th century Jean Baptiste Senac wrote about the heart's actions and diseases and he recognized that the symptoms of orthopnea and dropsy were related to a decrease in cardiac function.

The first recorded evidence of an understanding of left sided heart failure has to be credited to Jean Nicholas Corvisart (1755-1821) who made this statement concerning heart diseases, "the difficulty of respiration appears to belong solely to the accumulation of the blood in the vascular system of the lungs---" (6). In addition, James Hope (1804-1841) furthered the concepts of Corvisart by elaborating more on cardiac decompensation and extending the theory to include right heart failure with symptoms of venous congestion. Sir James Mackenzie continued with the ideas of Corvisart and Hope and assumed that when the heart failed it was due to a failure of the pumping action and that the symptoms of heart failure were due to an inadequate blood supply to the tissues. According to this theory dyspnea was due to hypoxia to the respiratory center and edema was due to hypoxia of the blood vessels themselves (7).

If the history of congestive heart failure can be divided into three sections, then the work of Sir James Mackenzie culminated the thoughts for over 1,918 years and would conclude the first section. Next, the work of Starling makes up the second phase of the history of congestive heart failure. This work also became known in the year 1918. Starling suggested that congestive heart failure was due to back pressure behind a diseased chamber of the heart. Due to the failure of this chamber, blood would back up behind into the veins and result in a secondary increase in venous pressure. It was this increase in venous pressure which produced transudation of fluid into the interstitial space. Dyspnea was explained as being due to a congestion of the lung which resulted in a decreased vital capacity.

The third concept of congestive heart failure is known as the "forward failure" theory and was published in 1944 by Warren and Stead and Merrill (8) (9). They have shown that in certain cases there is a salt and water retention in the tissues before the development of an elevated venous pressure and also that with a reduced cardiac output there is a more marked reduction of renal blood flow than to other vital organs. So from 1944 the importance of electrolytes was given added significance.

Electrolytes have been studied in the serum, in muscle biopsies, by balance studies, by radioactive ions and now intracellularly.

The study of intracellular potassium has been delayed by lack of suitable methods and instruments. The first estimate of the average concentration of cellular potassium was made by Corsa in 1950 (10). He measured the total body potassium with radioactive K_{42} and the serum potassium concentration with a flame photometer. He assumed the volume of intra and extra cellular fluids and calculated the average intracellular potassium concentration to be 106 meq/L. Deane and Smith (11) used the same method as Corsa but they actually measured the extracellular (sucrose) and intracellular (antipyrine) fluid volumes. They estimated the intracellular potassium concentration to be 115 meq/L.

Hutt (1) used a method of subtracting the plasma potassium from the whole blood potassium to determine the red blood cell potassium. By the use of the flame photometer the determination of both plasma and whole blood potassium was comparatively easy. The principle as used by Hutt was used in this study with modifications.

III. Incidence:

The exact incidence of congestive heart failure is

unknown as it occurs with other types of heart diseases and is not recorded as congestive heart failure in each case. However, a few facts from the National Office of Vital Statistics are pertinent. Heart and circulatory diseases accounted for 51.6% of all deaths in the United States for 1952. Heart and circulatory diseases accounted for almost twice as many deaths as the total of the next five high causes of death which were; 2. Cancer, 3. Accidents, 4. Pneumonia, 5. Tuberculosis and 6. Diabetes. About 1 in 16 persons in the United States suffers from some form of heart or blood vessel disease.

The observation of a cross section of patients as seen in a general practitioner's office brings out the number of "heart cripples" and the high percentage of patients who keep returning because of heart disease. Congestive heart failure ranks high among these heart diseases.

IV. Body Water in Normal and Congestive Heart Failure Patients:

It is well known that body water diffuses freely through the various cellular and vascular membranes maintaining a dynamic equilibrium and providing a homeostasis for which the living cell is dependent. Also, it is known that the body water may be grouped into compartments and that the volume of each compartment is regulated by the

vascular and cellular membranes. The vascular membranes are relatively impermeable to serum proteins and the cell membranes are in a like manner impermeable to cellular protein and in addition selectively permeable to various electrolytes. Friedberg (12) shows the distribution of body water in normal persons and in congestive heart failure (See Table #1).

TABLE #1

Distribution of Body Water in Normal Persons and Congestive Heart Failure Patients

	Normal % of body wt.	Heart Failure % of body wt.
Plasma	5	5
Interstitial water	11	28
Extracellular water	16	33
Intracellular water	40	30
Total body water	56%	63%

These percentages as given for congestive heart failure patients are only approximations due to the large increase in extracellular fluid which impairs the uniformity of mixing of the testing material and the increased effusions into serous cavities as the mixing process occurs.

Thus the excess of retained water in congestive heart failure is seen to remain in the interstitial fluid. The plasma volume remains unchanged and the intracellular water diminishes.

V. Pathogenesis of Edema of Congestive Heart Failure:

The study of the development of edema formation has

received the attention of many workers and yet the etiology of this condition still leaves much to be learned. The words "forward-failure" and "backward-failure" are names given to hypotheses. Consideration will be given to these theories since the present concepts of congestive heart failure rests on them. That a reduction in cardiac output usually occurs in congestive failure is fairly well agreed upon. Following the decrease in cardiac output, the pressure in the failing chamber rises and with this a rise in the diastolic pressure of the veins and capillaries leading to this chamber. Thus, the elevated capillary pressure becomes eventually greater than the oncotic pressure of the plasma proteins and transudation of fluid into the interstitial space results. In addition, it is further postulated that with the decreased cardiac output, which is further diminished by the loss of plasma water to the interstitial space, vasoconstriction occurs and ischemia to the kidneys, adrenals, pituitary and liver is the result. A decrease of blood flow to the kidneys results in sodium and water retention. This results then in hypervolemia and the cycle of edema formation is complete. This then is the backward-failure theory.

The forward-failure theory postulates that the decreased cardiac output first affects the kidneys and other endocrine organs by ischemia which in the same way results in sodium and water retention and hypervolemia, but that it is this hypervolemia which results in elevated venous pressure which in turn raises the hydrostatic pressure on the capillaries above the oncotic pressure of the plasma proteins and thus edema.

There remains no general agreement as to which theory is correct although the present data is more consistent with the forward-failure hypothesis. Neither the "forward-failure" nor "backward-failure" theory accounts for the lack of correlation between cardiac output and congestive failure as decompensation and recompensation may occur in a patient with very little change in the level of cardiac output (13).

It is interesting that as early as February 1944, Warren and Stead had precipitated decompensation in several cardiac patients by the administration of large amounts of sodium chloride. The first patient remained well compensated on a limited salt intake and diuretics but when the use of the diuretics was stopped and salt was

given, the patient's weight increased and a concommitant increase in plasma volume was observed. The venous pressure, however, stayed within normal limits. There was water retention by the kidneys and hemodilution without elevated venous pressure. The retention of salt and water by the kidneys may be hormonal or renal in origin. The work of Vier and Oliver would lend emphasis to a volume receptor mechanism probably located in the hypothalamus as a possible explanation.

In 1928 it was suggested that an increased permeability of the capillaries to protein due to anoxemia might be the causative factor for edema formation in congestive failure (14). But rather than an elevated protein content in the edema fluid as would be expected the protein content of the edema fluid is low (8) (15). Also a faulty lymphatic flow has been suggested as the cause for the development of the edema. However, here again a high protein content of the edema fluid would be necessary to be consistent with the theory and as stated above this is not true. The fact that the sodium ion itself is the significant offender in congestive failure was shown (16) (17) when a patient in congestive failure was given a very low intake of sodium chloride and water was not retained by the kidneys. But salts as potassium chloride or ammonium chloride do not cause

retention but produce diureses. Sodium bicarbonate was found to act in almost the same manner as sodium chloride in producing water retention. So the sodium ion is now considered as a primary factor in the retention of salt and water.

Since sodium is being retained by the kidneys one wonders if the normal sodium concentration would not be exceeded. However, it has been shown that there is an absolute increase of extracellular sodium but that in view of the increase of extracellular fluid from 16% of body weight to 33% the sodium ion shows a relative decrease in concentration (18). The factor of dilution will account for some of the relative decrease in sodium ion concentration, however, the chloride ion is not necessarily reduced which fact indicates that besides dilution the kidneys are playing a part and in addition the large volume of intracellular water may be affecting the sodium ion as well.

VI. Method for Determination of Intracellular Potassium:

A study of normal intracellular potassium was necessary to determine a method and control series for any determinations on congestive heart failure patients. The following method was used for determinations on control subjects and heart failure patients.

Venous blood drawn from the median anticubital vein was used for all analyses. The alcohol used to wipe the arm was allowed to dry before venepuncture to prevent hemolysis. A #21 gauge needle was used in all cases and 10 cc of blood was withdrawn and mixed with 4 mgm of powdered heparin gently so as to avoid hemolysis.

Packed cell volumes were determined in duplicate by the Wintrobe tube method and agreement of .5% or less was obtained in all determinations. One cubic centimeter of whole blood was measured into a weighing bottle for determination of whole blood water. A second cubic centimeter of heparinized whole blood was placed in 50 cc of water to permit hemolysis of all cells. This sample was allowed to stand for 20 minutes, then 15 cc of 20% trichloracetic acid was added and the sample was then diluted to 100 cc. This was then centrifuged for 30 minutes at 3000 rpm. One cubic centimeter of the supernatant was then diluted to make a final dilution of 1:200 of the original blood sample and was then ready to be analyzed for intracellular potassium.

The remainder of the original sample of heparinized whole blood was then centrifuged for 30 minutes at 3000 rpm and 1 cc of plasma was removed and added to 6 cc of

water and 3 cc of 20% trichloracetic acid. This was then centrifuged for 30 minutes at 3000 rpm and 1 cc of the supernatant was diluted to make a final dilution of 1:20. This sample of plasma was then ready to be analyzed for potassium.

The separation of the serum for analysis of serum potassium was done within 15 minutes from the time of venepuncture in all instances to avoid hemolysis. Triple distilled water was used throughout the experiment.

The normal controls were patients taken at random from job applicants and dispensary patients. All patients were in good health and were suffering from no diseases with the exception of several diabetic patients.

Blood cell potassium was determined by the following equation:

$$K_{wb} - K_p (1-H) = K_c (H)$$

wb - whole blood
p - plasma
c - intracellular
H - Hematocrit

The amount of water in the whole blood and serum was determined by des iccation of a sample to constant weight in an oven at 100 C. Desiccation was continued for 3 days in all cases before the weighing bottles were cooled to room temperature in a desiccator to avoid condensation.

The determination of whole blood and plasma potassium was done by means of the Beckman DU Spectrophotometer

with flame attachment at a wave length of 768 mu.

The percentage of water in the blood and serum was determined by the fraction of the weight lost by desiccation of the sample to a constant weight, to the weight of the sample before being desiccated. In all cases a chainomatic balance was used and weights were carried out to four places. The determination of the percent of weight of water in the cells was done by the following equation:

$$\text{Gms of } H_2O \text{ in RBC/cc of Blood} = \text{wt/cc blood } (H_2O \text{ \% of wt})_b - \text{wt/cc }_p(1-H)\ (H_2O \text{ \% of wt})_p$$

The determination of the potassium per meq/L of cell water and potassium in meq/L of plasma water was done by the following equations:

$$\frac{\text{meq } K^+/L \text{ of cells}}{H_2O \text{ \% wt of cells}} = \text{meq } K^+/L \text{ of RBC } H_2O$$

$$\frac{\text{meq } K^+/L \text{ of plasma}}{H_2O \text{ \% wt of plasma}} = \text{meq } K^+/L \text{ of plasma water}$$

To check on the accuracy of the method a comparison was made of the results obtained by using this method with the findings of other workers using similar methods. This will be considered in Section X. Also the accuracy of the method was checked by ascertaining the reproducibility of the results from one sample of blood.

The blood was separated immediately after being drawn into three portions and each was treated as a separate specimen.

Thirty milliliters of blood were drawn and divided into three 10 milliliter portions. Four mgm of powdered heparin was added to each portion as the anticoagulant and the method was followed as outlined.

The results obtained are given in Table #2.

TABLE #2

Reprpducibility of Results

	PCV	K plasma	K whole blood
Control #1	40.5 mm	4.8125 meq	42.916 meq
Control #2	40.0	4.8062	42.916
Control #3	40.5	4.8125	42.583

VII. A Study of Normal Intracellular Potassium Concentration:

Using the method outlined, a series of 26 normal persons were used to check on the method as to accuracy and reliability. The results obtained are given in Table #3.

TABLE #3

Determination of Normal Intracellular Potassium

Pt.	PCV	K_{WB}	K_{Pl}	K_{cell}	Water % weight Serum	Water % weight Cell	K meq/L Plasma	K meq/L Cell
Mor.	42.0	44.0	5.00	97.85				
Woo.	41.0	41.0	4.50	93.52	.9088	.6463	4.951	144.701
McD.	35.0	37.0	4.20	97.91	.9024	.6940	4.654	141.081
Hus.	40.0	44.0	5.20	102.20	.9017	.6752	5.766	151.362
Kuh.	43.0	48.0	4.40	105.79	.9027	.6607	4.874	160.421
748	39.0	42.0	5.00	99.87	.9076	.6567	5.509	152.078
Mei.	45.0	44.0	4.40	91.05	.9128	.6558	4.820	138.838
She.	43.0	44.0	4.76	96.01	.8972	.6711	5.33	143.06
761	42.0	41.0	4.40	91.56	.9104	.6669	4.833	137.29
747	42.0	43.8	4.00	98.76	.9204	.6576	4.345	150.18
1588	50.0	50.0	3.90	96.10	.9060	.6569	4.304	146.29
1604	49.0	50.0	4.88	96.96	.9041	.6544	5.397	148.17
758	42.0	42.0	4.24	94.14	.9095	.6581	4.661	143.05
1600	45.0	42.4	4.64	88.55				
Rad.	45.0	43.6	4.20	91.75	.9082	.6433	4.625	142.62
3053	38.0	41.2	4.76	100.65	.9125	.6302	5.216	159.711
Eng.	42.5	46.4	4.36	103.27	.9125	.6258	4.778	165.021
Fau.	39.5	41.8	4.36	99.14	.9082	.6678	4.801	148.457
Cas.	47.0	49.0	4.76	98.88	.9190	.6685	5.179	147.913
Fau.	47.0	49.0	4.76	98.88	.9047	.6747	5.261	146.554
Flo.	45.0	42.2	4.76	87.96	.9045	.6467	5.262	136.014
Mat.	42.0	41.2	3.88	92.64	.9075	.6700	4.275	138.269
Mor.	43.0	43.8	4.76	95.55	.9081	.6686	5.241	142.910
Will.	39.5	40.0	4.30	94.67	.9061	.6600	4.745	143.439
Gei.	42.0	49.1	5.19	109.68	.9026	.6897	5.750	159.028
Jen.	43.0	43.6	5.19	94.61	.9000	.6621	5.766	142.898
Mean	43.15	43.97	4.569	96.84	.9101	.6557	5.014	148.529
Sigma			.3866	5.066	.07166	.01529	.43977	7.849

VIII. A Study of Intracellular Potassium Concentration in Chronic Congestive Heart Failure:

Three selected patients in chronic congestive heart failure were studied. This was done in an effort to determine if their intracellular potassium concentration was normal after having had heart failure and years of diuretic therapy. A short clinical course of these three patients is given below. The results are given in Table #4.

L.R. is a 53 year old white male with a two year history of cardiac failure, which was preceeded by a known 10 year history of high blood pressure. In 1951 the patient became short of breath, edematous and showed marked fatigue with a weight gain of 20 pounds. He was admitted to UNH where he was treated with mercuhydrin, ammonium chloride, digitalis, low salt diet and rest. Within a two year period the patient has been hospitalized four times in failure. At the time the blood sample was drawn for this study the patient had a 2 plus ankle edema, blood pressure of 210/140 R&L, liver down 4 fingers and was slightly icteric.

W.M. is a 67 year old white male with a two year history of cardiac failure also. This patient was treated at another hospital for a decompensated heart in 1951 at which time he lost 74 pounds. Subsequently the patient came to UN Clinics with dyspnea, orthopnea, ankle edema, and a 19 pound weight gain. He stated at that time that he slept in a chair. Since 1951 the patient has had a consistently high blood pressure and has had edema varying from 2 to 4 plus. Venous pulsations in the neck have also been prominent. PE--Fibrillating with a pulse of 128 and HR of 152. PMI 2 cm to left of MCL. Liver down 4 to 5 fingers. Rx--Digitoxin and NH_4Cl as well as a salt free diet.

A.McG. is a 70 year old white female who has had a diagnosis of arteriosclerosis with coronary artery disease and cardiac failure with auricular fibrillation since 1941. Dyspnea and ankle edema have varied during this period from moderate to severe. In 1940 the patient while on a weight reduction diet gained 30 pounds. During this 12 year period the patient has been treated with digitalis, ammonium chloride, aminophyllin, salt poor diet, diamax and rice and skim milk diet, as well as sodium removing resins.

TABLE #4

Determination of Intracellular Potassium in Chronic Congestive Heart Failure Patients

Pt.	PCV	K_{WB}	K_{pl}	K_{cell}	Water % wt. Serum	Water % wt. Cell	K meq/L Plasma	K meq/L Cell
L.R.	42.0	47.08	4.73	105.57	.9074	.6597	5.213	160.028
McG.	42.0	44.79	5.33	99.28	.9016	.6538	5.911	151.851
W.M.	54.5	57.71	4.62	100.99	.8991	.6629	5.138	152.338
Mean			3.89	101.95	.9027	.6591	5.421	154.739

IX. A Study of Intracellular Potassium Concentration in Acute Congestive Heart Failure:

Table #5 gives the findings on a patient in acute congestive heart failure subsequent to a coronary occlusion. No diuretics had been given this patient which rules out any change in electrolytes by this method.

E. B. is a 53 year old white male with a history of two previous myocardial infarctions as well as hypertension for 30 years. Four days prior to admission for the present illness the patient had had ankle edema and dyspnea. The patient entered the University of

Nebraska Hospital with symptoms of a coronary occlusion which was later verified. The patient had a subsequent myocardial infarction while in the hospital and 33 days after admission the patient expired. Electrolyte studies were done in conjunction with intracellular potassium studies and are reported in Table #5.

On physical examination the patient showed grade II arteriosclerotic retinopathy, coarse rales over both bases, HR 132 and a tender pulsating liver palpable 12 to 14 cm beneath the right costal margin in the mid-clavicular line. A grade II pitting edema of the extremities was present.

TABLE #5

Determinations of a Patient in Acute Congestive Heart Failure

	11/30	12/3	12/5	12/7	12/8	12/11	12/27
TSP	6.35					6.7	Expired
Alb	3.15					3.02	
Glob	3.20					3.68	
CF24	2+						
48	3+						
TT	3.2						
CO_2	23.3	24.6		25.9	25.9	26.3	
Cl	103	98		100		104	
Na	135	140		140		140	
K	4.9	6.0		5.5		5.6	
PO_4				3.8		2.64	
NPN	58	64		38.4			
PCV			53.5	57.5	55.0		
K_{WB}			60.625	57.51	58.75		
K_{pl}			4.875	4.479	4.333		
K_{cell}			109.080	96.706	103.272		
H_2O Serum % wt.			.7519		.9191		
H_2O Cell % wt.			.6037		.6816		
K Plasma meq/L			5.290		4.714		
K Cell meq/L			180.670		151.509		

X. Discussion:

Table #3 gives the laboratory results of the potassium determinations of 26 normal persons. The mean of the results is given in Table #6.

TABLE #6

	K meq/L		Water % wt		K meq/L of water	
	Plasma	Cell	Serum	Cell	Plasma	Cell
Mean of Normal Patients (26)	4.569	96.84	.9101	65.57	5.014	148.529
Sigma (S.D.)	.3866	5.066	.07166	.01529	.4398	7.849
Mean of Chronic Cong. Ht. Failure Pts. (3)	3.89	101.95	.9027	65.91	5.421	154.739
Determinations of acute cong. ht. failure pt.	4.875	109.080	.7519	60.37	5.290	180.670
	4.479	96.706				
	4.333	103.272	.9191	68.16	4.714	151.509

Table #7 gives the results of Hutt (1) who studied various clinical conditions by means of the flame photometer.

TABLE #7

The Potassium Content of Cells and Plasma of 14 Fasting Normal Subjects and 1 Heart Failure Patient

Patient	K meq/L		Water % wt.		K meq/L of water	
	Plasma	Cell	Serum	Cell	Plasma	Cell
Mean of 14	4.4	94.5	91.6	65.2	4.8	145
Sigma (S.D.)	0.4	3.6	0.6	1.2	0.4	3.5
Heart Failure (1)	4.1	90.2	90.9	64.9	4.5	139

It is seen that the results of the normal determinations as done by the author (Table #6) compare favorably

with those of Hutt (Table #7). However, the results of the patient in acute congestive heart failure do not compare with the single determination of a heart failure patient as reported by Hutt. Since Hutt did not present information concerning his patient as to the clinical condition, one is not able to interpret his determination.

In Table #8 the results of Hold (19) are given for the concentrations of Potassium in Blood, Serum and Cells as determined on eight patients.

TABLE #8

Concentration of Potassium in Blood, Serum and Cells

	Potassium Blood meq/L	Potassium Serum meq/L	Potassium Cells meq/L
Average of 8 Patients	44.8	4.4	95.1
Maximum	48.8	5.3	100.0
Minimum	40.3	3.1	91.8

The determination of Serum Potassium levels has a much longer history than the intracellular determinations just given. In Table #9 the results of various workers is gathered along with the method of determination.

TABLE #9

Normal Ranges of Potassium in Serum

No. of Determinations	Potassium meq/L	Method	Author
10	4.8 - 5.1	Unashed Serum	Kramer 1921 (20
37	3.9 - 5.6	Electrodialysis	Talbott1940(21)
6	3.7 - 5.6	Colorimetric	Albanese1945(22)
107	3.6 - 6.2	Flame Photometer	Marinis1947(23)

This study indicates that in some cases of congestive heart failure there is no significant shift of potassium out of the cells. Also that the potassium level in the red blood cells remains within the limits of normal in acute or chronic congestive heart failure in some cases. The finding of an elevated potassium concentration in the erythrocytes in congestive failure is contrary to the assumptions of Iseri (24). Iseri showed that in a significant number of patients (59%) the plasma potassium concentration was greater than the mean plus twice the standard deviation. The mean plasma potassium concentration fell slightly in the cases he studied after compensation. Therefore the following hypothesis was made by Iseri.

"The magnitude of the elevation of plasma sodium concentration in many of our cases indicates a significant rise in the osmolarity of the extracellular fluid. This, in turn, probably reflects a rise of osmolarity

within the cells, since adjustments in extracellular fluid must take place in order to maintain osmotic equilibrium across the cell membrane. This is in accord with the hypothesis set forth in a previous communication from this laboratory (25) and recently advanced independently by Squires, Crosley and Elkinton (26) (27) that circulatory insufficiency causes an alteration in cellular metabolism manifested by liberation of base from osmotically inactive constituents of the protoplasm. A rise in cellular osmolarity would lead to the transfer of sodium and potassium into the extracellular compartment and cellular uptake of water, which apparently accompany the development of congestive heart failure."

This is a present concept of the electrolyte changes intracellularly as congestive heart failure develops. Iseri's studies have been on plasma sodium and potassium determinations and he states that it is presumed that there is intracellular storage of potassium as compensation occurs.

Elkinton has shown a loss of intracellular water during diuresis of edema fluid. This is in agreement with Squires who reports that from 15 to 62% of the total water (27) lost in diuresis comes from the intracellular phase. Both of these findings would lend support to the theory

of Iseri. In addition Miller (28) reports that both sodium and potassium enter cells during diuresis and also interprets this to mean that these ions leave this phase during the development of edema.

However, when a direct measurement of intracellular potassium was made on a patient in acute congestive failure the unexpected result of an increased intracellular potassium level was found. The work of Talso (29) on skeletal muscle biopsies may clarify this finding. Talso reported on 8 patients in congestive failure and of these three did not demonstrate a deficiency in intracellular cation concentration. He states that an intracellular hypotonicity is not a universal feature of congestive heart failure and that other features, such as alteration in acid-base balance and prior therapy, influence the intracellular cation concentration. So the possibility exists that the patient studied in acute heart failure in this paper may be one of the group of heart failure patients who do not show an intracellular hypotonicity as reported by Talso in 3 of his 8 patients.

Because of this unexpected finding which may be one of the many idiosyncrasies of the syndrome of congestive heart failure or may be a significant finding in intracellular electrolytes, further study of intracellular

potassium is indicated in patients in acute congestive heart failure who have had no diuretic therapy.

XI. Summary:

This is a study of potassium both intra and extra-cellularly in acute congestive heart failure. In previous reports it has been theorized that in the development of congestive heart failure there is an increased osmolarity of the extra-cellular fluid due to hypernatremia of the plasma. This increase of osmolarity reflects a concomitant rise of osmolarity within the cells in order to maintain osmotic equilibrium across the cell membrane. Then according to the theory altered cellular metabolism results in transfer of potassium from the cells and at the same time cellular uptake of water. Since the theory of Iseri was unsubstantiated by determinations on patients in acute congestive failure, the determinations as reported were done to test the theory. The intracellular and plasma potassium levels of a patient in acute congestive heart failure were determined and compared with the same determinations on normal persons.

Blood and plasma were analyzed for water content and potassium in twenty-six normal persons to determine an accurate mean. The accuracy of the method was checked

by determining the reproducibility of results and also by a cross check with other reports for similar determinations on normal persons.

The mean of the intracellular potassium of the normal controls was found to be 148.5 meq of K/L of cell water and 4.4 meq of K/L of plasma water. The mean of the water in percentage of weight was for the cells 65.57 and for the serum 91.01.

Three patients in chronic congestive heart failure were studied for comparison with the determinations of the normal contrbls and the acute congestive heart failure patient. The mean of the intracellular potassium of the chronic congestive heart failure patients was 154 meq of K/L of cell water and 5.4 meq of K/L of plasma water. The mean of the water in percentage of weight was for the cells 65.91 and for the serum 90.27.

One patient in acute congestive heart failure was studied. The intracellular potassium determinations were 180.7 meq of K/L of cell water and 151.5 meq of K/L of cell water. The first determination was more than twice the standard deviation and the second was within normal limits. The plasma potassium was 5.3 and 4.7 meq of K/L of plasma water. The determinations of the water in percentage of weight was for the cells 60.37 and 68.16

and for the serum 75.2 and 91.9.

XII. Conclusions:

1. It was found that the intracellular potassium concentration is not lowered in all cases of acute congestive heart failure as theorized.

2. In these determinations a normal to elevated intracellular potassium level was found with a normal plasma potassium concentration. Two possibilities exist for the finding of an elevated intracellular potassium concentration. First, the presence of protein bound potassium intracellularly must be considered. If this is true then the previous theories are untenable. Secondly, the syndrome of congestive heart failure has certain idiosyncrasies for which no answers can be given. It is possible that the determination of an elevated intracellular potassium concentration as reported may be one of these idiosyncrasies for which as yet no answer is available.

3. Since this is the first intracellular potassium determination on a patient in acute congestive heart failure and it does not support the theories of Iseri, Miller, Danowski and others, it is concluded that further studies of intracellular potassium in acute congestive failure are indicated.

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