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A LOW SODIUM, HIGH WATER, HIGH POTASSIUM REGIMEN IN THE SUCCESSFUL MANAGEMENT OF SOME CARDIOVASCULAR DISEASES

PRELIMINARY CLINICAL REPORT

DEMETRIO SODI-PALLARES, M.D.,*
BERNARDO L. FISHLEDER, M.D.,*
FERNANDO CISNEROS, M.D.,*
MARIO VIZCAINO, M.D.,*
ABDO BISTENI, M.D.,*
GUSTAVO A. MEDRANO, M.D.,*
BURTON J. POLANSKY, M.D.,† and
ALFREDO DE MICHELI, M.D.,*
Mexico City, Mexico

THE IMPORTANCE of restriction of sodium in the treatment of œdematous patients, particularly those with cardiac insufficiency, is almost universally accepted. There is no unanimity in respect to the degree of this restriction, but the general tendency is to reduce the ingestion of sodium significantly in order to achieve worth-while therapeutic results. Another illness in which the restriction of sodium has many adherents is arterial hypertension. It is also of interest to note the work of Raab,[72] who studied the role of catecholamines in angina pectoris and found that sodium had a potentiating effect. Finally, of great significance are the recent investigations of Selye[79] in the experimental production of myocardial necrosis by the combined effect of the adrenal hormones and sodium. All of these factors suggest that it is possible to influence the various manifestations of cardiac disease by means of restriction and/or increased elimination of the sodium ion.

A very different picture is seen in relation to the amount of liquid that must be ingested by a patient on a low-sodium program. A large number of cardiologists still follow the recommendation of Hippocrates, that the œdematous patient should eat "only things dry and bitter" and "drink very little". The majority probably let their patients take water *ad lib*, which means that ingestion of water depends mainly on the individual habits and customs of the patient. The early experiences of Schemm,[75] and also the investigations of Wolf[93] and Gorham and co-workers,[34] demonstrated that the volume of liquid ingested during a low sodium regimen is a most important factor.

The recent introduction of drugs with a marked saluretic effect, such as chlorothiazide and derivatives, has been of great value in the treatment of patients with fluid retention, as well as of those with arterial hypertension. However, such drugs also have the inconvenience of producing an excessive loss of potassium, an ion which plays an important role as a protector of the myocardium when one considers again the experiments of Selye.[79]

The original method of treatment that will be outlined in this presentation has been evolved over the past five years for the routine management of various cardiovascular ailments.

We believe that our regimen may be a contribution to the therapeutic armamentarium of every physician, inasmuch as it has proved to be very useful in our hands after repeated application. Moreover, in many cases we have practically been able to abandon other adjunctive agents, such as mercurial diuretics, xanthine derivatives, and ganglionic blockers, and even further to restrict the use of digitalis.

The types of cases in which we successfully use the regimen has grown to be very extensive: all forms of cardiac failure, particularly refractory cardiac failure, angina pectoris, essential hypertension and some of the secondary varieties, acute myocardial infarction, chronic cor pulmonale and pulmonary congestion of mechanical origin such as that of mitral stenosis.

The response to the regimen is usually prompt even in refractory cardiac failure. In hypertension the blood pressure falls to normal or near normal levels; pulmonary congestion as in mitral stenosis is significantly decreased, and in many instances the patients are then considered better candidates for commissurotomy. In acute myocardial infarction the course with our program is usually uneventful, thus reducing the period of absolute bed rest and the hazards of return to active life.

In regard to the reference to restriction of digitalis, we should point out that we use digitalis only in cases of tachyarrhythmia, i.e. rapid auricular fibrillation, or in paroxysmal dyspnœa which

*From the Instituto Nacional de Cardiologia, Mexico City.
†Postdoctoral Research Fellow, National Heart Institute, Public Health Service, U.S.A.

presages acute pulmonary œdema. With pulse rates below 90 per minute we have not observed consistently good results with digitalis, and on the contrary we have been impressed by the results of our program in such cases.

METHOD

The eight fundamental points of the regimen are:

1. *High water intake,* consisting of two to three litres of "natural" water per day. The use of a high water intake was originally proposed by Schemm.[75-77] This method was not generally accepted and was soon abandoned, very probably because of failure to use or observe the other principles set forth in this paper. The water should be "natural" or flavoured by very small amounts of fruit juices. The physician must always keep in mind that there are localities in which the tap water contains large amounts of minerals, mainly sodium salts. Carbonated beverages are particularly notorious in this respect.

The ideal amount of water necessary for a favourable result will vary from patient to patient, but we consider, along with Wolf,[93, 94] that two and a half litres per day is the amount which usually achieves the greatest diuresis.

2. *Salt restriction.*—Restriction of salt is variable according to the status of the patient. In general terms, in severe cases the allowance does not exceed 300 mg. sodium ion per day. In cases under good control we sometimes permit up to 1.5 g. per day in association with saluretic drugs (hydrochlorothiazide, etc.) in order not to attain a positive sodium balance. On the other hand we have found it necessary to avoid a fall in serum sodium below 130 mEq./l. In such cases we permit small increments of salt but adhere rigorously to the other aspects of the regimen.

3. *Foods prohibited because of naturally high sodium content.*—Those foods which contain more than 100 mg. of sodium per 100 g. of food must be absolutely prohibited. We have found that it is necessary to educate the patient carefully in this respect since many misconceptions are encountered even among physicians and dietitians. Some examples of foods and types of foods rich in sodium and therefore to be avoided are: ham, bacon, salami, all types of sausages and most cheeses; and all types of sea foods—shrimp, lobster, lagostinas, clams, oysters, sardines, anchovies, snails, caviar, tunafish and salmon. Some white fresh-water fish may be permitted. Also prohibited are many types of canned foods: juices, marmalades, jellies, etc., because sodium benzoate is often used as a preservative; also foods that are bottled, such as olives and pickles. Many packaged dry cereal foods are not to be permitted (oatmeal may be taken, since it is prepared without salt). French bread, white bread, rye bread and other types are to be avoided (in Mexico, tortillas are used and these contain no appreciable sodium). Salt crackers are not permitted, but again in Mexico we have a very palatable cracker free of sodium. The whites of eggs must be prohibited, but the yolks are permitted. Three vegetables which are high in sodium content must be avoided—spinach, beets and celery. Finally, the amount of milk and milk products (ice cream) must be restricted.

The listing given above includes most but not all of the common offenders that negate any attempt at a truly low sodium diet.

In general terms we recommend the following foods for inclusion in the diet: sodium-free milk (Lonalac), rice, meat, beans, chicken, white fish (as mentioned previously); practically all vegetables with the exception of spinach, beets, and celery; and desserts prepared at home (gelatine desserts, sherbet, etc.). In Mexico we allow chile sauce for seasoning and salt substitutes such as Zalima or Co-Salt or even lemon juice.

4. *A well-balanced diet* must be calculated for each patient. In our experience improvement is usually obtained and maintained only if the patient eats well.

5. *Saluretic agents* (hydrochlorothiazide, acetazolamide, etc.).—The use of saluretic drugs is of great importance inasmuch as it helps to make the restriction of salt less mandatory. However, it is necessary to be alert for side effects from the use of these drugs, particularly potassium loss. This is one reason why we usually give potassium as outlined below.

6. *Potassium.*—As pointed out above, the loss of potassium from the action of the saluretic drugs, or from sodium diuresis, should be watched for by periodic plasma determinations and serial electrocardiograms. The anticipated excess elimination of potassium is counterbalanced by the use of complementary doses of potassium chloride (0.5 to 1.0 g., t.i.d.) in order to maintain the level of this electrolyte above 4.2 mEq./l. In our regimen we consider that hypokalæmia is present when levels are lower than this figure.

7. *Steroids.*—In some cases of refractory cardiac failure or in the presence of persistent hypotension due to recent myocardial infarction, we add corticosteroids (prednisolone, triamcinolone, etc.) to the regimen; these do not reduce but rather increase the diuresis and aid in restoring the blood pressure to normal levels.

8. *Hyponatræmia secondary to use of saluretics.*—In a small number of instances we have observed hyponatræmia with or without hypochloræmia as a complication of the use of saluretic agents such as hydrochlorothiazide. In this situation we substitute acetazolamide in combination with ammonium chloride.

Clinical Indications of Improvement

The ability to titrate each of these principles in order to obtain maximum improvement can be reached only with practice, and it must be re-

TABLE I.—RESULTS IN TREATMENT OF CONGESTIVE HEART FAILURE.

Case	Sex	Age	Œdema		Dyspnœa		Pulmonary congestion		Liver size		Loss of weight lb.	Time days	Diagnosis. Added treatment. Comments
			Before	After	Before	After	Before	After	Before	After			
1	F	76	+	0	++++	+	++++	0	+	0	7.5	16	ASHD. HHD. Previously on digitalis
2	M	73	++++	++	+++	++	++	+	+++	+++	10	14	ASHD. MI. Liver Ca. Previously on digitalis
3	F	32	+	0	+++	0	+++	0	++	0	7	7	Post M. Comm. #
4	F	48	0	0	+++	0	+++	0	0	0	7	5	Post M. Comm. #
5	F	85	+	0	+++	+	++	0	0	0	3	5–7	HHD. Recurrent failure on digitalis
6	M	73	0	0	+++	+	++++	0	0	0	1	15	ASHD. Old MI
7	M	67	+++	0	++	0	++	0	0	0	9.5	15	HHD. Pulm. embolism. Chlorothiazide
8	F	67	+	0	++	0	++++	+	0	0	4	8	ASHD. Previously on digitalis. KCl on admis.
9	M	67	++	0	+++	0	++	0	+	0	7	6	CAD. CCP
10	M	74	+	0	+++	0	+++	0	++	0	8	6	ASHD. HHD. #
11	M	65	++	0	+++	+	++	++	++	++	4	10	ASHD
12	M	58	+	+−	++	0	++	+	+−	0	3	30	CCP. Digitalis
13	M	44	++	0	+++	0	+++	0	++	0	?	5	Recent MI
14	F	28	+	0	++	0	++	+	+	+	4	12	RHD. MS
15	M	55	0	0	+++	0	++	0	0	0	3	4	CAD
16	M	62	++	+−	+++	+−	++	0	+	+	6	7	HHD. Digitalis
17	M	57	++	0	++	0	++	0	++	0	8	28	ASHD
18	M		0	0	++	0	++	0	0	0	4.5	56	ASHD
19	F		+	0	+++	0	+++	+	+	0	3.5	14	RHD. DML
20	F		++	0	++++	0	++++	0	++++	+	1	49	RHD. DML. DAL
21	F		++	+	+++	0	+++	0	++	0	14.5	21	ASHD
22	M		+	0	+++	0	+++	0	++	0	1	10	RHD. DML. TI
23	M		++	0	+++	0	+++	0	+++	+	5	21	RHD. DML. TI
24	M		++	0	+++	0	+++	0	+++	+	2	7	RHD. DML. DAL. TI
25	M		+	0	++	0	++	0	++	0	8.5	7	ASHD
26	M	58	+	0	++++	0	+++	0	++	0	11	7	ASHD. CAD. HHD. CCP. Aminophylline
27	M	63	+++	0	+++	0	++++	0	++	0	17	14	ASHD. A.F. A-V block. Digoxin
28	F	65	++	0	+++	+	+++	+	+	0	4.5	7	ASHD. HHD. Recurrent failure on digitalis
29	F	81	+++	+	+++	0	++	0	++	0	3	5	ASHD. Varicose veins
30	M	21	+	0	++	0	++	0	+++	++	4	10	RHD. DML. TI. Pulm. embolism. AF. Digitalis. Tromexan®
31	F	48	+	0	+++	0	+++	0	+++	++	6	14	RHD. DML. TI. AF. digitalis
32	F	34	++	0	++	0	++	0	+++	++	5	18	RHD. DML. TI. AF. Digitali
33	F	60	+++	0	+++	0	+++	0	++	0	10	21	ASHD. HHD. Digitalis
34	M	57	0	0	+++	+	+++	+	+	0	3	10	ASHD. CAD
35	M	78	+	0	+++	++	+++	+	+	0	2	15	ASHD. CCP. #. Kyphoscoliosis
36	F	58	0	0	++	0	+	0	0	0	2.5	7	CAD. Old MI
37	M	64	+	0	++	+	++	0	+	0	3	7	CAD. Old MI
38	M	71	++	0	+++	0	+++	+	++	+	12.5	21	ASHD. CAD. Obesity
39	F	19	++	0	++	0	++	0	+	0	4	14	RHD. DML. AF. Digitalis
40	F	42	0	0	+++	+	+++	+	++	+	5	14	CCP. Chronic bronchitis. Aminophylline, antibiotics
41	M	65	++	0	++++	+	+++	+	+++	+	8	15	ASHD. CCP. Chronic bronchitis. Aminophylline, antibiotics

TABLE I.—(*Continued*)

Case	Sex	Age	Œdema		Dyspnœa		Pulmonary congestion		Liver size		Loss of weight lb.	Time days	Diagnosis. Added treatment. Comments
			Before	After	Before	After	Before	After	Before	After			
42	F	53	0	0	++	0	++	0	0	0	2.2	10	CAD. Old MI. Tromexan®
43	M	60	+	0	++	0	++	0	++	+	4.5	15	ASHD. HHD
44	F	65	+++	0	++++	+	++++	+	+++	+	10	21	Luetic aortitis. AI. ASHD. CAD. Angina pectoris. Digoxin. Iproniazid
45	M	28	+++	0	++++	+	++++	+	+++	++	11	19	RHD. DML. DAL. TI. AF. Digitalis
46	M	65	+	0	+++	0	+++	0	++	0	4.5	8	ASHD. Pulm. embolism (after prostatectomy) Tromexan®. Antibiotics
47	M	50	++	0	++++	0	++++	0	++	0	6.5	16	Recent MI. Pulm. embolism. Pleural effusion. Tromexan®.
48	F	80	++	0	+++	0	+++	+	++	+	6	15	ASHD. Acute hæmorrhagic anæmia. Transfusions
49	F	85	+++	0	++	0	++	0	++	0	7	14	ASHD. Prednisone treatment (discontinued)
50	M	67	++	+	++++	++	+++	++	++	++	3	21	CCP. ASHD. Aminophylline
51	F	57	0	0	+++	+	+	0	0	0	3.3	?	HHD. CAD
52	M	60	+	0	+++	0	+++	0	++	+	13	10	HHD. CCP
53	M	60	+++	0	++++	+	+++	0	++	0	6	15	CCP
54	M	68	++	0	+++	++	+++	0	+++	++	9	12	CCP. Pulmonary Ca. AF. Digitalized
55	M	67	++	0	+++	+	+++	0	++	+	9	9	CCP
56	F	55	0	0	++	0	+	0	0	0	2	14	MS. AI. AF. Digitalized
57	M	60	+	0	++	0	++	0	0	0	?	10	MI. Diabetes
58	F	58	+	0	++	0	++	0	0	0	6.5	10	HHD. CAD
59	F	51	0	0	++	0	++	0	0	0	6.5	?	HHD
60	M	64	0	0	+++	0	++	0	0	0	?	36	AI. Luetic coronary insufficiency
61	M	64	+	0	++	0	++	0	0	0	7	46	HHD. CCP. 1.5 g. NaCl permitted
62	M	44	+	0	++++	0	++++	0	+	0	?	7	Recent MI
63	M	65	0	0	++	0	+++	0	+	0	?	10	DAL. No chlorothiazide
64	M	60	+	0	++++	0	++++	0	++	0	9	10	CAD. Digitalized
65	M	55	++	0	++	0	+++	0	0	0	9	?	CCP. CAD
66	F	71	0	0	+++	+−	+++	0	++	+	?	14	CAD
67	M	58	0	0	++	0	++	0	++	0	6.5	7	MS. AF. Digitalized
68	F	66	+	0	+++	0	++	+−	0	0	6.5	60	HHD. CAD. Average diuresis 4 litres daily
69	F	63	+	0	+	0	++	0	0	0	6.5	60	CCP. CAD. Marked intolerance to digitalis
70	M	37	0	0	+++	0	+++	+	0	0	2	15	Coarctation of the aorta with AI. Data before Huffnagel valve. No treatment required postop.
71	F	60	++++	0	+++	0	+++	0	++	+	45	19	CCP. CAD. Acetazolamide and NH_4Cl instead of chlorothiazide
72	F	35	++++	0	++++	+	++++	0	++++	++	33	32	DML. TI. Digitalized; previous failure to all medical therapy
73	F	36	+++	0	++++	+	+++	0	+++	+	22	10	DML. DAL. TI. AF. Return of failure when pt. stopped therapy
74	M	49	+	0	+++	0	++	0	0	0	6.5	10	Chronic glomerulonephritis. Secondary hypertension. Return of failure when pt. stopped therapy

TABLE I.—(*Continued*)

Case	Sex	Age	Œdema		Dyspnœa		Pulmonary congestion		Liver size		Loss of weight lb.	Time days	Diagnosis. Added treatment. Comments
			Before	After	Before	After	Before	After	Before	After			
75	F	45	+++	0	+++	+	+++	0	+++	+	13	30	DML. TI. Rheumatic activity; on steroids, but diuresis was still obtained
76	F	52	0	0	+++	0	++	0	0	0	?	?	HHD. CAD
77	M	67	+	0	+++	0	+++	+	0	0	6	15	CCP
78	M	60	+++	0	+++	0	+++	0	+	0	11	18	MI. A-V block. Hemiplegia
79	M	60	0	0	++++	0	0	0	0	0	4.5	30	HHD. Blood pressure 170/100, 170/70
80	M	68	++	0	+++	0	++	0	0	0	4.5	17	CAD. Prostatic Ca.
81	F	50	+++	0	++	0	+	0	0	0	6.5	?	CAD. Hypothyroidism. On thyroid
82	M	60	++	0	+++	0	++	0	0	0	29	25	CAD. MI. Diabetes
83	M	73	+	0	+++	0	+++	0	+++	0	11	11	CAD. CCP. Digitalized. Acetazolamide instead of chlorothiazide

KEY TO ABBREVIATIONS

ASHD	=	arteriosclerotic heart disease	DAL	=	double aortic lesion
HHD	=	hypertensive heart disease	AI	=	aortic insufficiency
CAD	=	coronary artery disease	TI	=	tricuspid insufficiency
CCP	=	chronic cor pulmonale	MI	=	myocardial infarction
RHD	=	rheumatic heart disease	Post M. Comm.	=	post-mitral commissurotomy
DML	=	double mitral lesion	Liver Ca.	=	cancer of the liver
MS	=	mitral stenosis	AF	=	auricular fibrillation
#	=	NH_4Cl, acetazolamide and dexamethasone for initial three days of treatment			

membered that each patient is a different problem. Nevertheless, we have been able to make a sufficient number of clinical observations to set forth the following points:

Very often when a patient improves he spontaneously diminishes his intake of water, and we have become accustomed to checking on this point as the patient improves, for we believe that a high water intake is one of the cornerstones of the program.

Many patients forget to avoid one or two of the sodium-rich foods that are prohibited. Thus, we review the diet at each of the first few visits and if there is failure to improve we search even more carefully for the offending foods.

The action of the saluretic agents such as hydrochlorothiazide is less effective if there is not a high water intake.

We feel that it is a common observation that many patients have great difficulty in drinking 10 glasses of water a day. In such cases we reduce the intake to 1500 c.c. per day (6 glasses), but we emphasize very strongly the importance of achieving at least this level of intake of water in each 24 hours.

Some patients will complain of great weakness because of the reduction of sodium levels. In these cases we reduce the amount of hydrochlorothiazide and allow the salt intake to range between 0.5 and 1.0 g. per day.

Finally, one of the best indices of improvement is the patient's weight. We attempt to maintain weight at the level at which we observe the greatest amount of improvement. Further, we will permit a greater intake of salt slowly, as long as this optimum weight remains stable.

RESULTS

Results in Congestive Heart Failure

The results of treatment of 83 patients with cardiac insufficiency are given in Table I. The effects of therapy on the major signs and symptoms—œdema, dyspnœa, pulmonary congestion, hepatomegaly and loss of weight—are noted during the period of observation of each case, and the diagnoses are given. The majority were patients with arteriosclerotic heart disease, coronary heart disease or hypertensive heart disease, but we also followed up a fair number of cases of rheumatic heart disease and chronic cor pulmonale. Furthermore, most of the rheumatic patients had tricuspid insufficiency, probably on an organic basis; this is a relatively frequent lesion in Mexico.[7]

Of the 83 patients, digitalis was given to 18. In eight of these the basic reason for using the drug was auricular fibrillation with a rapid ventricular response. In many patients there had been no previous response to digitalis and conventional therapy, yet improvement was obtained with the use of our program.

The duration of the observation varied from four to 56 days, averaging 16.7 days. The weight loss varied from 1 to 45 lb., averaging 7.6 lb. in the 76 cases for which sufficient data exist on this point.

The results of treatment are summarized in Table I. In 43 cases (57.8%) the signs of insufficiency disappeared completely, in 32 cases (38.5%) they were reduced to a minimum, and in eight cases (9.6%) there was only slight or moderate reduction. Thus excellent to good results were obtained in 90.3% of the cases. Œdema, pulmonary congestion and dyspnœa were the parameters that

responded most rapidly, while hepatomegaly responded somewhat less favourably and rapidly. This was seen particularly in the rheumatic patients with tricuspid insufficiency who had long-standing histories of cardiac failure, suggesting that "cardiac cirrhosis" may have been a factor.

In summary, the clinical results in cardiac insufficiency have been extremely impressive with this program. The major points are that the regimen has been of great help even in the severe cases of refractory failure, and we have become accustomed to using it before the more conventional types of therapy. Finally, we have been able to discontinue use of digitalis in some of our patients, thus avoiding the real hazards of overdosage with this drug.

Results in Hypertension

Table II summarizes the effects of the use of this program in 100 patients with arterial hypertension. We have compared the mean systolic and diastolic blood pressure before and after therapy, and the difference is given. We have also entered the duration of observation in each case, and the amount of weight lost when this was recorded. Table III gives the statistical analysis of the results of therapy. These results are statistically significant, and the decrease in systolic and diastolic pressure is greater than that reported by other workers using chlorothiazide or its derivatives alone.[15, 30]

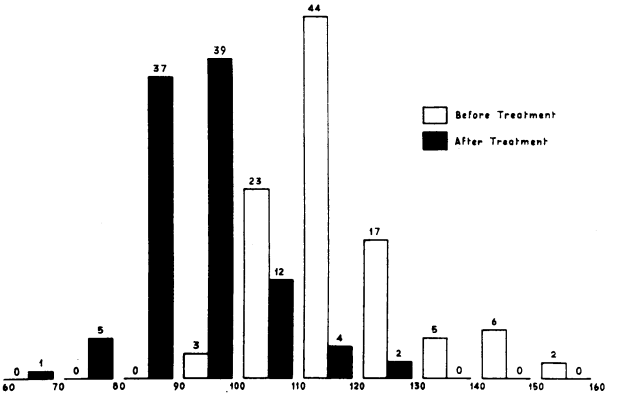

Fig. 1

Distribution of Cases According to Diastolic Pressure (mm. Hg) Before and After treatment

Fig. 1 shows the frequency of distribution of diastolic pressure levels before and after therapy. It may be seen that there is a shift of the distribution to lower levels after therapy.

In Figs. 2 and 3 we show the differences of systolic and diastolic pressures before and after therapy. Note that the diastolic differences are regular (Fig. 2) while the systolic curve (Fig. 3) has two peaks, one at a level of 31-40 mm. Hg and the other at a level of 51-60 mm. Hg. This irregular distribution cannot be explained from our data. It may possibly be due to factors which

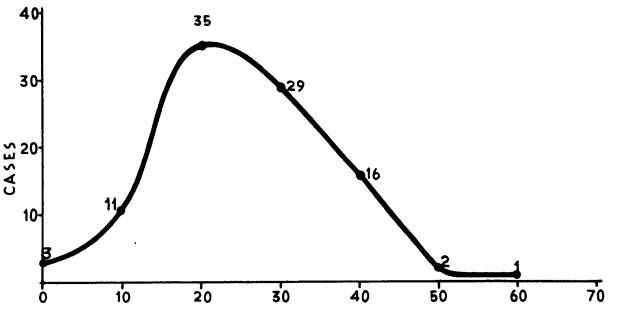

Fig. 2

Decrease in Diastolic Pressure (mm. Hg) After Treatment

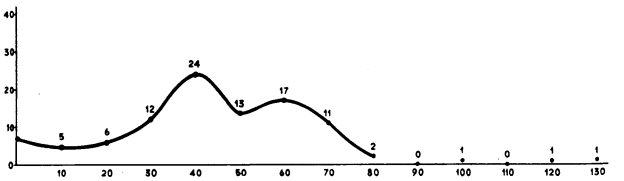

Fig. 3

Decrease in Systolic Pressure (mm. Hg) After Treatment

were not controlled or analyzed in our series, such as bed rest or the emotional status of the patient, which in general influence the systolic more than the diastolic pressure.

As may be seen from Table II, there are some cases in which no significant pressure changes were observed. It is possible that these patients did not follow the program carefully, for we have cases (Cases 27, 37 and 38) in which the pressure fell and rose again when the program was discontinued. In other cases, when the patients discontinued the KCl (Case 40), we noted a rise in the pressure.

In two cases (Cases 31 and 32) we obtained falls in blood pressure with the regimen but not using diuretics. In three cases previously refractory to drug therapy, including chlorothiazide, we obtained blood pressure decreases by only a low-salt, high-water and supplementary-potassium regimen.

In a large number of the cases, there was loss of weight even in the absence of œdema or insufficiency. However, we could not establish a relationship between the weight loss and its effect on the pressure. Patients with insufficiency or angina pectoris showed improvement of these conditions as the pressure decreased.

Of great interest are the two patients with toxæmia of pregnancy who had elevated diastolic pressures. In one patient with severe nausea we administered 5% glucose intravenously in order to obtain a high water intake. In both cases the response of the blood pressure and the diuresis was rapid and the further course was practically uneventful. In our one case of malignant hypertension with uræmia, the pressure fell considerably, but the patient died in uræmia. Perhaps some of the failures may have been due to advanced renal involvement, but we do not have sufficient data to allow this conclusion.

TABLE II.—EFFECT OF THE REGIMEN ON SYSTOLIC AND DIASTOLIC BLOOD PRESSURE IN AMBULATORY HYPERTENSIVE PATIENTS

			Systolic pressure			*Diastolic pressure*				
Case	*Sex*	*Age*	*B. T.*	*A. T.*	*Difference*	*B. T.*	*A. T.*	*Difference*	*Time (days)*	*Observations*
1	F	55	220	165	−55	120	95	−25	15	Weight loss 5 lb.
2	F	63	230	170	−60	120	90	−30	4	Weight loss 4 lb.
3	M	65	155	165	+10	105	105	0	30	No response
4	F	54	210	170	−40	110	100	−10	90	Weight loss 21 lb.
5	M	65	210	140	−70	110	84	−26	24	
6	M	36	165	170	+ 5	100	100	0	60	No response
7	F	66	200	160	−40	120	85	−35	12	Angina
8	F	47	235	170	−65	130	95	−35	21	
9	F	48	210	140	−70	125	90	−35	21	Loss 3 lb.; no response with other hypotensive drugs
10	F	61	240	180	−60	140	110	−30	28	Loss 2 lb. Previous drug failure
11	F	52	210	160	−50	110	95	−15	7	
12	M	65	240	200	−40	140	115	−25	21	Previous drug failure
13	F	58	190	135	−55	110	85	−25	7	
14	M	38	190	130	−60	110	85	−25	14	Loss 2 lb.
15	M	65	210	170	−40	100	90	−10	7	Loss 1 lb.
16	F	50	200	150	−50	115	100	−15	15	Loss 4 lb.
17	F	48	180	130	−50	100	85	−15	21	
18	M	63	250	240	−10	130	125	− 5	14	No response; previous drug failure
19	F	72	210	200	−10	115	100	−15	30	Loss 2 lb.
20	F	61	175	160	−15	105	90	−15	30	Loss 2 lb.
21	M	58	220	140	−80	115	80	−35	7	Loss 11 lb. Congestive heart failure
22	F	65	200	160	−40	110	90	−20	7	Loss 4.5 lb. Congestive heart failure
23	F	60	205	175	−30	120	100	−20	21	Loss 10 lb. Congestive heart failure
24	M	60	180	140	−40	100	90	−10	14	Heart failure which disappeared
25	F	57	160	160	0	110	98	−12	12	Angina, which disappeared
26	M	46	180	140	−40	115	80	−35	10	
27	M	40	160	120	−40	110	90	−20	63	Rise in pressure with each self-discontinuation of treatment
28	M	44	180	125	−35	115	90	−25	8	Heart failure which disappeared
29	F	58	250	210	−40	110	85	−25	10	
30	F	68	200	140	−60	90	60	−30	15	
31	F	47	180	130	−50	110	80	−30	27	Only low sodium, high water. No chlorothiazide
32	F	51	190	170	−20	115	100	−15	68	Only low sodium, high water. No chlorothiazide
33	F	69	200	160	−40	100	95	− 5	60	
34	M	41	170	150	−20	110	95	−15	11	
35	M	38	140	135	− 5	110	95	−15	57	
36	F	56	220	200	−20	140	125	−15	2	
37	M	46	190	145	−45	110	95	−15	20	Rise in pressure with each self-discontinuation of treatment
38	M	50	180	160	−20	110	90	−20	?	Rise in pressure with self-discontinuation of treatment
39	M	49	165	130	−35	110	85	−25	20	
40	M	57	155	140	−15	110	85	−25	19	Patient discontinued only KCl, and pressure rose 180/90
41	M	64	220	150	−70	110	85	−25	31	Heart failure disappeared
42	F	52	200	155	−45	100	85	−15	?	
43	M	44	200	140	−60	130	90	−40	20	With 1 g. dietary NaCl pressure rose to 160/100
44	M	91	200	170	−30	100	90	−10	15	
45	M	48	260	140	−120	150	80	−70	70	Failure of previous drug therapy
46	F	69	180	138	−42	110	95	−15	40	Patient decreased water intake, and pressure rose to 150/108
47	M	65	190	160	−30	110	95	−15	7	
48	F	55	180	140	−40	120	90	−30	14	Mild constipation forced reduction of chlorothiazide
49	M	47	200	130	−70	120	80	−40	14	
50	M	52	170	110	−60	110	80	−30	21	
51	F	52	170	170	0	110	90	−20	?	

TABLE II.—(*Continued*)

Case	Sex	Age	Systolic pressure			Diastolic pressure			Time (days)	Observations
			B. T.	A. T.	Difference	B. T.	A. T.	Difference		
52	M	56	185	150	−35	100	80	−20	13	
53	M	66	210	150	−60	110	90	−20	120	Failure of previous drug therapy
54	M	60	170	170	0	100	70	−30	30	
55	F	77	195	150	−45	100	80	−20	35	
56	M	42	180	125	−55	120	95	−25	210	Gradual but steady decrease of pressure in terms of months
57	F	50	210	140	−70	110	80	−30	12	
58	F	85	240	190	−50	100	80	−20	15	
59	F	64	190	140	−50	110	90	−20	15	
60	F	57	205	175	−30	110	100	−10	15	
61	M	26	170	130	−40	120	85	−35	8	
62	M	62	170	140	−30	105	90	−15	7	
63	M	58	190	180	−10	110	90	−20	7	
64	F	69	200	175	−25	105	90	−15	6	
65	M	65	185	130	−55	95	80	−15	10	
66	M	54	190	150	−40	110	80	−30	12	
67	F	65	220	190	−30	120	110	−10	12	
68	M	58	220	125	−95	140	80	−60	13	Disappearance of ECG signs of subendocardial injury. Moderate improvement of retinopathy
69	F	62	270	140	−130	140	80	−60	25	
70	F	58	200	170	−30	120	90	−30	15	
71	F	37	220	190	−30	120	100	−20	10	
72	M	39	125	120	− 5	100	70	−30	7	Hypothyroidism. Purpura probably due to chlorothiazide
73	F	55	195	145	−40	110	90	−20	8	
74	M	74	200	140	−60	105	80	−25	15	Heart failure disappeared. Diabetic
75	F	39	210	140	−70	130	95	−35	10	
76	F	39	185	130	−55	110	85	−25	13	
77	F	36	170	110	−60	95	70	−25	7	
78	M	31	150	155	+ 5	105	100	− 5	6	Purpura, probably due to chlorothiazide. Phæochromocytoma? under investigation
79	M	62	200	170	−30	120	100	−20	9	
80	M	53	200	140	−60	120	70	−50	15	
81	M	23	230	160	−70	150	100	−50	15	Malignant hypertension with drop in pressure under therapy, patient rapidly developed uræmia and expired
82	M	66	160	110	−50	110	80	−30	14	
83	F	53	220	180	−40	110	85	−25	14	
84	F	50	180	150	−30	110	90	−20	8	
85	F	40	200	165	−35	105	90	−15	8	Latent chronic glomerulonephritis
86	F	72	200	145	−55	110	70	−40	10	
87	F	25	170	135	−35	130	90	−40	10	Toxæmia of pregnancy. Uneventful delivery
88	M	49	185	125	−60	115	80	−35	12	
89	M	55	180	150	−30	100	90	−10	13	
90	F	74	185	150	−35	105	85	−20	5	
91	M	52	170	135	−35	110	90	−20	7	Disappearance of angina
92	M	59	210	145	−65	115	95	−20	6	
93	M	75	180	190	+10	100	110	+10	13	No response
94	F	57	210	140	−70	115	80	−35	10	
95	M	60	170	135	−35	100	90	−10	8	
96	F	51	205	130	−75	120	80	−40	8	
97	F	52	185	140	−45	110	85	−25	7	
98	F	23	200	130	−70	140	80	−60	15	Toxæmia of pregnancy 8th month. Initial water intake was intravenous
99	M	43	200	160	−40	120	80	−40	10	Serum Na fell to 112 mEq./l. Pt. extremely asthenic, but urinary output remained high
100	F	55	230	180	−50	120	80	−40	17	

KEY TO ABBREVIATIONS

B. T. = before therapy A. T. = after therapy

TABLE III.
EFFECT OF THE REGIMEN ON SYSTOLIC AND DIASTOLIC PRESSURES IN AMBULATORY HYPERTENSIVE PATIENTS.
(100 cases)

	MEAN Systolic pressure	*MEAN Diastolic pressure*
Before therapy	199.90	117.00
After therapy	155.90	92.10
Mean of difference	47.30	27.40
Standard error of the mean	2.26	1.31
t	18.41*	15.66*
p	< 0.01	< 0.01

* Statistically significant

The electrolyte status of the patients varied little. With the rigid sodium restriction, the levels of sodium rarely fell below 130 mEq./l. In one case (Case 90) it fell to 112 mEq./l., and the patient developed marked asthenia but maintained a diuresis of two litres of urine daily. His general status was improved by the administration of salt, which elevated his reduced pressure very little.

In the majority of the cases the decrease in the pressure began quickly in the first two or three days of therapy; occasionally this fall was marked. In the next few days the pressure gradually decreased until by day 4 to day 15 the low plateau was reached, with little fluctuation thereafter. In some cases the pressure showed a tendency to increase in spite of the rigid continuation of treatment (Case 56).

Similar results have been reported recently[2] with the use of a low-sodium, high-potassium diet, bed rest and chlorothiazide but no high intake of water. Our patients were for the most part ambulatory, and thus the factor of bed rest is much less important.

Results in Angina Pectoris

Using as our criterion the disappearance or diminution of cardiac pain, as has been proposed by Levine,[55] we may state that our program was of benefit to all of the 34 cases of our series.

Five patients and possibly six presented with cardiac insufficiency and four with hypertension. Of great interest was the patient (Case 25) who had global cardiac insufficiency and severe angina even while at rest, secondary to luetic aortic insufficiency. He was given 150 mg. of iproniazid daily for seven days, with no alleviation of the frequency or intensity of his pain. The subsequent use of our regimen resolved the signs of cardiac insufficiency and resulted in complete disappearance of his angina while at rest. The angina was, however, still present as he returned to physical activity but was then controlled with 100 mg. of iproniazid daily. It should be noted that relief of pain did not parallel improvement of the insufficiency or decrease in blood pressure in all cases. In Case 2, for example, the angina disappeared completely, while there was no change in the diastolic pressure.

The results were rather surprising in the 24 patients who did not have cardiac insufficiency or hypertension with the anginal syndrome. These included one case with a double aortic lesion and one with an aneurysm of the sinus of Valsalva. The benefit was frequently dramatic and occurred within a few days of the onset of therapy, and was maintained as the patient adhered to the therapy. In Cases 22 and 23 there was reappearance of slight pain as the patients increased their physical activity. Exercise tests were not done in a sufficient number of cases to enable us to draw any conclusions.

The large number of factors that may influence the frequency and intensity of anginal pain cause great difficulty in the evaluation of any type of therapy, be it surgical or medical. In our patients several were at absolute bed rest, while the remainder were ambulatory; thus with different degrees of activity it is not a homogeneous group. We may look on these results as only preliminary and tentative. They must be tested by a larger more carefully controlled series of cases. However, clinically the results are sufficiently impressive that we may suggest that the low-salt, high-water, high-potassium and chlorothiazide regimen may be of benefit in the management of the anginal syndrome.

GENERAL DISCUSSION

Possible Mechanism of Action in Cardiac Insufficiency

Many studies, such as those of Gamble[32] and of Stewart and Rourke,[83] have demonstrated that the administration of a large quantity of water to healthy subjects produces a diuresis which is larger in volume than the amount of liquid ingested. Wolf[93] gave healthy subjects water every half hour in amounts corresponding to an intake of 6.10 c.c. per minute and found that the volume of urine excreted was 8% more than the volume of ingested water. This worker concluded that the administration of water without electrolytes had a dehydrating effect, probably because of the excretion of salt with the diuresis. Schemm[75-77] has reported good results in the treatment of congestive cardiac insufficiency by the use of a moderate low-salt regimen combined with forcing the ingestion of 5 litres or more of water daily. Subsequent investigations of Wolf[94] and of Gorham *et al.*[34] showed that in order to obtain an optimum negative balance of sodium and water it was not necessary to use such large volumes of fluid. According to these authors, the loss of sodium and water from patients with congestive cardiac insufficiency, who are taking one gram of sodium per day, was maximum when the ingestion of water was 3000 c.c. daily; the ingestion of more water did not increase the loss of sodium and water, and the ingestion of less water decreased such losses. Moreover, these authors believed that the basic consideration was not only the volume of water ingested but the relation

TABLE IV.—RESULTS IN ANGINA PECTORIS.

Case	Sex	Age	Intensity and frequency of pain: Before	Intensity and frequency of pain: After	Loss of weight (lb.)	Time (follow-up) days	Observations
1	M	60	+++	+	10	1 year	ASHD
2	F	66	+++	0	—	180	HHD. B.P. 210/100; after, 180/100
3	F	60	+++	0	20	60	ASHD
4	M	62	++++	+	—	195	ASHD
5	M	66	+++	0	7	120	ASHD
6	M	60	++++	0	—	180	ASHD
7	F	49	+++	+	—	45	CAD
8	M	55	+++	0	2.5	90	CAD
9	M	43	+++	++	23	150	CAD. Chronic alcoholism
10	M	42	+++	+	5	225	CAD
11	F	66	++++	0	—	90	HHD. Old MI
12	M	50	++++	+	—	10	CAD
13	M	54	++	0	—	4	CAD
14	M	58	+++	0	—	18	CAD
15	F	61	++++	++	—	30	CAD
16	M	45	++++	+	—	7	CAD
17	F	64	+++	0	—	14	CAD
18	M	57	+++	+	—	45	CAD
19	M	54	+++	0	—	30	CAD
20	M	58	++	0	11	30	ASHD. HHD. CHF
21	F	58	+++	0	2.5	60	Old MI. CHF
23	M	71	+++	+	12.5	90	CHF. Obesity
24	F	53	++	0	2.2	30	Old MI. CHF
25	F	65	++++	+	12	120	Luetic aortitis. AI. CHF. The angina disappeared completely with iproniazid 100 mg. daily
26	M	57	+++	0	4	90	CAD. Heparin intramuscularly
27	M	35	++++	+	—	120	CAD. Persistent presystolic gallop rhythm
28	M	63	+++	+	—	12	HHD. 170/110, 150/90
29	M	66	+++	+	6	30	CAD. Diabetes
30	F	35	+++	+	8	20	DAL
31	M	56	++	0	—	20	CAD
32	M	40	++	0	3	10	CAD
33	M	63	+++	0	—	20	CAD
34	M	43	+++	+	2	120	Aneurysm of sinus of Valsalva

KEY TO ABBREVIATIONS

ASHD = arteriosclerotic heart disease
HHD = hypertensive heart disease
CHF = congenital heart failure
MI = myocardial infarctoin
AI = aortic insufficiency
CAD = coronary artery disease
DAL = double aortic lesion
BP = blood pressure
\+ = Mild pain on walking
++ = Moderate pain on exertion and walking
+++ = Pain after eating and marked pain on walking
++++ = Pain at rest (nocturnal) or episodes of severe recurrent angina
0 = No pain during the treatment in usual activities

between salt and water intake, in that the sodium ingested was reduced significantly while the above-mentioned level of water intake was maintained.

On the other hand, the marked restriction of the ingestion of water has been questioned by numerous authors.[17, 53, 78] Thus the majority of physicians and cardiologists permit patients with cardiac failure to take liquids *ad lib.* The intake is then dependent on the sensation of thirst which, varying from patient to patient, may be depressed owing to cardiac failure, and is influenced by habit, general physical condition, etc. This usually means, in our experience, that the ingestion of liquids is much less than the requirement for the optimum elimination of the retained sodium and water.

In regard to the use of potassium in our regimen, it should be noted that considerable evidence has been accumulated to indicate that in cardiac failure there is usually an intracellular deficit of potassium, even though the levels of serum potassium seem normal.[20, 51, 82, 84, 85] In our cases we frequently encountered electrocardiographic signs suggestive of hypopotassæmia with normal serum levels of this cation. Thus we have come to the viewpoint that the administration of potassium chloride in conjunction with the low-sodium, high-water regimen not only substitutes for the potassium loss due to the diuresis and that due to the use of chlorothiazide, but also protects against the potassium deficit which could be an important factor in congestive cardiac insufficiency.

Furthermore, we feel that the generally accepted low normal values of serum potassium between 3.5 and 4.2 mEq./l. should be considered as repre-

senting a relative hypopotassæmia for the conditions under discussion and calling for supplementary administration of potassium chloride. Thus with values as given above for serum potassium we have often seen the appearance of various arrhythmias (extrasystoles, paroxysmal tachycardias) which subsequently disappear when we increase the dosage of potassium chloride, and raise the level of serum potassium to higher than 4.2 mEq./l.

Selye[79] has experimentally demonstrated in animals that a high intake of sodium salts and of corticosteroids can provoke cardiac necrosis, which can be prevented by the administration of potassium or magnesium. Thus cardiac insufficiency, associated as it is with retention of sodium and decrease of potassium (intracellular), as well as being a "stress situation" which causes excess adrenal activity, is, at least theoretically, fertile ground for the production of the type of infarct and damage that Selye has experimentally observed.

The mechanism or mechanisms of action that allow for the successful use of the low-sodium, high-water intake regimen in cardiac insufficiency are not completely clear. Indeed the factors controlling the flux of water and electrolytes in this condition are very complicated and poorly understood. Any discussion concerning the mechanism of action can only be in terms of probabilities and speculations, and not in terms of certainties.

We know, however, that the kidney plays a fundamental role in the regulation of salt and water in the organism. The kidney in turn is influenced by various endocrine factors, particularly the antidiuretic hormone of the posterior pituitary gland (ADH) and the adrenal hormones, especially aldosterone.

ADH is one of the continuous regulators of water balance of the body[13] and probably acts chiefly on the distal tubules of the kidney, and as Smith[39] has shown, governs the "facultative reabsorption" of water. Its absence produces the clinical picture of diabetes insipidus. The primary stimulus for the production of ADH, as Verney[88] so brilliantly demonstrated, is the increase in osmotic pressure of the plasma, which specifically affects the osmo-receptors of the internal carotid. This is most concisely stated by Elkinton and Danowski:[26] "The absorption of several hundred cubic centimetres of ingested water at a time when body stores are intact will dilute body fluids. Such a decrease in osmotic pressure or tonicity of the body fluids will be registered in the osmo-receptors and less ADH is elaborated and the excess water as a consequence is eliminated via diuresis. A similar sequence of events will follow the administration of artificial extracellular fluid, suggesting that there are receptors which also detect changes in the volume of the body fluids. On the other hand, with water restriction the concentration of body solutes rises and the volume of body water diminishes as the consequence of continuous losses of water via the lungs, skin, bowel, and kidney. An increased supply of ADH then becomes available and marked reabsorption of glomerular filtrates ensues. The volume of urine decreases and its specific gravity becomes high."

This sequence of exquisite adjustments between response and stimulus that occurs in the normal subject is a good example of what is spoken of as a "negative feed-back system". Notwithstanding, there is no unanimity of opinion in respect of the role that ADH plays in cardiac insufficiency. Black[13] believes that ADH is probably elevated during the active phase of retention of water as œdema, but that it does not operate continuously during the stable phase of the œdematous condition.

The studies of Leaf and his colleagues,[52] as well as Weston and co-workers,[90] suggest that in cardiac insufficiency there exists a new equilibrium between the volume and composition of the body water mediated by antidiuretic substances in which ADH participates.[92] It is possible from this evidence to suggest further that the administration of appropriate amounts of water may affect this new equilibrium, diminish the stabilized production of ADH, and thereby facilitate a diuresis of water. The hyperproduction of ADH in the low-salt syndrome is not at variance with the above suggested hypothesis, for this syndrome appears to represent a "resetting" of the osmo-receptor renal response mechanism at a new low level and therefore is different from the situation that usually obtains in cardiac insufficiency.[26] The hyponatræmia of the low-salt syndrome has been attributed to a primary diminution of the intracellular osmotic pressure which in some way reduces the extracellular tonicity to a subnormal level so that it may conform to that of the intracellular space. In this situation there may have been a previous substantial loss of potassium from the cells and in some cases the administration of potassium alone has elevated the level of serum sodium.[10] It seems possible that the absence of patients in our series who developed the low-salt syndrome after long periods of salt restriction, may be due in part to the fact that we gave supplementary doses of potassium.

In regard to the role of aldosterone in the regulation of body water and electrolytes in cardiac insufficiency, it may be stated that it seems to be more important than ADH.

Many workers have confirmed that in œdematous conditions there is a great increase in the excretion of aldosterone which is presumably responsible for the excessive reabsorption of sodium and thus the retention of water.[57] However, it is not known what the primary stimulus is that produces the "secondary hyperaldosteronism" of cardiac insufficiency, or the mechanism by which hæmodynamic changes may influence the adrenal glands.[37]

There is sufficient evidence that secretion of aldosterone is in some way regulated by the levels of electrolytes and water of the body. In man reducing the amount of sodium intake, as by a low-

salt diet, mediates an increase in the secretion of aldosterone. Some workers have found that restriction of sodium in man, and also in the dog, even though it is accompanied by a fall in the concentration of serum sodium, results in only a slight change in the production of aldosterone, unless potassium is added to the diet.[10] However, other workers consider that the principal factor in the secretion of aldosterone is not only the electrolytic status but the changes in the volume of body water, particularly the extracellular fluid volume.[9] Acute depletion of sodium accompanied by a loss of water causes an increased production of aldosterone. If changes in the volume of body fluid are avoided by the administration of water, only minor alterations in the production of aldosterone are observed.[11, 56, 63]

Thus the beneficial effect of the administration of significant amounts of water as we propose, in association with a true low sodium diet, may be due to the avoidance of rapid contraction of the extracellular fluid space, thereby preventing the increase of and even decreasing the production of aldosterone. This ultimately then favours the continuing diuresis of water and sodium.

Arterial Hypertension

The restriction of salt in the diet was alluded to as far back as the beginning of this century by Ambard and Beaujard.[7, 8] These workers erroneously concluded that the retention of chloride was responsible in some cases for the elevation of the pressure and in others for the retention of water and œdema. Subsequently other workers[11, 58, 70] demonstrated that the ion responsible for the retention of water was sodium and not chloride. It was the common practice in French and German clinics to restrict the dietary intake of salt as part of the treatment of various cardiovascular diseases including arterial hypertension.

Allen and his collaborators[4-6] introduced the low sodium diet in the United States for the treatment of arterial hypertension and reported excellent results in cases of severe hypertension. However, the negative reports of other investigators[12, 26, 62, 65] discouraged the use of this diet until the works of Kempner were published.[41-46] He introduced the rice and fruit diet and reported very good results in severe hypertension. This stimulated considerable investigation concerning the role of diet in hypertension and particularly that of sodium. Subsequent research[31] demonstrated that the hypotensive effect of the diet used by Kempner was fundamentally due to the low sodium content. The evidence that sodium restriction significantly decreases high levels of arterial pressure in hypertensive individuals is almost unequivocal and does not require amplification. Furthermore, the decrease in the arterial pressure frequently observed in obese hypertensives who reduce their weight, has been attributed[24] recently not to the weight reduction but rather to the restriction of salt that goes along with a weight-reducing diet.

The administration of desoxycorticosterone acetate (DOCA) and salt has been a standard method of producing hypertension in animals for some time.[49, 80] Increased intake of dietary salt and fluid restriction (the use of hypertonic saline as the basic fluid ingested) produces hypertension in chickens[54] and rats[36, 73] without the use of supplementary corticosteroids. Finally, Meneely *et al.*[60, 61] demonstrated that the chronic ingestion of excessive amounts of sodium chloride produces a pathological picture in rats similar to that seen in human hypertension.

It is well known that the hypertensive patients who respond to this restriction will manifest a rise in arterial pressure if salt is added to the diet.[67, 89] Normotensive adults who have been given increased amounts of salt for short periods of time have not shown consistent elevation of arterial pressure,[22] and in diabetic children ingestion of salt has been shown to elevate arterial pressure rapidly.[66] Dahl[23] has suggested that since essential hypertension is rare before 40 years of age and since salt is an etiological factor, its effect depends on the duration of excessive ingestion. Data obtained from another field, that of epidemiology, though limited, also suggest the importance of sodium as an etiological factor in essential hypertension. The basic studies of Love[56a] demonstrated that people with low levels of salt ingestion have an incidence much lower than average. The studies of Dahl[23] summarize statistical and epidemiological viewpoints which have shown that the incidence of arterial hypertension is closely correlated with the amount of salt ingested by the groups of humans studied. These investigations provided data which allow the conclusion that the excessive ingestion of salt over a long period of time is very probably a causal factor of great significance.

Certainly many studies that can be cited suggest that the retention of sodium plays an etiological role in arterial hypertension and leads one to ask a question which was alluded to in the initial hypothesis of Ambard and Beaujard.[8] Why can many normal subjects tolerate large quantities of sodium chloride without changes in arterial pressure and why in conditions in which there is marked retention of sodium, such as cardiac insufficiency, lipoid nephrosis, and chronic hepatitis, is there no accompanying arterial hypertension?

There are observations which may allow for a hypothesis to explain this problem. It has been known for a long time that the capacity of the kidney to conserve water is altered in essential hypertension.[47, 48] Even though the hypertensive kidney retains its ability for "economy of water" (free water saved for the organism), this capacity is less than normal.[18] The water economized for the body, in relation to sodium as well as chloride, is less in hypertensives than in normals.[21, 35] That is to say, the hypertensive eliminates these ions as

rapidly as or even more rapidly than normal subjects, but in so doing uses and therefore excretes more water. These same findings are encountered in rats with experimental hypertension;[16, 28, 68] the amount of antidiuretic hormone in the urine is increased,[27] and the concentration of serum sodium is also slightly elevated.[3, 38, 50] Thus Sapirstein[74] proposed the theory that the fundamental difficulty in hypertension was not the simple retention of sodium, but the inability of the organism to maintain a normal osmolarity because the capacity of the kidney to retain water is decreased. The hypertension is not produced by the excess of sodium but in reality by the deficit of water and the consequent increase of the osmolarity of the body fluids. We believe that it is of great value to quote the conclusions arrived at by Sapirstein:[74]

"This working hypothesis would imply that an excessive consumption of sodium chloride can induce the hypertensive state if, and only if, there is at the same time a failure to adjust body water to body sodium. In this view, the intake of sodium is of less importance than the relationship between sodium balance and water balance. Abnormal metabolism of water—for example, excessive losses of free water in sweating, or habitual disregard of thirst—may be more significant in the pathogenesis of hypertension than abnormal intake of the sodium ion. In the same way, it is quite conceivable that the favourable effects of the low salt diet are more directly referable to the removal of the osmolar load on the body-water than to any specific effect of sodium.

"Perhaps the most intriguing aspect of the proposed hypothesis is that, if it is correct, it may add an important new substance to the medical armamentarium against hypertension, namely water. If the basic deficiency in hypertensive disease is hyperosmolarity of the body fluids, generated either through renal inability to save 'free water' for the body or through any combination of these, the rational remedy would appear to be increased consumption of tap water. *To my knowledge, there have been no studies made on this point.*"

In keeping with these conclusions, our results of the treatment of arterial hypertension with a low-sodium, high-water regimen and small doses of chlorothiazides are superior to those reported by other authors[15, 30] who use chlorothiazide alone.

However, we believe that precise comparative studies are required to prove or disprove this interesting and important hypothesis.

Angina Pectoris

Our results with the proposed program in patients with angina pectoris have been much better than we would have expected prior to investigation. The decrease or disappearance of pain has been a fairly constant finding. Of course, the complete mechanism of the production of cardiac pain is not clearly understood. The older clinicians[19, 87, 91] accepted the theory of angina offered by Jenner and Parry[40] at the end of the eighteenth century, particularly in relation to decubitus angina, where they related it to insufficiency of the left ventricle. This concept seems to have been overlooked or discarded by the majority of investigators who have dealt with the difficult problem of angina pectoris. However, Gold[33] has recently called attention to the effective treatment of cardiac pain by mercurial diuretics, particularly in patients in whom it occurs with the assumption of the reclining position. These patients did not have clinically demonstrable pulmonary congestion, but had worsening of symptoms on exertion and no improvement unless they lost weight with the mercurials. Gold's summary[33] is of great pertinence to our discussion: "Not all patients respond but some do in a dramatic way. I have the impression that the pain in those patients who also have exertional dyspnœa or nocturnal dyspnœa is more apt to respond well. Because of a clear-cut relationship between the relief of dyspnœa and the pain by dehydration in some cases which have both symptoms, I am inclined to think that in some cases cardiac pain is the sole clinical manifestation of left heart failure. If you treat them as cases of left heart failure their capacity for exertion without pain is enhanced, and nocturnal pain may either lessen or vanish." These results were also confirmed by Soloff[81] and by Paul,[69] and more recently similar findings have been reported with the use of chlorothiazide.[59]

The investigations of Muller and Rorvich[64] help to clarify some of the hæmodynamic changes that occur during an attack of angina. These workers catheterized the right heart of patients with angina who had normal blood pressures and heart size and no evidence of cardiac insufficiency. Some of the patients had previous myocardial infarction but others did not. All had angina pectoris. During the absence of pain the hæmodynamic data were almost normal, but during the attacks of pain induced by exercise, they encountered a surprising elevation of the pulmonary capillary pressure which they felt was due to left ventricular insufficiency. This was seen not only in the patients who had pain induced by exercise but also in a patient whose pain appeared spontaneously without exercise during catheterization. The administration of nitroglycerine prevented not only the pain but also the signs of left ventricular insufficiency after exercise.

The difficulty of determining the exact effect of a therapeutic program on the course of angina pectoris is well known. But we feel that our results have been so consistent that it is not out of place to speculate on the possible mechanisms. Further carefully controlled studies are needed. Our results would suggest that the theory of Rabb, who considers that anginal attacks are produced by an excess liberation of catecholamines which cause anoxia of the myocardium, is correct. He found that the effect of the catecholamines was potentiated by thyroid hormone as well as by a high

content of intracellular sodium. Thus he stated that high intracellular sodium potentiated the vasoconstrictor action of extrinsic or intrinsic catecholamines and that a decrease in intracellular sodium weakens this action.[71] Other workers[29] have shown that the muscular tone of the blood vessels is related to the extra-intracellular gradient of sodium—as the gradient decreases with an increase of intracellular sodium, the contractile capacity of the musculature of the vessels increases. Also, Tobian[86] found an increase in water and sodium content in the aorta of experimental hypertensive animals.

Thus we suggest that the low-sodium, high-water regimen when combined with chlorothiazide produces a diuresis of water and sodium and reduces the work load of the heart, thereby improving the status of the left ventricle particularly. This would then eliminate the factor of cardiac insufficiency which we discussed. At the same time these changes of water and sodium balance would tend to modify favourably the responsive capacity of the coronary arteries as well as the myocardial fibres to the hormonal factors operative. These two modes of action would account for the success of the program in many of the anginal patients. Finally, the use of potassium is justifiable in the light of Selye's work[79] in which he showed its protective role for the myocardium against the chemical factors which experimentally produce cardiac necrosis.

SUMMARY

The results of treatment of patients with cardiac insufficiency, arterial hypertension and angina pectoris by a low-sodium, high-water, high-potassium regimen have been presented. In the light of the evidence from the literature that has been reviewed, it is suggested that a revision of some of the therapeutic concepts for cardiovascular conditions may be in order. It would appear that rigid sodium restriction may not be enough in the majority of cases, but that administration of potassium as well as large amounts of water may also be necessary. As Sapirstein[74] has so succinctly pointed out, water is not merely an inert portion of the diet of the patient but is a part of the therapeutic armamentarium and should be regarded as a drug to be taken in specified required doses.

The excellent results obtained in the treatment of angina pectoris suggest anew to the clinician that a relationship exists between cardiac insufficiency, electrolyte status of the myocardium and the status of the coronary tree.

Our knowledge of the basic mechanisms involved in the success of this program is limited, as is knowledge in many areas of cardiovascular physiopathology. Further work with clinical as well as experimental approaches is needed in order to clarify and qualify our concepts.

It is hoped that this preliminary report will serve to stimulate further investigation of the mechanism of this regimen, and that it will be of use to the clinician in the everyday treatment of his cardiac patients, many of whom represent severe and refractory problems at the present time.

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RÉSUMÉ

Les auteurs présentent les résultats de leur traitement de malades atteints d'insuffisance cardiaque, d'hypertention artérielle et d'angine de poitrine par un régime pauvre en sodium et riche en eau et en potassium. D'après les données de la littérature médicale, les auteurs suggèrent qu'une revision des conceptions thérapeutiques s'appliquant aux affections cardio-vasculaires est de mise. It semble que la simple restriction rigide de sodium ne soit pas suffisante dans la majorité des cas, mais que l'on doive aussi administrer du potassium ainsi que de fortes quantités d'eau. Comme l'a fait remarquer Sapirstein, l'eau ne constitue pas seulement une portion inerte du régime alimentaire de ces malades, mais elle fait partie de l'arsenal thérapeutique et doit être considérée comme un médicament dont la posologie n'est pas négligeable. Les excellents résultats obtenus dans l'angine de poitrine, soulignent de nouveaux aux yeux du clinicien le rapport qui existe entre l'insuffisance cardiaque, l'état électrolytique du myocarde et celui de l'arborescence coronarienne. Notre connaissance des mécanismes fondamentaux impliqués dans le succès d'un tel programme, est limitée, comme c'est le cas dans plusieurs champs d'activité physio-pathologiques cardio-vasculaires. Il faudra donc continuer le travail clinique et expérimental afin de clarifier et de délimiter nos conceptes. Les auteurs espèrent que ce rapport préliminaire stimulera une recherche plus poussée des mécanismes mis en jeux par ce régime et aidera le clinicien à surmonter les obstacles, que présente souvent le traitment quotidien de malades atteints d'affections cardiaques.

TREATMENT OF THE MINOR EPILEPSIES*

JOHN A. SIMPSON, M.B., Ch.B.(Glasg.), M.R.C.P., F.R.F.P.S., M.R.C.P.E.,
Edinburgh, Scotland

PETIT MAL, "the little illness"—a disparaging term, almost affectionate—is described as "a minor form of epilepsy" by the dictionary. So often in science, the simple and the commonplace hold the key that opens the door of knowledge. Understand petit mal and you understand epilepsy. It is for this reason that a close study of this "little disease" is worth making, and it is encouraging to reflect that there are more specific forms of therapy for this disorder than for other types—since a therapeutic trial is merely an experiment in chemical pathology.

It is then understandable that there should be obvious disappointment in the letter received by every neurologist: "Dear Doctor, this patient has petit mal, but shows no response to trimethadione." In the majority of instances it turns out that the patient does *not* have petit mal, but another of the minor epilepsies.

Before reviewing treatment, let me say a few words about "the minor epilepsies", for they are many; to their elucidation we acknowledge a tremendous debt to Dr. Wilder Penfield.

True petit mal is the characteristic type of a related group associated with neuronal discharges arising in the upper diencephalon and rapidly spreading to both hemispheres synchronously. The patient is usually a child who suddenly pales, becomes silent, looks vacant, with eyes staring or rolling up at a rhythmical three per second and, perhaps with fingers or hands twitching at the same rate, and then suddenly resumes the normal stream of consciousness without post-ictal disturbance. Related to this are simple "absences", slowing of reaction time, akinetic spells, petit mal with myoclonus and petit mal with automatism. The latter is not a common feature, yet it is epileptic automatism of other types that is most frequently erroneously described as petit mal.

Unlike the petit mal group proper, the other minor epilepsies are manifestations of a discharge arising from a limited area of cortex or subcortical tissue, without generalized propagation of the discharge. If the local sign of the disturbed area is motor or sensory, the true nature of this minor epilepsy as a "focal seizure" is readily apparent. If the local sign is a disturbance of thought or of the stream of consciousness or memory, it is much less obvious that the fit is of the same nature. The

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†Senior Lecturer in Neurology, Edinburgh University; Physician in Charge, Neurological Unit, Northern General Hospital, Edinburgh.