tistically significant changes, although the electrocardiograms remained within clinically normal limits. In 20 cardiac patients, mostly definite or suspected coronary disease, we recorded the standard limb leads, 3 chest leads (CF_1, CF_2, CF_4) and the heart sounds before and at 30 and 60 minutes after a 1000-calorie meal. In 2 patients additional chest leads were taken. The location for the chest leads was marked on the chest by means of a colored pencil.

Out of 10 patients with some symptoms of angina pectoris but with normal electrocardiogram before the meal and without any signs of decompensation, the electrocardiogram became abnormal after the meal. The abnormality involved inversion of the T-wave in lead CF_2 or CF_4 or increase in the size of a Q-wave in lead III. These patients felt no discomfort after the meal.

In 5 patients with coronary disease and abnormal electrocardiogram before the meal, the electrocardiogram became more abnormal with inversion of the T-wave in leads 1, 2 or CF_4. Slight changes of the QRS-contour were also observed. In one patient, a transitory *pulsus trigreminus* appeared after the meal.

In 2 patients with abnormal electrocardiograms before the meal the chest leads appeared to be more normal after the meal; previously inverted T-waves in CF_2 and CF_4 became positive. Similar changes have been observed after exercise in coronary patients and cannot be interpreted as a sign of improvement.

In 2 patients with coronary disease and abnormal electrocardiograms, the meal produced violent discomfort, associated with a pronounced ST-depression, especially in lead II. The discomfort as well as the ST-depression was instantaneously removed by nitroglycerine. In normal subjects the ST-segment does not change after the meal. It seems probable that the ST-depression is due to a transitory coronary insufficiency, produced by an abnormal reflex coronary constriction. In only one patient with an abnormal ECG were the changes after the meal comparable to those observed in normal subjects.

The present series is only of an exploratory nature, and no attempt is made to correlate the effect of meals on the electrocardiogram to the nature of the existing pathological changes. However, the series appears to show that the effect of meals is of importance for the clinical interpretation of electrocardiograms and for the standardization of procedure.

15666

Radiosodium Tracer Studies in Congestive Heart Failure.*

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Extensive studies in this laboratory on the distribution and turnover of sodium in cardiovascular states with Na^{24} (14.8 hour ½ life) as a tracer led to the possible investigation of long-term phenomena associated with congestive heart failure and edema. For such studies a long life isotope is necessary. Radioactive sodium 22 (3 year ½ life) is listed in the isotope tables but has not been reported as used in biological studies. Through the cooperation of Professors M. D. Kamen and A. L. Hughes of the Washington University Cyclotron, an experimental supply was made available for investigation. The details of preparation, standardization, determination and safety will be described later. In view of the significant results as well as for the introduction of this technic in the

* Aided by grants from The Helis Institute for Medical Research, Mrs. E. J. Caire Fund for Cardiovascular Research, and The Life Insurance Medical Research Fund.

study of the mechanism of edema this report is presented.

Two patients were followed simultaneously for 10 weeks. All voided and catheterized urine specimens and daily blood samples were collected during the first 3 weeks for the control and in the first 4 weeks for the heart failure patient. Samples of feces, vomitus, ascitic fluid and edema fluid were obtained when possible. Over 1500 5-minute counts were made. All samples were done in triplicate.

The congestive heart failure patient (elderly colored female) had hypertensive cardiovascular disease with acute failure and anasarca. This patient showed little if any improvement during her illness and died of acute heart failure 11 weeks after the study was started. The control was a young, colored female with vague arthraligic complaints of unknown cause. Both patients received the Na^{22} (less than 0.1 millicurie) as 200 cc of a 1% aqueous sodium chloride solution.

These patients were allowed to reach equilibrium with respect to the introduced sodium (more than 12 hours) before the results presented below were obtained. The determinations were made with a TA-Bl and scale-of-64. Technical Associates Geiger-Muller Counter.

Results. The effect of sodium intake on the excretion of sodium and water in the normal, and in congestive heart failure with and without the use of a mercurial diuretic (sodium salt of methoxyoximercuripropylsuccinylurea with theophylline,—"Mercuhydrin," 1 cc l.M.)† was studied. It was found that the control required 5 days to reach a steady state of sodium excretion when placed on a low sodium diet. The results summarized in Fig. 1 are based on the succeeding 4 days. The congestive heart failure patient was on a low sodium diet (1.7 g NaCl or less, daily) without a diuretic for 9 days. During this time the mean sodium output of the control was 3.1 times that of the abnormal. This is to be expected because the available sodium was reduced in both patients. However, when it became readily available, such as when they were on a regular hospital diet (10 g or more NaCl) with salt *ad lib.*, the difference became quite marked. During 6 days (without a diuretic) for the abnormal and 10 days for the control the latter excreted 90 times as much sodium. In one 24-hour period this exceeded 200 times as much. That this was not due to the difference in urine volume is indicated by the fact that the latter were essentially the same on a low sodium intake and only 3.5 times greater in the control on a regular intake.

The individual urine concentrations of Na^{22} for the control were quite variable and no regular relationship existed between urine volume and Na^{22} concentration. A 1 cc dose of the diuretic produced no appreciable effect in this patient. The congestive heart failure patient's urine concentrations of Na^{22} were fixed at a very low level and in many instances the counts were at background. There was little relationship to volume, *e.g.*, a 10-fold change in volume was accompanied by no concentration changes. It might be added that the 6-day normal salt intake period for the congestive heart failure patient was initiated by a slow infusion of 1000 cc of physiological sodium chloride solution.

The question of selective sodium excretion after a mercurial diuretic is conclusively answered for this patient. During the salt-free period (20 days) 10 1-cc injections of the diuretic were given intramuscularly. The average response was a 7-fold increase in salt output (Fig. 1). When salt was made available for 6 days this response consisted of an average increase of 75 times. In one 24-hour period it reached a 160-fold increase. Following the diuretic, the water output increased only 2.3 times with salt restriction and 5.3 times with salt given *ad lib.* The sodium diuresis preceded the water diuresis by 2-4 hours. The diuretic became effective in less than 2 hours, reached a maximum in 4-6 hours, and lasted rather uniformly for almost 24 hours when given intramuscularly.

The question next arose as to the degree of normalcy approached by the treated congestive heart failure patient as determined by a comparison with the control under

† Courtesy Lakeside Laboratories, Milwaukee, Wis.

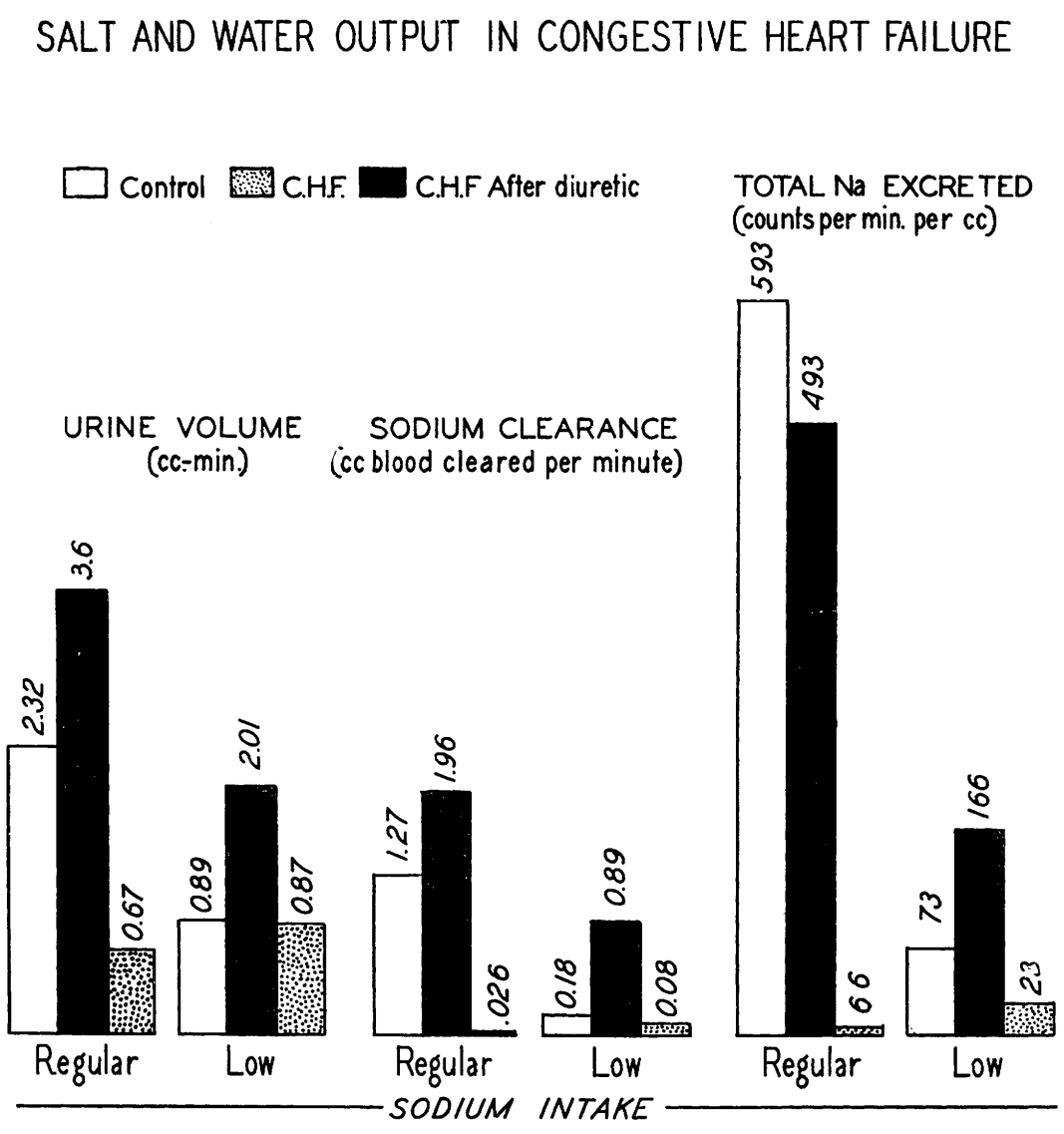

FIG. 1.

A comparison of the urine output, sodium clearance, and total sodium excretion on regular and low sodium diets in a congestive heart failure patient with and without a diuretic and a control subject. The heart failure patient was on a regular diet for 6 days and on a salt-free diet for 9 days, without a diuretic being administered, and 20 days during which 10 injections of a diuretic were given. The control subject was on a salt-free diet for 9 days (with only the last four used in the calculations) and on a regular diet 10 days.

identical conditions of salt and water intake. With mercurial diuresis the congestive heart failure patients' excretion of sodium was practically identical with the control and the excretion of water was greater (Fig. 1). In addition to the above data it was noted that: (a) The feces and vomitus counts were low and close to background. (b) The ascitic fluid and edema fluid were not appreciably different from the blood serum levels. (The removal of 1500 cc of ascitic fluid yielded as much sodium as would be excreted during 20 days without a diuretic). (c) In the control subject the blood serum Na^{22} concentration was found to decrease proportionately as the Na^{22} was excreted in the urine. In

the congestive heart failure patient the presence of edema when the sodium was injected made similar calculations impossible. (d) The Na^{22} was 50% excreted by the control subject in 12 days and had disappeared in 10 weeks. In the congestive heart failure only 45% had been excreted in 10 weeks.

Discussion. The urine concentration of sodium is somewhat dependent upon the blood concentration at the time the urine is being formed. The exact relationship is unknown. Sodium clearances were employed to express this relationship. It must be remembered, however, that the term "clearance" cannot be used in the strict sense for sodium since the blood is less than 1% cleared of sodium during a single passage through the kidney. These patients formed urine of similar maximal concentration throughout the experiment. In the control this was equal to the blood concentration. In the congestive heart failure case it was lower but approached the blood level as the latter declined. It appears that the sodium concentrating ability in the congestive heart failure patient is fixed and not related to the blood level, whereas marked variations were possible in the normal.

Summary. The use of a radioactive tracer, Na^{22}, on an apparently normal control and a congestive heart failure patient showed a marked difference in respect to the behavior of this substance. (1) The control patient excreted an average of 90 times as much sodium as the congestive heart failure patient when both were given salt *ad lib.* (2) A mercurial diuretic resulted in an increase in sodium excretion of 75-fold when the congestive heart failure patient was receiving salt *ad lib.* (3) A reduction of salt excretion occurred in both when salt intake was restricted. However, the use of the diuretic still resulted in a 7-fold increase in the output of sodium in the congestive heart failure patient. (4) Other significant findings are presented.

The valuable technical assistance of Miss Shirley Wiederecht and Messrs. G. Morgavi, F. M. Parks, J. Fruthaler, and R. Schramel is gratefully acknowledged.

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Effect of Glycine Feeding on Renal Hemodynamics of the Rat.*

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The feeding of excess protein or its constituent amino acids has been found generally to increase the urea clearance in man[1,2] and in dog.[3,4] However, other than the studies of Van Slyke *et al.*,[3] little is known about the effect of these substances on the renal blood flow. Moreover, some investigators[5,6] have observed that the creatinine clearance did not rise after the ingestion of excess amino acids. It seemed important then, to study the effect of the common amino acid, glycine on the renal hemodynamics of the rat. This amino acid was employed because most investigators[2,4] are agreed that whatever effect protein does have on renal function, resides in its amino acid content which in turn almost invariably con-

* Aided by a grant from the Dazian Foundation for Medical Research.

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