Renal Factor in Congestive Heart Failure

By Eugene A. Stead, Jr., M.D.

Patients with edema of congestive heart failure may be divided into two groups: (a) those with edema caused by an abnormal redistribution of the fluid normally present in the body, and (b) those with edema caused by an absolute increase in the amount of fluid present in the body. The patient with no previous history of dyspnea, who has sudden pulmonary edema caused by a massive myocardial infarct, belongs to the first group. Edema of the lungs develops suddenly without a change in body weight. The fluid collecting in the lungs comes from that originally present in the blood stream and from fluid pulled into the blood stream from the tissues. The second group is exemplified by the patient with slowly progressive generalized failure of the heart who over a period of weeks has gained 35 to 100 pounds. In this patient the fluid intake has exceeded the fluid output over a long period of time. In the last analysis, the fluid has been retained in the body because the kidneys have failed to excrete it. This retention of fluid by the kidney is the subject of our present discussion of the renal factor in congestive failure. In most patients with congestive failure both the abnormal distribution of fluid and the abnormal increase in weight from edema are present.

Observations of patients with heart failure who gain weight from edema show the following generally agreed upon findings: (1) The renal excretion of sodium chloride is markedly reduced. (2) The night volume of urine is increased and the day volume decreased. (3) The ability to excrete water at a maximal rate is impaired, but if salt is not given, the average patient in moderate congestive failure can excrete water sufficiently well to tolerate a fluid intake of several thousand cc. of water without difficulty. (4) The concentration of sodium and chloride in the blood is frequently moderately lowered. (5) The plasma volume is increased. (6) The venous pressure is raised.

An excess of Cl⁻ produced by the giving of an acidifying salt, as ammonium chloride, does not cause edema. During the excretion of the excess Cl⁻, a variable amount of Na⁺ and water is lost. It is generally stated that Na⁺ causes retention of fluid. In most instances the Cl⁻ has been available in the diet and the effects of giving excess Na⁺ with rigid restriction of Cl⁻ has rarely been tried. Potassium does not lead to water retention.

An understanding of the mechanisms causing retention of sodium chloride and water in heart failure has been hampered by the lack of knowledge of factors controlling excretion of sodium chloride and water in normal subjects. This problem is now being studied extensively in many laboratories.

In normal man, increases and decreases in water excretion are controlled by changes in the amount of water reabsorbed by the tubules and not by changes in renal blood flow and glomerular filtration. The posterior lobe of the pituitary gland produces an antidiuretic hormone (ADH) which causes marked oliguria by increasing the tubular reabsorption of water. The secretion of ADH is inhibited by lowering of the total osmotic pressure of the plasma (not colloid osmotic pressure). The secretion of
ADH is caused by a rise in osmotic pressure or by many emotional, neurogenic, and pharmacologic stimuli. The osmoreceptors which respond to changes in osmotic pressure are located in the area supplied by the internal carotid artery.

There is no clearcut evidence that variations in ADH secretion have any effect on Na⁺ and Cl⁻ excretion in normal man. Injections of minute quantities of Pitressin produce the same changes in urine volume and sodium chloride concentration as does the production of endogenous Pitressin by the administration of 0.9 per cent sodium chloride solution intravenously. ADH does cause an increase in urine concentration but the product of urine volume and salt concentration is unchanged. When concentrated sodium chloride solutions are given intravenously, a large output of water results which cannot be stopped by the injection of Pitressin. Thus, water excretion can be increased by mechanisms which cause increased sodium chloride excretion, but sodium chloride excretion is not changed by varying the water output by the injection of Pitressin.

These observations on normal subjects have led most observers to believe that posterior pituitary ADH is not of primary importance in the edema of congestive failure and that its presence in the urine in patients with congestive heart failure represents an effect on the osmoreceptors secondary to the retention of salt. The finding of a tendency towards reduced concentration of sodium and chloride in the serum of patients with congestive failure raises the question of the stimulus for the production of ADH in the presence of a decreased concentration of electrolytes, as this condition normally inhibits ADH production. It is possible that the "set" of the osmoreceptors may change in many illnesses and that in chronic heart failure a moderate reduction of electrolyte concentration will no longer stimulate the osmoreceptors. Other antidiuretic hormones may be present and important in congestive failure. It is also possible that the action of posterior pituitary ADH in patients with congestive heart failure differs from that in normal subjects.

The excretion of Na⁺ and Cl⁻ in alkalosis and acidosis has been studied rather extensively. This does not seem to be the real crux of the problem in congestive heart failure. In the latter both Na⁺ and Cl⁻ are retained, and our problem is what controls the excretion of the balanced mixture rather than the excess of either Na⁺ or Cl⁻.

A decrease in the excretion of Na⁺ and Cl⁻ occurs in normal subjects during exercise, sitting, motionless standing, and sleep. When sodium chloride is restricted in the diet, the extracellular fluid volume decreases and the excretion of sodium chloride in the urine decreases. When the intake of sodium chloride is increased, the extracellular space expands and the excretion of sodium chloride in the urine rises. Retention of salt occurs at various times during the menstrual cycle. The administration of large quantities of testosterone, adrenocorticotropichormone (ACTH) and cortisone usually causes retention of sodium chloride. The available data indicate that these variations in excretion are produced by changing the amount of sodium chloride reabsorbed by the tubules and not by changing the renal blood flow and glomerular filtration rate. In this respect, the control of excretion of sodium chloride seems to parallel the mechanism for the control of the excretion of water. The sodium chloride control differs in that it is much more sluggish and the factors acting on the tubules to increase and decrease the excretion of sodium chloride have not been defined. It is known that ACTH in large doses will usually cause initial retention of sodium. Whether ACTH in physiologic doses causes similar sodium retention remains to be determined. It is likely that the degree of salt loading and salt depletion will influence the action of the hormone. Whether the normal hourly variations in sodium chloride excretion are caused by the action of various hormones on the kidney tubules, by changes in filtration rate, by changes produced directly in the kidney, by changes in the electrolyte composition of the blood circulating through them, or by some other mechanism remains to be determined.

Sodium chloride retention is a characteristic finding in chronic congestive heart failure. The inability to excrete salt is relative rather than
absolute. The patient with heart failure varies his sodium chloride excretion as does a normal subject with exercise, infection, trauma. The abnormal change is quantitative rather than qualitative. The cardiac patient under a given stimulus for salt retention merely retains more than the normal amount of salt and under conditions where the normal person loses salt rapidly, the patient with chronic failure loses it slowly. The patient with heart failure does show one qualitative peculiarity. He excretes more salt during the night than during the day. This may be an expression of the fact that his circulation becomes increasingly abnormal with exercise and tends to become more normal during rest.

There are several possible explanations for the slow excretion of sodium chloride in patients with heart failure. Many persons believe that the backing up of blood behind the failing ventricles causes an increase in venous pressure in the systemic venous system. This in turn causes a rise in capillary pressure and water is forced out into the tissues. Salt and water taken in the diet then pass through the blood stream to the tissues and are not excreted by the kidneys because of the prerenal deviation of water and salt. This thesis seems unlikely because the plasma volume in chronic congestive failure is increased rather than decreased and because the quantitative difficulties in handling sodium chloride persist after the venous pressure has been returned to normal by the use of salt restriction and mercurial diuretics. This explanation also fails to account for the similar retention of salt which occurs after hemorrhage or trauma.

Other investigators have felt that the impairment of sodium chloride excretion results from the high venous pressure in the kidneys produced by backward failure. It has been shown in animal experiments that a rise in venous pressure will cause a decrease in sodium chloride output without a change in renal blood flow or filtration rate. Whether this change occurs in man and whether it is of the order of magnitude seen in congestive failure and whether this stimulus for sodium retention remains effective for the weeks and years which a patient may stay in failure are problems for the experimental laboratory. The observation that in man the abnormal sodium chloride retention persists after the central venous pressure returns to normal remains to be explained. This thesis will not explain similar retention of sodium chloride after hemorrhage.

Some investigators have believed that the primary cause for salt retention in congestive failure is the increased avidity of the renal tubules for salt because of hormonal stimulation. They point out that ACTH, cortisone, and testosterone cause salt retention in normal subjects. An insufficient circulation is certainly a stress and would be expected to stimulate the pituitary-adrenal mechanism. Increased urinary corticoid excretion has been reported in chronic failure, and studies of sweat secretion are compatible with increased adrenal cortical function. One would expect to find comparable retention of sodium chloride when the circulation is decreased by hemorrhage. The weakness of this argument lies purely in its quantitative aspects. Patients with heart failure show the same qualitative changes to stress, exercise, and anoxia as normal subjects. It remains to be shown that the body produces sufficient salt-retaining hormones to cause the massive edema of chronic heart failure. Either some other factors are operative or, in comparison to other stresses, the stress of congestive failure produces unusually large amounts of salt-retaining hormones.

There is a marked disturbance in renal hemodynamics in patients with chronic heart failure. In subjects who form edema at rest on an unrestricted diet, the findings are surprisingly uniform. The renal blood flow is greatly reduced and the amount of glomerular filtrate is decreased. The amount of filtrate obtained from each unit of plasma flowing through the glomeruli is, however, greatly increased. The fall in filtration rate causes a decrease in the amount of sodium chloride presented to the tubules. The tubules reabsorb nearly all of the filtered sodium chloride, but the absolute amount of sodium chloride filtered is so small that the absolute amount of sodium chloride reabsorbed is much less than in the normal subject. This remains true if 100 per cent of the filtered sodium chloride is reabsorbed. In
chronic failure, the per cent of filtered sodium chloride which is reabsorbed is increased, but the absolute amount compared to that reabsorbed by a normal subject is decreased. The disturbed renal hemodynamics of chronic failure are not correlated with changes in venous pressure, but they do correlate with the reduced cardiac output of chronic failure.

Some investigators, including the author, have believed that this reduction in filtered sodium chloride was the primary factor in causing the edema of chronic heart failure. They have reasoned that the renal tubules normally have as one of their main functions the retention of these ions and that the tubules cannot avoid reabsorbing nearly all the sodium chloride when the amount presented to them becomes very small. Attention is called to the interesting fact that tubular function remains surprisingly good in congestive failure and that there is only a moderate reduction in renal oxygen consumption. Comparable decrease in filtration rate in glomerular nephritis or vascular disease of the kidney results in much lower rates of oxygen consumption than is seen in congestive failure. This thesis states that there is a normal balance between filtered sodium and tubular reabsorptive function and that when glomerular filtration is lowered without a corresponding decrease in tubular function, edema occurs; if glomerular filtration is lowered with a corresponding decrease in tubular function because of disease of the tubules, the tendency to edema is decreased.

Many objections have been raised to the glomerular-tubular imbalance concept of sodium retention. In normal subjects, the variations in sodium excretion are controlled to a greater degree by changing tubular function than by changing filtration rate. Likewise, in patients with chronic failure, changes in sodium excretion can be produced which seem to be related to changes in tubular function. The proponents of the glomerular-tubular imbalance hypothesis answer that the directional changes produced in normal subjects are also produced in patients with cardiac failure, but that the extent of the change is governed to a large degree by the amount of sodium filtered. For example, light exercise, which in a normal subject causes only slight retention of salt and water, will produce massive edema in the patient with heart failure.

Various investigators have pointed out that edema may disappear without demonstrable change in filtration rate. Again it should be emphasized that there are many situations which influence sodium excretion. Massive edema from heart failure rarely persists at bed rest unless the filtration rate is markedly reduced. On the other hand, on a sodium restricted diet, edema may disappear even though the filtration rate remains low.

The fact that reduced glomerular filtration in other diseases, as chronic glomerular nephritis and marked nephrosclerosis, does not cause the same tendency to edema so characteristic of patients with congestive failure has been given as an objection to the glomerulotubular imbalance hypothesis. This observation actually supports the hypothesis because, in these diseases, tubular destruction is going along with glomerular destruction and the reduced filtration is balanced by the decrease in tubular function.

In summary, there is still no general agreement on the relative importance of the mechanisms by which salt and water are retained in chronic heart failure. In recent years more emphasis has been placed on determining the role of the kidney in controlling salt and water metabolism and less attention has been paid to mechanical factors diverting salt and water from the blood stream to the tissues. The student of heart failure has become interested in the means by which a reduced cardiac output and elevated venous pressure affect renal function. He has been pulled into the fields of endocrinology to evaluate the effect of the stress of reduced circulation and decreased venous oxygen tension on the pituitary-adrenal relationship and on other aspects of metabolism. He has had to observe the effects of diets restricted in protein and salt on the function of the pituitary, adrenal, and thyroid glands and to consider the effects of chronic illness on the electrolyte composition of cells. Problems in physical chemistry loom large as one tries to define the mechanisms by which osmoreceptors operate and attempts to evaluate the scattered
evidence that the "osmotic set" of these receptors may vary. The means by which the body regulates the concentration of electrolytes and the amount of extracellular and intracellular fluids remain problems for the future.

Once the salt and water are present in the body there is general agreement that the distribution of the retained water is largely determined by local factors. The greatest swelling occurs where the capillary pressure is the highest, the tissue pressure the lowest, and the lymphatic flow least. When a normal subject lying in the recumbent position is given physiologic saline solution at a faster rate than his kidney can excrete the fluid, he gains weight. As there are no areas of abnormally high capillary pressure, the fluid accumulates in areas where a considerable increase in volume can occur with a minimum rise in tissue pressure. The edema first becomes visible in the soft tissues about the eyes. If the subject now stands erect, he will have a high capillary pressure in the portion of the body below heart level. Fluid will now be deposited in the lower part of the body. In either position there will be no tendency for fluid to accumulate in the lungs.

The situation is entirely different when fluid is given intravenously to a patient with left ventricular failure. The high capillary pressure in the lungs causes an unusual portion of the fluid given to accumulate in the lungs, and frank pulmonary edema may be precipitated with a minimal increase in body weight. If during the course of heart disease the right ventricle is weakened to the same degree as the left, one loses this marked predisposition for pulmonary edema, and the patient gains large amounts of weight without drowning.

The treatment of edema of congestive heart failure can be divided into two phases: (1) Measures which make the circulation adequate for the needs of the body. When these measures are effective, edema will not develop on a normal diet. (2) Measures for preventing edema when the circulation remains inadequate. If the circulation cannot be restored to a level adequate for the activity of the patient, edema will occur on an unrestricted diet.

(1) To make the circulation adequate for body needs

- a. Increase the output of the heart and restore the circulation to a normal level. Digitalis is the only effective drug for this purpose.
- b. Decrease activity of the body so that fewer liters of blood have to be pumped per day. This reduction in the requirements of the body for blood allows the damaged heart to supply normal quantities of blood to all vital organs. This is accomplished by weight reduction, limitations on stair climbing, and on work.
- c. Correct any diseased states which increase the requirements of the body for blood. Anxiety, hyperthyroidism, anemia, beriberi, arteriovenous fistula, and patent ductus arteriosus all increase the output of a normal heart. Removing this extra load may make the output of the heart adequate for the needs of the body.
- d. Correct any diseased states which have an adverse effect on myocardial function. Hypertension, pulmonary infections, pulmonary infarctions, asthma, anoxemia, and myxedema decrease the functional capacity of the heart.

(2) To prevent edema in the presence of an inadequate circulation.

- a. Restriction of the sodium chloride in the diet. This is the most satisfactory measure with intelligent and cooperative persons. The restriction must be marked enough to produce the desired results. In many patients, the sodium intake must be reduced to 150 to 200 mg. per day. This means a marked reduction in protein intake unless the diet is supplemented with special protein preparations low in sodium, such as dialyzed milk. Many physicians have felt that the restriction in protein intake was undesirable and have devised diets to supply approximately 1 Gm. of protein per Kg. Others have felt that the metabolic adjustment that the body makes to the low protein intake is desirable and has a favorable effect on the patient with chronic heart failure. This problem needs further investigation.

The diet should be controlled by following the excretion of Cl⁻ in the urine. For this reason salt substitutes are not desirable.

- b. Increased excretion of sodium chloride by the use of diuretics. The mercurial diuretics are the most useful. (The intravenous route should be avoided.) They should be given sufficiently often to maintain the patient at a constant
weight. They must be used cautiously if the patient is on a restricted intake of sodium chloride. Ammonium chloride is useful in increasing the effectiveness of the mercurial diuretics.

c. Removal of the sodium from the gastrointestinal tract by the use of ion exchange resins. This method is still in the experimental stage.

d. Removal of fluid from the body by mechanical means. Thoracentesis and abdominal paracentesis may hasten convalescence. Large quantities of subcutaneous edema may be drained off by inserting several number 14 needles into the subcutaneous tissues above the ankles. After a few minutes the needles are removed and the fluid drains freely along the needle tract.

This discussion of congestive failure differs from that present in any standard text book of medicine of 10 years ago in four ways. (1) It is recognized that the reduction of sodium chloride to 2 Gm. per 24 hours is inadequate in many patients and that diets containing 200 mg. or less of sodium are practical. (2) The old Karell diet of 200 cc. of milk four times per day contains about 400 mg. of sodium and is not the best diet for the severest forms of congestive failure. (3) Treatment by sodium restriction is preferred to treatment by diuretics, and the dietary therapy is controlled by the measurement of the chloride output. (4) No mention is made of fluid restriction.

In the years of fluid restriction without salt restriction patients were miserable from thirst. It was gradually learned that the cardiac patient's difficulty was in the excretion of salt and that in the absence of salt he could tolerate a large amount of water. It also became obvious that the craving for water disappears as the salt intake is restricted. The amount of water needed by the patient with congestive heart failure varies greatly. If he is dehydrated, febrile, and in a hot environment, his water requirements may rise to between 3000 to 6000 cc. per 24 hours for a short period of time. If he is on a diet which contains a minimum of nitrogen and electrolytes, his water requirements will be reduced below that of a person on a normal diet.

The emphasis on low sodium diets in congestive heart failure has led to the occasional development of weakness and anuria from Na+ depletion. This syndrome of Na+ loss is not uncommonly seen in patients with renal disease who are placed on a rigidly restricted sodium intake, as the kidneys may have reduced ability to retain sodium because of disease of the renal tubules. It is rarely seen in congestive heart failure unless sodium restriction has been combined with the use of mercurial diuretic agents.

In severe failure the mercurial diuretic may cause a diuresis of salt with very little increase in the output of water. This leads to a lowering of the sodium and chloride concentrations in the blood. It is probable that shifts of sodium from extracellular fluids to cells occur in the severest forms of failure and that a low concentration of Na+ does not necessarily mean excess loss through the urine. Finally, the "set" of the osmoreceptors regulating the output of the posterior pituitary ADH may be altered so that the body accepts a lowered level of electrolytes. The administration of sodium chloride in a 3 to 5 per cent solution may cause a dramatic improvement in some of these patients. In others it is without effect. In still others acute pulmonary edema may be precipitated.

REFERENCES

Renal Factor in Congestive Heart Failure
EUGENE A. STEAD, JR.

Circulation. 1951;3:294-299
doi: 10.1161/01.CIR.3.2.294
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1951 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/3/2/294.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/