SCIENTIFIC PUBLICATIONS BY WALTER KEMPNER, MD

Volume II

Radical Dietary Treatment of Vascular and Metabolic Disorders

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Special camera for eyeground photographs.

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Radical Dietary Treatment of Vascular and Metabolic Disorders

Edited with a Foreword by Barbara Newborg, MD

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Note to the reader

The German, Spanish, and Italian papers reprinted here are included without editorial interpretation or comment, as they are either paraphrases or direct translations of the original English version reproduced in this volume.

The papers reprinted in this collection retain their size and pagination as originally published. The page numbers of this volume appear in the upper outer corners above the running headers.

FOREWORD

In October 1934, at the invitation of Dr. Frederick Hanes, Dr. Walter Kempner left Germany to accept a position as a research member of the Department of Medicine in the fledgling Duke University Medical Center in Durham, North Carolina. Initially, he spent most of his time in the laboratory pursuing his interest in the role of oxygen tension in biological reactions; he also was a consultant on the public medical wards and taught medical students. Once, while discussing metabolic functions of the kidney with students, he voiced his growing conviction, based on his laboratory findings, that renal disease might actually be influenced through diet. A student asked, Why don't you try this out on a patient, instead of just talking about it? In this casual challenge lay the beginning of the Kempner rice diet, which, as this volume documents, revolutionized medical knowledge about the effects of diet on renal, cardiovascular, and metabolic diseases.

In 1942, one of the first patients to be put on the rice diet in the hospital was sent home, after a stay of two weeks, with instructions to stay on the diet and return after two weeks. Misunderstanding the instructions, she returned after two months. To the surprise of everyone—including Dr. Kempner—she had improved enormously: her blood pressure was lower, her heart size smaller, her blood chemistry improved. The rest is history.

Dr. Kempner did not rely on patients' subjective reactions—increased well-being, fewer headaches, etc.—to measure the efficacy of his treatment; he wanted and got objective evidence. Blood pressures were charted, serial blood and urine tests recorded, and retinal photographs, chest films, and electrocardiograms taken at intervals. At a medical meeting in 1944 where chest films were presented, he was accused of forgery; the x-rays, like fingerprints, could be identified as of the same patients, but it was suggested that the dates had been reversed. An ophthalmologist from Boston wrote Dr. Banks Anderson, head of the Duke Department of Ophthalmology, questioning the validity of the eyeground photographs, implying that they must in some way have been falsified. The chairman assured him that the photographs were made by Duke's medical illustration department, and added, "I have seen these amazing results for myself." In 1950, after consulting on a patient who had been on the rice diet for some months, Dr. Anderson noted, "This patient's eyegrounds are improved to an unbelievable degree. I have never previously seen such an extensive papilledema subside with such minimal retinal scarring, nor for that matter do I think I have ever seen a patient with this degree of hypertensive retinopathy alive after this length of time."

Volume I of Dr. Kempner's papers covers the years 1926-1945. The first paper in Volume II is a comment by Dr. Kempner at a clinicopathology conference in 1943, in which he draws a distinction between metabolic and excretory functions of the kidney and points to the former as a main culprit in renal and hypertensive vascular disease. The second work is a report on the first major presentation of the benefits of the rice diet in the treatment of renal disease and of retinal and hypertensive vascular disease, and it tabulates the decrease in hypercholesterolemia. Dr. Reginald Smithwick, the father of surgical sympathectomy for hypertensive vascular disease, was struck by these dramatic findings on the rice diet's effectiveness in patients too sick for his surgery. He commented to Kempner, "You start where we end."

As Dr. Eugene A. Stead wrote of his colleague and friend, "Kempner has dedicated his life to the study of vascular disease and after all, his strikes have all been made in areas where the experts said there was no gold. Who in his right mind would have ever thought that rice and fruit could modify vascular disease appreciably? Who would have fed a protein-deficient patient, losing large quantities of protein in his urine, a protein-poor diet? Who would have dared to give a more than 90% carbohydrate diet to a diabetic? Every expert knew that cholesterol levels were not influenced by diet. Nevertheless, all these leads have paid off richly."

In 1949, writing about the beneficial effects of the rice diet in so-called benign essential hypertension and in malignant hypertension, Kempner wrote, "The important result is not that the change in the course of the disease has been achieved by the rice diet but that the course of the disease can be changed."

CASE REPORTS

Discussion by Dr. Kempner

tion the nonprotein nitrogen varied from 238 to 375 mg. per 100 cc. The phenolsulfonphthalein test revealed *no excretion at all* of the dye on several occasions. The total proteins were 6.4 Gm. per 100 cc.; albumin was 4.4 and globulin 2 Gm. per 100 cc.

The average serum calcium (seven determinations) was 4.8, and the phosphorus 11.2 mg. per 100 cc.—the reverse of the normal ratio—, and the ionized calcium ranged from 1.6 to 2.4 mg. per 100 cc. When the ionized, or physiologically active calcium is less than 3 mg. per 100 cc. tetany ensues, and this patient had active tetany on several occasions, which was relieved by large doses of calcium gluconate given intravenously. In passing, it should be noted that the convulsive phenomena of uremia may be due to hypocalcemic tetany. Phosphorus is excreted largely by the kidneys, and when it is retained in the blood because of poor excretion it is excreted in part by the bowel, with resulting hypocalcemia and tetany.

However, when either calcium or phosphorus rises abnormally in the blood, a colloidal complex is formed which is removed from the blood by the reticulo-endothelial cells. These cells store it and return these elements as they are required to maintain the jealously guarded proportion between plasma calcium and phosphorus[2].

The blood pressure, which was 170 over 90 on admission, fell to an average of 135 over 70, where it remained throughout his stay in the hospital. The heart was only slightly enlarged, and the electrocardiogram showed only left axis deviation. The patient was not in cardiac failure, and this fact leads one to speculation as to the absence of hypertension. Could it be that so little functioning kidney remained that the kidney was powerless to furnish a pressor substance to the blood?

During the last few days of his illness the patient was stuporous, and had a fever, doubtless due to some terminal infection, though the notes do not permit me to say what this might have been.

Discussion

DR. KEMPNER: Dr. Hanes has given you the story of this case of kidney disease, from the operation for bladder stones eighteen years ago to the terminal renal breakdown. It is a story of lost opportunities. When the patient finally came to the hospital the chemical functions of the kidneys had ceased, and, if Dr. Hanes's prediction is correct, his kidney parenchyma had been almost completely destroyed. This patient "without" kidneys could furnish the basis for a discussion of the whole clinical physiology of kidney disease. I want to draw your attention to only two points today.

1. Dr. Arthur Grollman has told you recently that hypertension should be regarded as being due to the absence of an anti-pressor substance which, he believes, is formed by the normal kidney, just as the high blood sugar in diabetes mellitus is due to the absence of insulin which is formed by the normal pancreas. According to this theory, our patient "without" kidneys should have had a very high blood pressure, but except for a blood pressure of 170 systolic, 98 diastolic on admission, and a systolic blood pressure ranging between 160 and 185 during the last four days of his life, the average of frequent daily blood pressure readings during the remaining twenty-seven hospital days was 134 systolic, 73 diastolic, although the phenolsulfonphthalein excretion at this time was recorded as zero, and the nonprotein nitrogen averaged 268 mg. per 100 cc.

On the other hand, I believe that a blood pressure raising substance, the production of which depends upon the activity of the kidney cells under pathological conditions, causes hypertension, and I would explain the absence of hypertension in this patient by the assumption that there was only a minimal amount of physiologically active kidney tissue left.

2. This patient up to his death excreted an adequate amount of urine, averaging in the last twenty days of his life 1664 cc. daily; and his urinary nitrogen and urea excretion in this period were considerably higher than we have frequently found them to be in nephritic patients with a normal nonprotein nitrogen.

This point is illustrated in the following table. Patient "B", a chronic nephritic with hypertension, received the same diet, consisting chiefly of carbohydrates, as did the patient under discussion in this conference.

2. Gersh, I.: The Fate of Colloidal Calcium Phosphate in the Dog, Am. J. Physiol. 121:589-94 (March) 1938.

	Blood NPN mg. per 100 cc.	Total urine excretion in 24 hours Volume cc.	Nitrogen Gm.	Urea Gm.
Patient A (under discussion)	300	2150	7.9	11.9
Patient B (chronic nephritis; hypertension)	24	1250	2.8	3.2

These figures illustrate again a point which I have made in previous papers[3,4]: that the high blood nonprotein nitrogen is *not* necessarily due to a *decreased excretion of urea* through the kidneys, but may be due to a *surplus formation of urea*. This surplus urea is formed from amino acids by the liver whenever there is an impairment of the chemical functions of the kidney cells. Normally the kidney cells participate to a great extent in the metabolism of amino acids, converting them into ammonia, which is more easily excreted in the urine than is urea.

3. Kempner, W.: Verminderter Sauerstoffdruck in der Niere als Ursache der "reversiblen" uraemischen Acidose, Klin. Wchnschr. 17:971-73 (July 9) 1938.
4. Kempner, W.: The Role of Oxygen Tension in Biological Oxidations, Cold Spring Harbor Symposia 7: 269, 1939.

Anatomical Discussion

DR. DOUGLAS H. SPRUNT: At autopsy the abdominal cavity contained 1000 cc. of clear fluid. The heart was hypertrophied, weighing 375 Gm. Some yellow areas, which microscopically were seen to be fat, were present in the myocardium.

The kidneys were about normal in size but weighed only 70 Gm. each. On section the kidneys, as shown in the illustration, were only shells, with greatly dilated pelves. The cortex was quite irregular and several yellow nodules were seen. In microscopic sections of the kidney only a few glomeruli were found, and all of these were damaged, showing all stages of necrosis, scarring and hyalinization. There was also extensive round cell infiltration, particularly just beneath the capsule. The larger and middle sized arteries were extensively sclerosed; the arterioles, however, showed only a slight amount of sclerosis. The tubules were dilated and frequently filled with a dense, laminated, eosin staining material. A microscopic prepara-

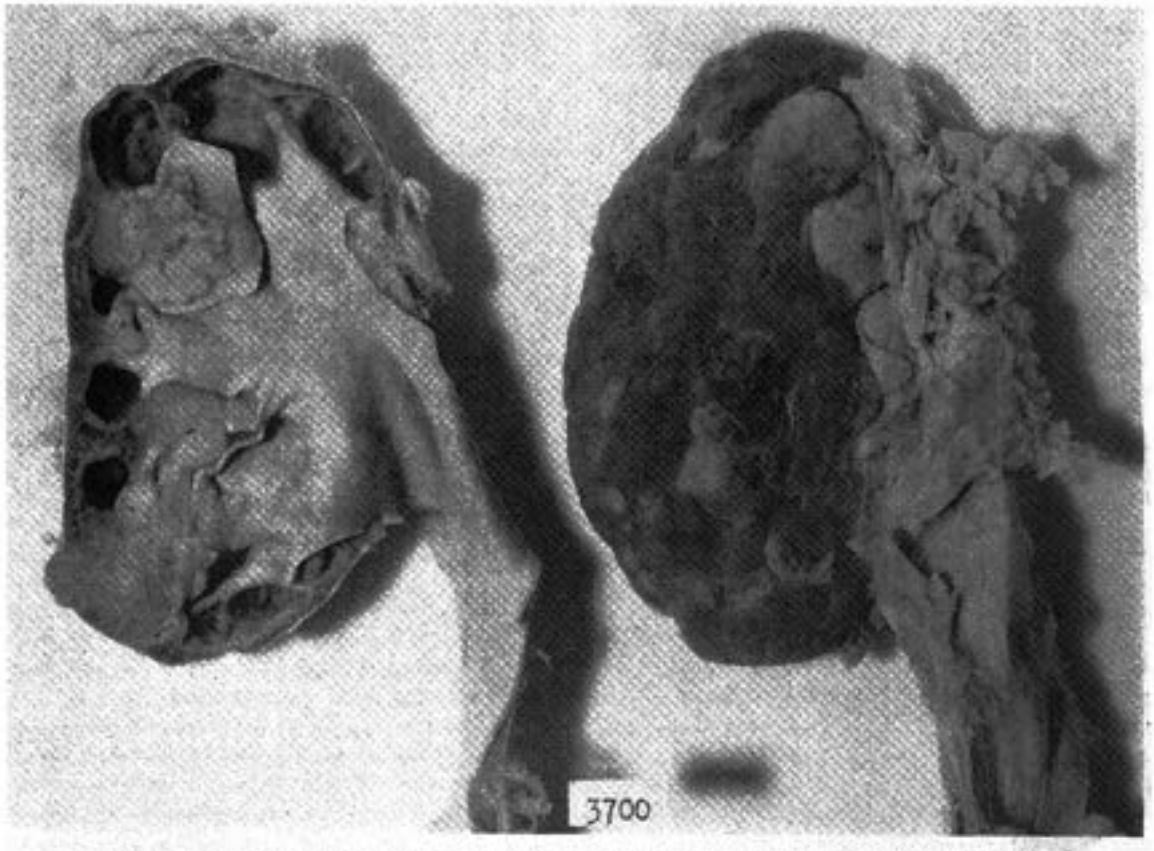

Fig. 1. Photograph of the halves of one kidney, showing the cut surface and the exterior, with the capsule stripped away.

Treatment of Kidney Disease and Hypertensive Vascular Disease with Rice Diet

Poster Presentation and Talk, Chicago Session of the Annual Meeting of the American Medical Association

THE CHICAGO SESSION

J. A. M. A.
May 6, 1944

WALTER KEMPNER, Duke University School of Medicine, Durham, N. C.:

Treatment of Kidney Disease and Hypertensive Vascular Disease with Rice Diet: Exhibit showing that a rice-fruit-sugar diet has proved to be beneficial to the majority of patients treated for acute or chronic kidney disease or hypertensive vascular disease. Blood pressure, nonprotein nitrogen, cholesterol decreased, and the angle of the electrical axis of the heart increased. Flat, diphasic, inverted T_1 waves became more upright, heart became smaller and retinal hemorrhages, exudates and papilledema disappeared. Summary of these effects and those on urinary chloride and nitrogen excretion, plasma proteins and hemoglobin, as well as the effects on individual patients together with photographs of eyegrounds, electrocardiograms and chest films.

This poster presentation was displayed in a large booth at the Chicago Session of the Annual Meeting of the American Medical Association. One of the posters contained the following statement:

The kidney, besides being an organ of *excretion*, plays an important role in the body as an organ of *metabolism* (deamination of amino acids, formation of ammonia, oxidation of keto-acids, etc.)

In kidney diseases there may be impairment of both the *excretory* and the *metabolic* function of the kidney, or of either one alone. Experiments with the Warburg technique have shown that the *metabolism* of isolated kidney cells can be altered quantitatively and qualitatively, reversibly and irreversibly (e.g., by changes in the oxygen concentration of the cell milieu).

Pathological conditions in the kidney (considered here only as an organ of metabolism) may lead to the following changes:

a. Substances which are normally metabolized by the kidney cells increase in amount.

b. Substances which are normally produced by the kidney cell metabolism decrease in amount.

c. Some of the substances normally metabolized by the kidney cells are vicariously metabolized by the liver cells with a resulting increase of the metabolism products of the liver cells.

d. "Abnormal" substances appear which under physiological conditions exist only in an intermediary (nonapparent) phase of the kidney cell metabolism, since normally they are immediately further metabolized to harmless end products.

WE HAVE ASSUMED AS A WORKING HYPOTHESIS:

1. That some of these "abnormal" substances which appear in disturbances of the metabolic function of the kidney cells are "harmful," playing a role either directly or indirectly in the development of hypertension, vascular retinopathy, encephalopathy, heart lesions, and new kidney disease.

2. That the ordinary mixed diet contains constituents which may increase the production of these "abnormal" harmful substances by the diseased kidney cells.

Treatment of Kidney Disease and Hypertensive Vascular Disease With Rice Diet

Walter Kempner, M. D.
Durham, N. C.

Treatment of Kidney Disease and Hypertensive Vascular Disease With Rice Diet

Walter Kempner, M. D.

Durham, N. C.

A dietary regimen consisting of rice, sugar, fruit and fruit juices supplemented by vitamins and iron has been used during the past four years in a series of patients with acute and chronic glomerulonephritis and hypertensive vascular disease. The diet contains in 2000 calories about 15-25 Gm. of protein, 4-6 Gm. of fat, 460-470 Gm. of carbohydrate, 0.25-0.4 Gm. of sodium, and 0.1-0.15 Gm. of chloride. The amount of fruit juices given daily is usually 700-1000 cc.

In a great number of the 140 patients who followed this regimen for periods ranging from four days to thirty months in the hospital and at home, the diet proved to be beneficial. Apart from the subjective improvement, there were favorable changes in the blood pressure, in the heart size, in the electrocardiogram, in the eyegrounds and in the urine and blood chemistry findings, and loss of edema. In no instance has the diet proved to be harmful. Careful medical supervision, however, including studies of blood and urine chemistry, is essential.

A detailed account of the results obtained with the rice regimen will be given elsewhere. The histories of 2 patients, one with chronic glomerulonephritis, the other with hypertensive cardiovascular disease, are given here as a preliminary report.

Case 1

F. C., a 25 year old white farmer, was admitted to Duke Hospital with the complaints of weakness, swollen ankles and "sick headaches".

History. His mother had died at 30 of "Bright's disease". The patient had "always been well;" he had had no childhood disease except "German measles" at the age of 20. A herniorrhaphy was done when he was 5, and a tonsillectomy when he was 10.

In November, 1942, he had a cold, with general malaise, and was in bed for two weeks. There was no sore throat, but he had pain in "both sides", bright red urine, burning on urination, and nocturia (two to three times nightly) for three or four days. He was told that he had albuminuria. In December, 1942, he noticed puffiness around his eyes and ankle edema. He had not been feeling "up to par" since and had been in bed most of the time. In February, 1943, he was rejected by the army because of marked albuminuria and high blood pressure. He had had sick headaches with vomiting spells for the past month. Since the onset of his illness he had been treated with bed rest and a high caloric, high vitamin, salt-poor diet, with restriction of fluids. He was referred to Duke Hospital with the diagnosis of chronic nephritis and nephrosis "which has failed to improve and in which the outlook is bad."

Examination. On June 2, 1943, his temperature was 36.8 C., his pulse 80, respirations 20, blood pressure 186 systolic, 110 diastolic. His height was 167 cm., his weight 74 kilograms. There was a 1 plus pitting sacral edema. His eyegrounds showed bilateral venous engorgement and tortuosity, with narrowing and tortuosity of the arterioles; there were small plaques of exudate around the macula on the left. His teeth were in good condition and his tonsils had been removed. There were no pathological findings in the lungs. His heart was enlarged bilaterally (fig. 2). The rhythm was regular. There was a soft systolic murmur over the entire precordium, loudest over the aorta. The liver was not enlarged. A flat plate of the abdomen showed nothing grossly abnormal.

The hemoglobin was 76 per cent and there were 3,610,000 red blood cells and 8920

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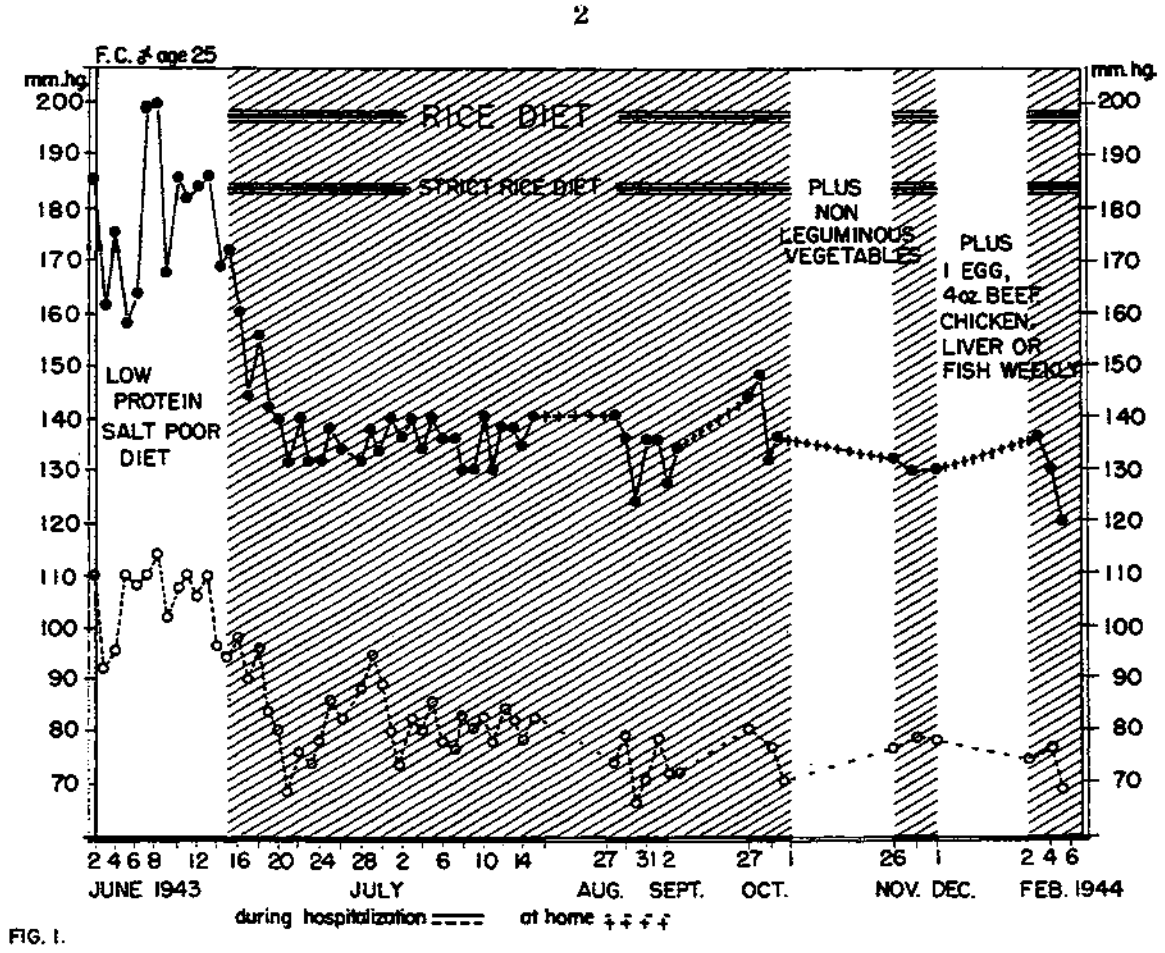

Fig. 1. Blood pressure of patient F. C.

white blood cells. The differential count showed 68 per cent polymorphonuclears, 3 per cent eosinophils, 5 per cent large lymphocytes, 15 per cent small lymphocytes, and 9 per cent monocytes. The corrected sedimentation rate was 27 mm. per hour. Kahn and Kline tests were negative. The blood chemistry was as follows: nonprotein nitrogen 59 mg. per 100 cc. of blood; total proteins 4.6-4.1 Gm. per 100 cc. of plasma, albumin 1.6-1.7 Gm., globulin 3.0-2.4 Gm., albumin-globulin ratio 0.53-0.74. Chlorides (as NaCl) were 662 mg. per 100 cc. of plasma, calcium 8.1 mg. per 100 cc. of serum, phosphorus 5 mg. per 100 cc. of serum. The cholesterol content was 368 mg. per 100 cc. of serum.

Urinalysis showed the specific gravity to be 1.004-1.016. The average amount of albumin during a twelve day period on a low protein, salt-poor diet was 1 Gm. per 100 cc. There were 30 to 40 white blood cells per high power field, 20 to 30 red blood cells. benzidine (3 plus), and cellular and granular casts. The phenolsulfonphthalein test showed 5 per cent excretion at the end of one-half hour, 7.5 per cent at one hour, 5 per cent at one and a half hours, and 5 per cent at two hours. The total excretion in two hours was 22.5 per cent. This test was repeated three days later, with the following results: one-half hour, 5 per cent; one hour, 10 per cent; one and a half hours, 7.5 per cent; two hours, 5 per cent; total excretion in two hours, 27.5 per cent. The family physician reported that in March the excretion in two hours had been 60 per cent.

Impression: Chronic nephritis following acute glomerulonephritis. Hypertension, vascular retinopathy, azotemia, edema, hypoproteinemia, hypercholesterolemia.

Course. The patient was placed on a low protein, salt-poor diet, with fluids limited to 1000-1200 cc., for thirteen days. His weight loss (edema) was 5 Kg. His blood pressure did not change during this period, the average being 178 systolic, 105 diastolic, and the lowest, taken during sleep induced by sodium amytal (0.6 Gm.), 150 systolic, 96 diastolic. The nonprotein nitrogen rose from 59 mg.

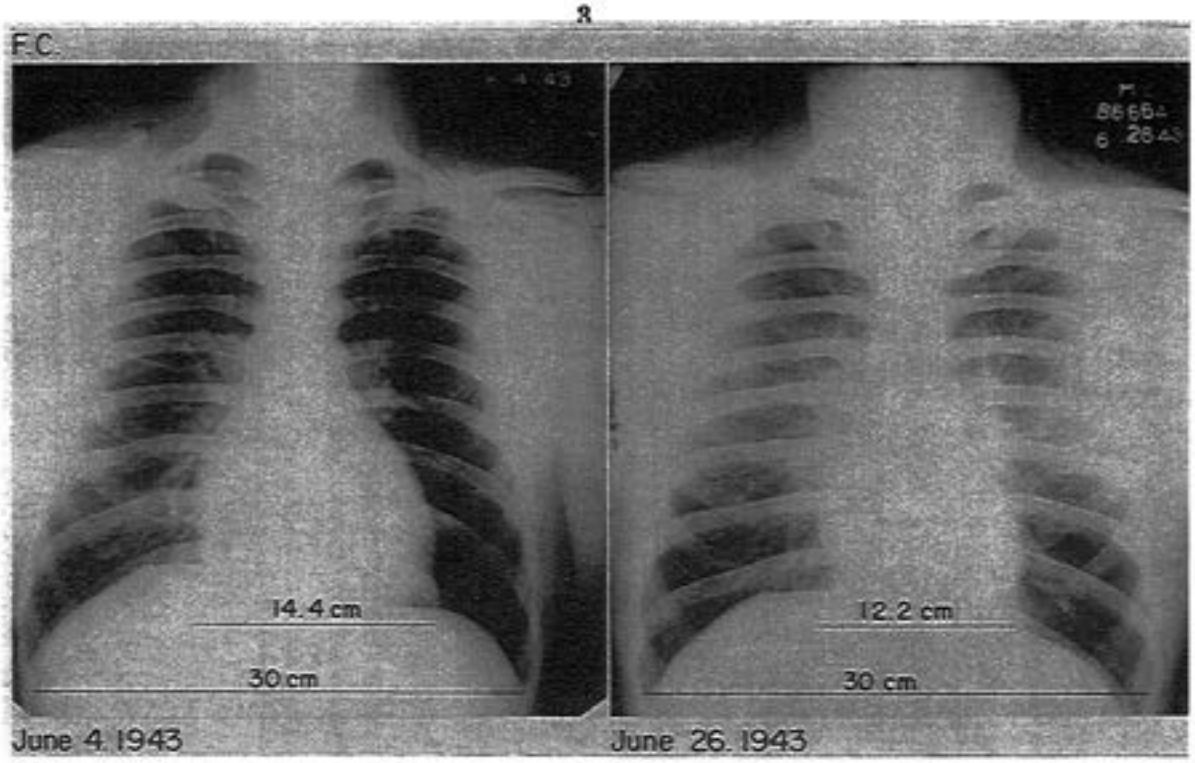

Fig. 2. Reduction of heart size in patient F. C. The transverse diameter is decreased by 18 per cent.

per 100 cc. of blood on admission to 72 mg.

On June 15 the patient was put on the rice regimen (2000 calories, 900 cc. of fruit juices). After six days his blood pressure decreased to 134 systolic, 74 diastolic (fig. 1). After eleven days his heart was much smaller. The transverse heart diameter before the rice diet was started was 14.4 cm.; after eleven days on the rice diet, it was 12.2 cm. (fig. 2).

The patient lost 10 Kg. of weight (edema) in seventeen days (fig. 3); during the remaining sixteen hospital days his weight was constant. After one month on the rice diet, the nonprotein nitrogen was 46 mg. per 100 cc. of blood, chlorides (as NaCl) 512 mg. per 100 cc. of plasma, cholesterol 390 mg. per 100 cc. of serum. The urine contained 0.3 Gm. of albumin per 100 cc.; the hemoglobin was 78 per cent. The patient no longer had headaches. An electrocardiogram showed the previously flattened T waves to be normally upright (fig. 4).

The patient continued the rice regimen at home faithfully except for a larger amount of tomatoes than was allowed. He was seen in the hospital from time to time, and was advised still to rest a great deal. He had no complaints. There was no edema, retinopathy had disappeared, and the heart was normal in size. The average blood pressure reading was 136 systolic, 74 diastolic. The lowest blood pressure reading, in sodium amytal sleep, was 106 systolic, 68 diastolic.

Below, the findings after five months of the rice regimen and partial bedrest in the hospital and at home (B) are compared with those after seven months of a high vitamin, salt-poor diet and bedrest at home and twelve days of a low protein, salt-poor diet and bedrest in the hospital (A).

	A. Before rice diet	*B. After rice diet*
Blood pressure	178/105	128/77
Hemoglobin	76%	69%
Gm. albumin per 100 cc. urine	1.00	0.21
Benzidine in urine	3 plus	0
PSP excretion in two hours	25%	25%
Total plasma proteins (Gm. per 100 cc.) (Fig. 3)	4.1	6.0
A/G ratio	0.71	1.07
Cholesterol (mg. per 100 cc. serum)	368	230
NPN (mg. per 100 cc. blood) (Fig. 3)	72	38

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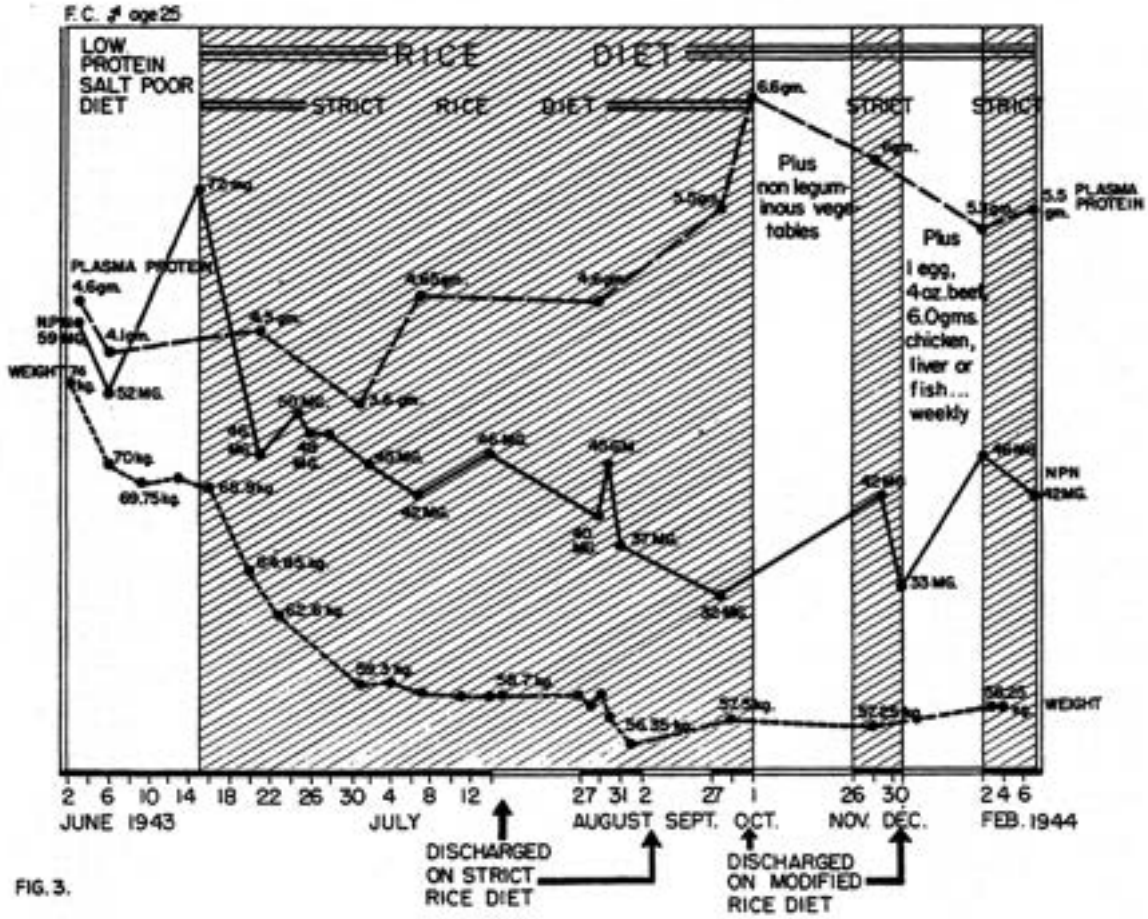

Fig. 3. Weight, nonprotein nitrogen, and total plasma proteins of patient F. C.

The patient was seen again in February, 1944. He was still on the rice diet because of the persistence of albuminuria. He has, however, for the past three months been allowed small amounts of meat and a few eggs. His blood pressure on the last examination was 128 systolic, 73 diastolic; the cholesterol content was 206 mg. per 100 cc. of serum. There was no edema. His eyesight was normal and he was able to carry on his former work as overseer on a small farm without any complaints.

Case 2

R. W., a 36 year old white mill worker, was admitted with the complaints of severe headaches, dizziness, failing vision, exertional dyspnea, and palpitation for about ten months.

History: His mother died at the age of 50 of "Bright's disease" and hypertension. One sister has hypertension; another sister died of hypertension at 33.

The patient had mumps, whooping cough, chicken pox and pneumonia in childhood, and measles at the age of 16. His general health was good, except for nasal obstruction and occasional head colds and sore throats. At 26 he noticed beginning deafness in the left ear. Since the age of 22 or 23, he has had epigastric pain one or two hours after meals, which was relieved by alkali or food and was improved by a bland diet. At 35 there was an episode of vomiting of coffee ground material, and tarry stools for one week.

He is known to have had hypertension for about five years, the systolic blood pressure ranging from 170 to 220, but usually remaining between 175 and 190. He had had headaches for three years, gradually increasing in intensity and becoming very severe in the last ten months. At first they came on early in the morning, awakening the patient after four to five hours of sleep, preventing further sleep, and forcing him to get up; later they occurred at any time of day or night. They were generalized, start-

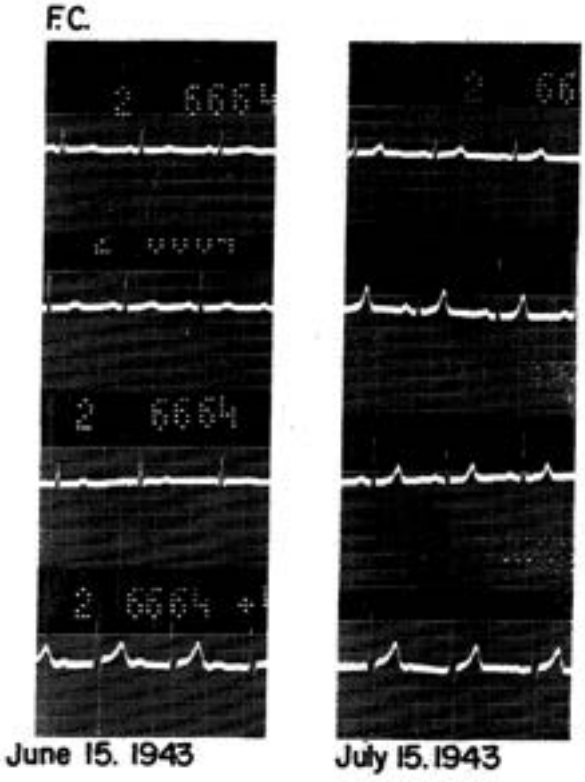

Fig. 4. Electrocardiograms of patient F. C. Flattened T-1, T-2, and T-3 have become normally upright.

ing in the eyeballs and spreading over the entire head into the posterior neck muscles and shoulders. For the past ten to twelve months the patient had noticed progressive dimness of vision "as though something was in front of my eyes." Sometimes he felt that "everything went black." For about the same length of time he had had dizziness, dyspnea on exertion and "pounding of the heart with rapid beating." He had nocturia once nightly, but no other urinary symptoms.

March 19-26, 1943, he was in the Baptist Hospital in Winston-Salem for examination. His blood pressure while he was there varied from 185-210 systolic, 120-144 diastolic. Examination of his eyegrounds there was reported as showing bilateral papilledema (3-4 diopters) with complete blurring of the margins, "silver wire" arteries, moderately distended veins, and arteriovenous nicking. Fluoroscopy of the chest showed cardiac enlargement, with a dilated, tortuous aorta. The pressure of the spinal fluid was 400 mm. The fluid gave a 2 plus Pandy reaction and showed 4 monocytes per cubic millimeter. The diagnosis made was hypertensive cardiovascular disease, hypertensive neuroretinopathy, hypertensive encephalopathy, angina pectoris, malignant hypertension, anomalous left sided colon, diverticulo-

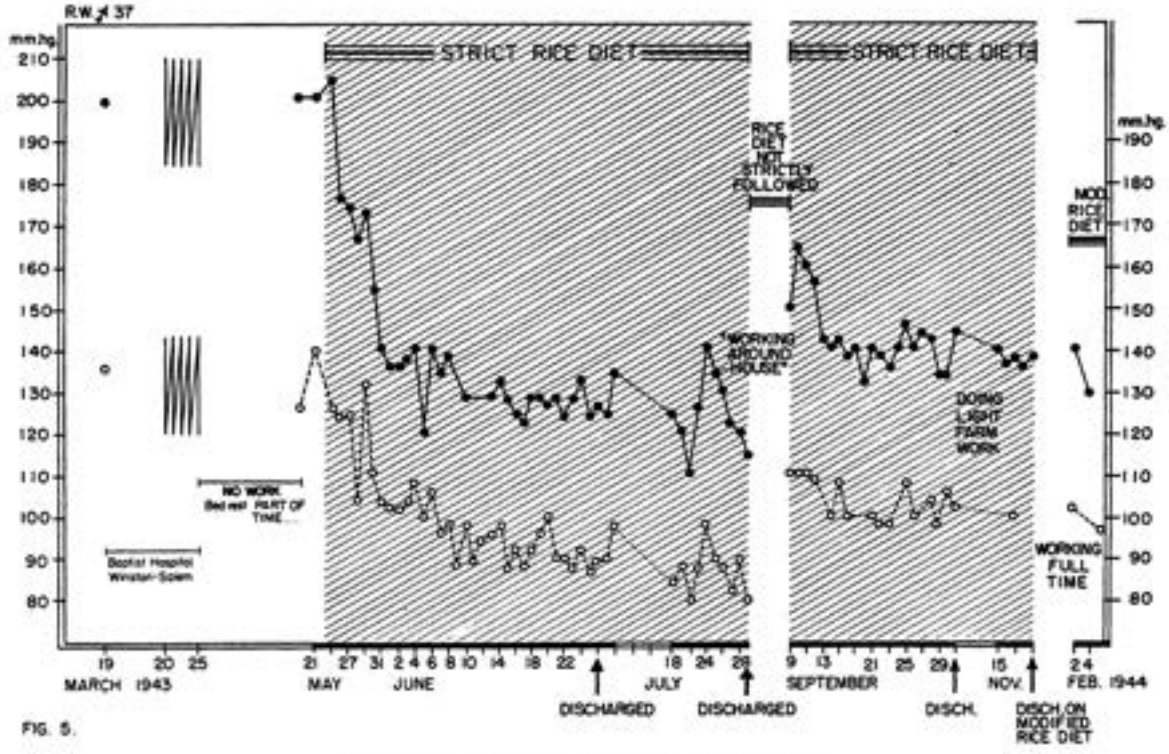

Fig. 5. Blood pressure of patient R. W.

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sis of the colon. The patient was treated with nitroglycerin and nicotinic acid.

During April, 1943, his condition became worse. He had marked substernal pain, severe headache, and further impairment of vision. He was sent to Duke Hospital with the diagnosis of "severe essential hypertension with choking of the discs."

Examination on May 21, 1943, showed the temperature to be 36.6 C., the pulse 66, respirations 20, blood pressure 200-204 systolic, 126-140 diastolic. His height was 170 cm., his weight 74.25 Kg. There was no edema. The pupils reacted well to accommodation and light. Examination of the fundi showed both discs to be very edematous, with extensive peripapillary edema. The veins were engorged and tortuous, with arteriovenous nicking; the arterioles were tortuous and partly covered by retinal edema (fig. 7). The eardrums were intact, but hearing was greatly impaired on the left; air conduction was better than bone conduction in both ears. The sinuses transilluminated well. The adenoids were large, and the tonsils were large and hyperemic. The teeth were in good condition.

The lungs were clear to percussion and auscultation. The heart was enlarged and the sounds forceful. The aortic second sound was greater than the pulmonic second sound. There were no murmurs. The liver was not enlarged and the spleen was not palpable. No tenderness was elicited in the kidney region. Neurological examination gave no pathological findings. A chest film showed the lungs to be clear, and the transverse diameter of the heart to be 14.7 cm.; the aorta was dilated (fig. 8). An x-ray of the abdomen revealed non-rotation of the duodenum, jejunum and ascending colon. The electrocardiogram showed a slightly flattened T_1, upright T_2 and T_3. The angle of the electrical axis was plus 30 degrees (fig. 6).

The hemoglobin was 93 per cent, the red blood cells 4,800,000, and the white blood cells 7200, with 70 per cent polymorphonuclears, 2 per cent eosinophils, 1 per cent basophils, 8 per cent monocytes, 2 per cent large lymphocytes, 17 per cent small lymphocytes. The blood chemistry was as follows: Nonprotein nitrogen 33 mg. per 100 cc. of blood, urea nitrogen 12.6 mg. per 100 cc., urea ratio 38 per cent. The total proteins were 6.6 Gm. per 100 cc. of plasma, albumin

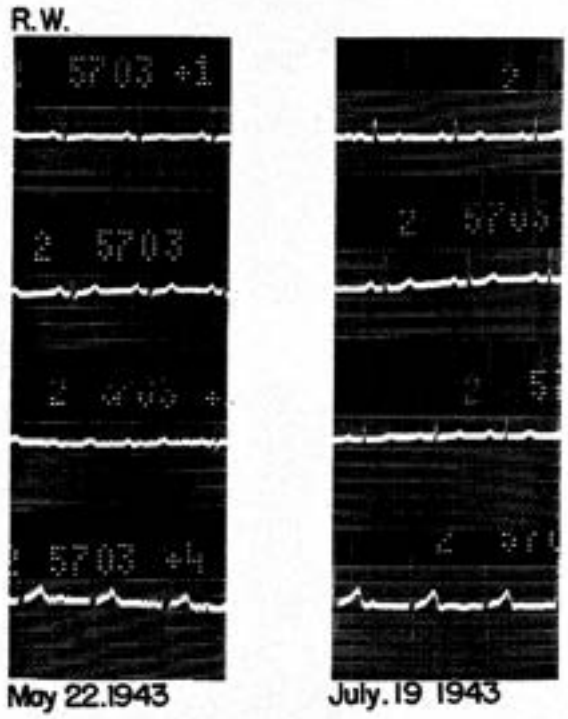

Fig. 6. Electrocardiograms of patient R. W. Flattened T-1 has become more upright. There has been an increase in the angle of the electrical axis from plus 30° to plus 50°.

3.7 Gm., globulin 2.9 Gm., albumin-globulin ratio 1.3. Chlorides (as NaCl) were 572 mg. per 100 cc. of plasma. calcium 8.7 mg. per 100 cc. of serum, phosphorus 3.5 mg. per 100 cc. of serum, cholesterol 260 mg. per 100 cc. of serum.

The urine showed a slight trace of albumin, 1-2 white blood cells per high power field, an occasional hyaline cast, and no red blood cells or benzidine. The total urinary nitrogen was 7.8 Gm. in twenty-four hours; the urea was 13.1 Gm. in twenty-four hours. A phenolsulfonphthalein test showed 17 per cent excretion in one-half hour, 26 per cent in one hour, 11 per cent in one and one-half hours, and 12 per cent in two hours. The total excretion in two hours was 66 per cent. The concentration test showed a range of 1.003-1.027.

Impression: Hypertensive cardiovascular disease; vascular retinopathy.

Course. Because of the severity of the papillitis and the engorgement of the retinal veins, the rice diet (2000 calories, 1000 cc. of fruit juices) was started on the second hospital day. The blood pressure dropped almost immediately (fig. 5), averaging during the first week 181 systolic, 123 diastolic;

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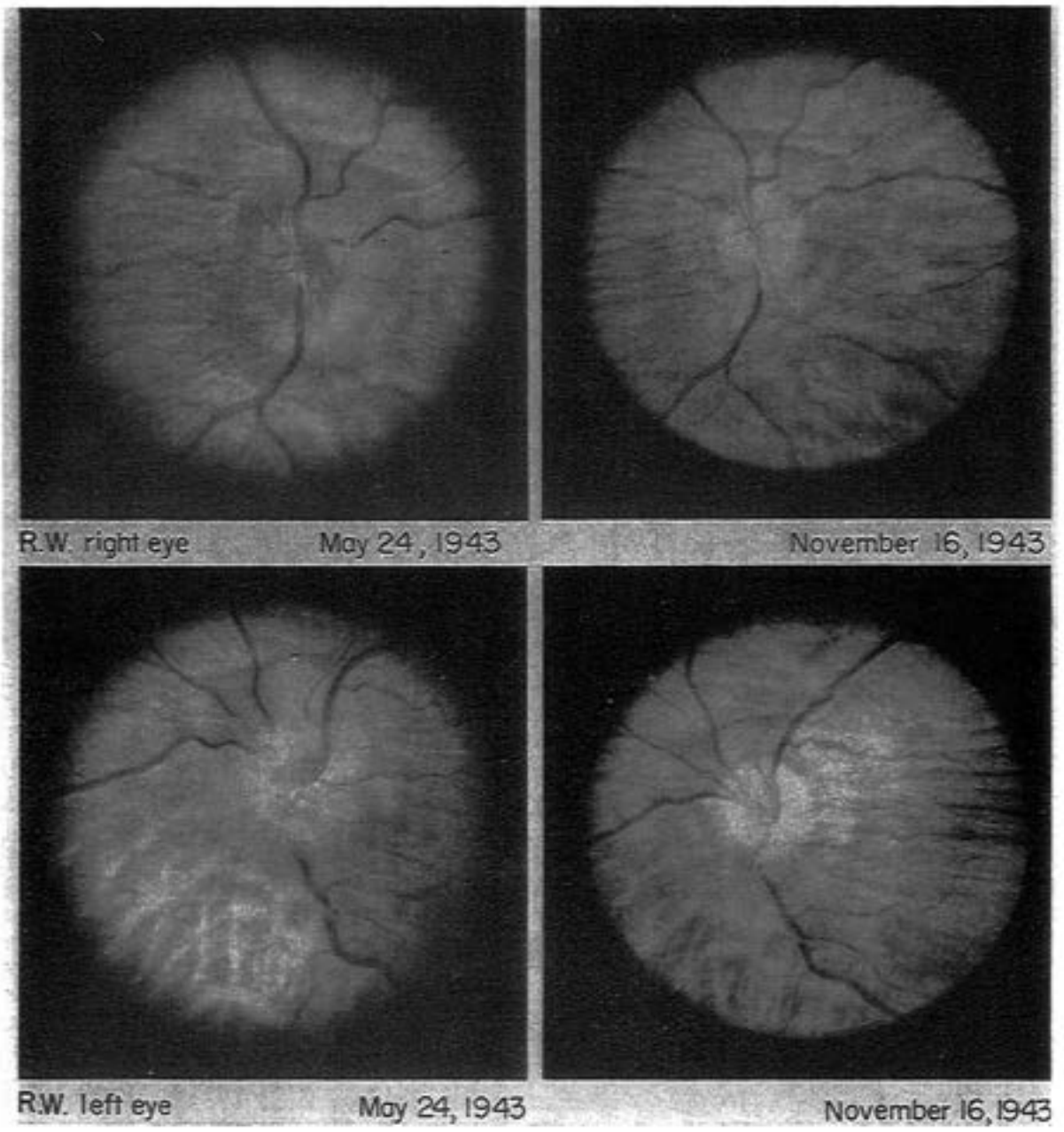

Fig. 7. Disappearance of marked papilledema and peripapillary retinitis in patient R. W. Engorged and tortuous retinal veins have become straighter and smaller in caliber.

during the second week 138 systolic, 104 diastolic; and during the third week 130 systolic, 95 diastolic. It remained at a level of 127 systolic, 92 diastolic until the patient's discharge on June 26 (five weeks after starting treatment). The intense headaches became much milder after two weeks, and disappeared completely in the fourth week. Papilledema and engorgement of the retinal veins began to subside. The patient continued the strict rice regimen at home for the next three weeks, staying in bed for the first two weeks and getting up about three hours daily during the third week. His headaches recurred only on three occasions and were very mild, in no way comparable to the intense headaches he had experienced for ten months before his first admission here. He had the impression that his eyesight had improved considerably, and he had no dyspnea or palpitation.

At readmission on July 19, his blood pres-

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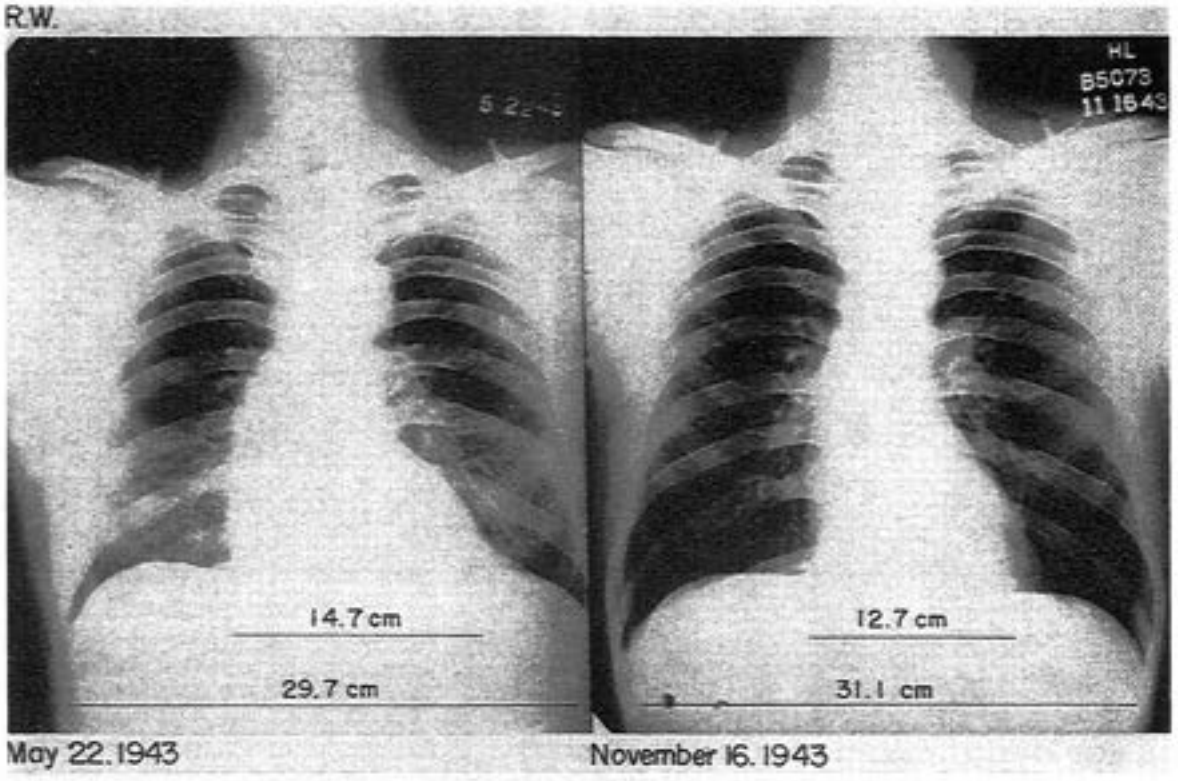

Fig. 8. Reduction of heart size in patient R. W. The transverse diameter is decreased by 16 per cent. The diameter of the great vessels is decreased by 30 per cent.

sure was 124 systolic, 84 diastolic, and it remained at a level of 125 systolic, 88 diastolic during the ten days of his hospital stay. His weight was 64.5 Kg. The hemoglobin was 90 per cent, with 4,420,000 red blood cells. The plasma proteins were 6.8 Gm. per 100 cc., the albumin-globulin ratio 0.88, nonprotein nitrogen 33 mg. per 100 cc. of blood, urea nitrogen 8.3 Gm. per 100 cc. of blood, urea ratio 25 per cent, chlorides (as NaCl) 524 mg. per 100 cc. of plasma, calcium 9.8 mg. per 100 cc. of serum, phosphorus 3.7 mg. per 100 cc. of serum, cholesterol 205 mg. per 100 cc. of serum. The average urinary albumin was 0.02 Gm. per 100 cc. Phenolsulfonphthalein excretion in two hours was 64 per cent. The average urea concentration per 1000 cc. of urine was 4 Gm. (as against an average of 10 Gm. at the start of treatment). An electrocardiogram showed the T waves in lead 1 to be more upright; the angle of the electrical axis was plus 50 degrees (fig. 6). The heart size was markedly decreased and the retinitis had cleared up considerably.

Two ounces of carrots and 2 ounces of onions daily were added to the strict rice diet at discharge. However, in the interval between discharge and the next readmission on September 9, the patient did not follow the diet as outlined, but added "very small quantities" of beans, peas. and corn, as well as butter and, on one occasion, beef. He had been up about eight hours every day during the past two weeks, working around the house. He had been feeling "completely well", had had only a few mild headaches of short duration, no urinary complaints, and only very slight exertional dyspnea. His "vision and strength had improved."

His blood pressure on readmission was 150 systolic, 110 diastolic: his weight was 68.5 Kg., the hemoglobin 91 per cent, plasma proteins 7.4 Gm. per 100 cc., albumin-globulin ratio 1.6, nonprotein nitrogen 30 mg. per 100 cc. of blood, urea nitrogen 4.9 mg. per 100 cc. of blood, urea ratio 16.3 per cent, chlorides (as NaCl) 528 mg. per 100 cc. of serum, calcium 10.1 mg. per 100 cc. of serum, phosphorus 3.6 mg. per 100 cc. of serum, cholesterol 205 mg. per 100 cc. of serum. The urinary albumin was 0.005 per 100 cc., the total nitrogen 1.8 Gm. in twenty-four hours. Urine chlorides averaged in the first three days 1.5 Gm. per 100 cc. (After two weeks of a strict rice diet the average

was 0.23 Gm. per 100 cc.) Phenolsulfonphthalein excretion in two hours was 47 per cent.

The patient was placed again on a strict rice diet. His blood pressure during the first hospital week averaged 151 systolic, 106 diastolic; during the second and third weeks, 139 systolic, 101 diastolic. Papilledema and peripapillary edema had almost completely disappeared. The arterioles were clearly visible. Venous engorgement, tortuosity and arteriovenous compression had markedly decreased. The patient was discharged on September 29, on a strict rice diet.

He returned to the hospital for a check-up on November 15. He felt very well, and had been up and done light work, such as milking. He had had no headache, dizziness, blurring of vision, or urinary symptoms except nocturia about twice nightly. For the last few days before readmission he had had a slight head cold with nasal congestion.

The average of blood pressure readings taken over five days was 138 systolic, 98 diastolic. The hemoglobin was 90 per cent and there were 4,880,000 red blood cells. The nonprotein nitrogen was 25 mg. per 100 cc. of blood. The plasma proteins were 5.9 Gm. per 100 cc., the albumin-globulin ratio 1.8. Chlorides (as NaCl) were 556 mg. per 100 cc. of serum, calcium 10.3 mg., phosphorus 4 mg., cholesterol 170 mg. There was no albumin, white blood cells, red blood cells, or casts in the urine; the urinary total nitrogen was 2 Gm. in twenty-four hours, the urea 2 Gm. in twenty-four hours (775 cc.). Phenolsulfonphthalein excretion in two hours was 58 per cent. The eyegrounds were almost normal (fig. 7).

The transverse diameter of the heart was 12.7 cm., as compared to 14.7 cm. in May (fig. 8); that of the great vessels was 5.7 cm. (7.4 cm. in May). The chest diameter was 31.1 cm., as compared to 29.7 cm. in May. The diet was again modified to include nonleguminous vegetables, one egg, and 2 ounces of beef or liver once a week.

The patient was last seen February 2-4, 1944. He was in excellent condition, and had been working up to eleven hours every day (in charge of a grocery). He had had no headache, dizziness or dyspnea, even when doing such heavy work as unloading feed trucks. His eyesight had greatly improved; he was able to read fine print. His blood pressure ranged from 130 to 140 systolic, 96 to 102 diastolic. His hemoglobin was 86 per cent, red blood cells 5,000,000, nonprotein nitrogen 26 mg. per 100 cc. of blood, urea nitrogen 2.4 mg. per 100 cc. of blood, urea ratio 9.2 per cent. Total plasma proteins were 7.4 Gm. per 100 cc., albumin-globulin ratio 0.8. Chlorides (as NaCl) were 552 mg. per 100 cc. of serum, calcium 9.2 mg., phosphorus 2.9 mg., cholesterol 237 mg.

The patient was told to continue a modified rice regimen with non-leguminous vegetables, plus two eggs and 4 ounces of lean meat a week. He was advised to stop carrying heavy loads and not to work more than eight hours daily.

Summary

The histories of 2 patients, one with chronic glomerulonephritis, and one with hypertensive cardiovascular disease, are given to illustrate the effects which a rice-fruit-sugar diet may have on hypertension, heart enlargement, electrocardiographic changes, edema, hypoproteinemia, nonprotein nitrogen, hypercholesterolemia, albuminuria and retinopathy.

Treatment of Kidney Disease and Hypertensive Vascular Disease with Rice Diet, II

Reprinted from the North Carolina Medical Journal
Vol. 5, No. 7, July, 1944

TREATMENT OF KIDNEY DISEASE AND HYPERTENSIVE VASCULAR DISEASE WITH RICE DIET, II

WALTER KEMPNER, M.D.

DURHAM, N. C.

It is a greater pleasure to talk for fifteen minutes about the treatment of kidney disease and hypertensive vascular disease with the rice diet than to eat this diet three times daily for fifteen days or for fifteen weeks or for fifteen months. Let me start with a number of unpleasant facts: (1) This is a monotonous diet and it does not taste good. It can never become popular. It is a disagreeable medicine. (2) One has to eat it for quite a while before its full effect becomes apparent. (3) The patients should be in the hospital until they are "regulated" on the diet, and constant checks on their blood and urine chemistry should be made. (4) The diet becomes worthless if it is modified by so-called "small" or "minimal" additions according to the patient's own taste.

The basic diet consists of rice, sugar, fruit, fruit juices, vitamins, and iron. No other "routine" medication, such as digitalis or sedatives, is given. The rice diet can be modified for some patients after a time by the addition of non-leguminous vegetables,

Read before the Section on the Practice of Medicine, Medical Society of the State of North Carolina, Pinehurst, May 3, 1944.

From the Department of Medicine, Duke University School of Medicine, Durham, N. C.

small amounts of lean beef, chicken, or liver, or a few eggs. Just so much may be included in the diet as the patient can stand without reacting by an increase in blood pressure, nonprotein nitrogen, or albuminuria.

There is only one excuse for such a therapy: It helps. And if there is a choice between an unpleasant diet on the one side and cardiac failure, uremia, encephalopathy or blindness on the other side, I think the diet is the lesser evil.

I will not discuss today the rationale of this treatment. Neither will I discuss the question as to whether we may be able in the future to substitute for the rice diet similar diets or diet combinations which taste better and have the same therapeutic effect.

Results[1]

Up until April 1, we have given the rice diet to 150 patients, many of whom were critically ill. The periods of treatment varied from four days to thirty months. In no instance has the diet been harmful. It has been ineffective in 41 of the 150 patients (27 per cent), if we judge according to rigid standards and include 18 patients who were in a critical condition when started on the diet and who died after an average time of twenty-two days. In 109 of the 150 patients (73 per cent), the rice diet has proved to be beneficial.

I will show you some of the results.

(Sixty lantern slides of blood pressure

1. Two cases were reported in detail in a previous issue of this Journal (Kempner, Walter: Treatment of Kidney Disease and Hypertensive Vascular Disease With Rice Diet, North Carolina M. J. 5:125-133 (April) 1944).

3

and nonprotein nitrogen charts, photographs of x-rays of hearts, electrocardiograms, and eyegrounds were shown, illustrating the response of patients with acute and chronic kidney disease and hypertensive cardiovascular disease to the rice diet.)

In a great number of patients, blood pressure and nonprotein nitrogen decreased markedly; the enlarged heart became normal in size; the left axis deviation and T-1 inversion in the electrocardiograms decreased; advanced vascular retinopathy improved so much that severe retinal hemorrhages, exudates, and papilledema healed completely and patients who had been blind regained their eyesight and were able to read fine print.

Abstract of Discussion

Dr. Frederic M. Hanes (Durham): Mr. Chairman, Ladies and Gentlemen: You have just listened to a paper by Dr. Kempner which presents the results of more than four years of intensive study of decompensated kidneys. So much that is inaccurate has been published upon the subject of hypertension that it requires some bravery to discuss the matter again. I can only say that Dr. Kempner's work, in my opinion, throws the only hopeful light that I have seen upon the therapy of certain types of hypertension.

Certain things should be made very plain. The study just reported is a meticulous, scientific study of the metabolism in the presence of kidneys which are so injured that they are no longer able to excrete properly the katabolic products of animal proteins. For such patients Dr. Kempner has substituted vegetable protein, derived largely from rice and fruits. There is probably no special virtue in rice, but to keep the prolonged experiment pure, Dr. Kempner has wisely adhered to his special diet with great rigidity. Once he has established the principle involved, it may be possible to alter the diet so as to make it more agreeable to the patient. However, in using his diet one must adhere to the strict limitations he has postulated.

Compensation of Renal Metabolic Dysfunction:
Treatment of Kidney Disease and Hypertensive Vascular Disease
with Rice Diet, III. Part 1

COMPENSATION OF RENAL METABOLIC DYSFUNCTION

Treatment of Kidney Disease and Hypertensive Vascular Disease With Rice Diet, III

WALTER KEMPNER, M. D.
Durham, N. C.

FROM NORTH CAROLINA MEDICAL JOURNAL, FEBRUARY, 1945, VOL. 6, NO. 2

Compensation of Renal Metabolic Dysfunction

Treatment of Kidney Disease and Hypertensive Vascular Disease With Rice Diet, III

Walter Kempner, M. D.

Durham, N. C.

In kidney disease, there may be impairment of both the *excretory* and the *metabolic* functions of the kidney, or of either one alone.

In previous papers[1], experiments with the Warburg technique were published which show that the metabolic reactions of surviving isolated kidney cells—for example, deamination of amino acids, formation of ammonia, oxidation of keto-acids — can be altered quantitatively or qualitatively, reversibly or irreversibly (as by changes in the oxygen concentration of the cell milieu). On the basis of these experiments, the impairment of the renal *metabolic* function was emphasized as an important factor in conditions such as uremic azotemia and acidosis.

This view seems to be supported by clinical observation. Two case histories may serve as examples. A 21 year old girl with mercury bichloride poisoning, who subsequently made a very good recovery, was completely anuric for four days, and from the fifth to the seventh day passed an average of only 128 cc. of urine per day. In spite of the very limited excretion (a total of 385 cc. of urine in seven days), the nonprotein nitrogen, which was measured daily during these seven days, averaged only 87 mg. per 100 cc. of blood and was never higher than 120 mg. (on the seventh day). The second patient, who subsequently died, had chronic glomerulo-nephritis. He had a urine output of 1200-1500 cc. per day, but his nonprotein nitrogen was more than 200 mg. per 100 cc. of blood.

In the first patient, there was no impairment of the *metabolic* function of the kidney, though the *excretion* of urine was almost completely suppressed. There was no rise in blood pressure, no retinopathy. In the second patient, the *excretory* function of the kidney was relatively satisfactory; with a protein intake of about 20 Gm. in twenty-four hours, the urinary excretion in twenty-four hours was 3.7 Gm. of urea nitrogen, 5 Gm. of total nitrogen. The *metabolic* function of the kidney, however, was inadequate, and there resulted hypertension, retinopathy and a nonprotein nitrogen level considerably higher than that of the first patient, whose urinary nitrogen excretion was 0.

That renal excretory insufficiency does not play a decisive role in the production of renal hypertension was shown by the experimental work of Goldblatt[2]. Constriction of the main renal arteries may cause persistent hypertension without disturbance of renal

From the Department of Medicine, Duke University School of Medicine, Durham, N. C.

1. Kempner, W.: (a) Anoxemia of the Kidney as a Cause of Uremic Acidosis: Inhibitory Effect of Low Oxygen Tension on the Deamination of Amino Acids in Kidney Tissue, Am. J. Physiol. 125:117-118 (July) 1938; (b) Verminderter Sauerstoffdruck in der Niere als Ursache der "reversiblen" uraemischen Acidose, Klin. Wchnschr. 17:971-978 (July 9) 1938; (c) Inhibitory Effect of Low Oxygen Tension on the Deamination of Amino Acids in the Kidney, J. Biol. Chem. 124:229-235 (June) 1938; (d) The Role of Oxygen Tension in Biological Oxidations, Cold Spring Harbor Symposia on Quantitative Biology 7:269-288. New Bedford, Mass., The Darwin Press, 1939.

2. (a) Goldblatt, H., Lynch, J., Hanzal, R. F., and Summerville, W. W.: Studies on Experimental Hypertension I, J. Exper. Med. 59:347-379 (March) 1934; (b) Goldblatt, H.: Experimental Hypertension Induced by Renal Ischemia; Harvey Lecture, Bull. New York Acad. Med. 14:525-553 (Sept.) 1938.

excretory function. In some of the experimental hypertensive animals which had no apparent renal excretory insufficiency, degenerative disease of the retinal arterioles developed.

If, for the moment, we disregard the renal *excretory* function and consider the kidney only as an organ of *metabolism* we can assume, as a basis for experimental approach, that pathological conditions in the kidney *may* lead to the following changes:

(a) Substances which are normally removed by the kidney cell metabolism may increase in amount in the blood or tissue fluids.

(b) Substances which are normally produced by the kidney cell metabolism may decrease in amount.

(c) Some of the substances normally metabolized by the kidney cells may be metabolized vicariously by the liver cells, with a resulting increase in the metabolic products of the liver cells[1b,d;3].

(d) "Abnormal" substances may appear in blood or tissue fluids which under physiological conditions exist only in an intermediary, non-apparent phase of the kidney cell metabolism, since normally they are immediately further metabolized to harmless end products.

If we assume that some of these "abnormal" substances which appear when the metabolic function of the kidney cells is disturbed are "harmful" and play a role either directly or indirectly in the development of hypertension, vascular retinopathy, encephalopathy, heart lesions, and new kidney disease, the *working hypothesis* suggests itself: That the ordinary mixed diet may contain constituents which increase the production of these "abnormal," harmful substances by the diseased kidney cells.

Starting from this *working hypothesis*, we have tried to compensate renal metabolic dysfunction by replacing the ordinary mixed diet with a diet limited to rice, sugar, fruit and fruit juices, supplemented by vitamins and iron[4].* The purpose of this paper is to describe the effects obtained with this rice-fruit-sugar diet. The therapeutic possibilities and limitations of similar diets or diet combinations will not be discussed here.

It is not a new experience that special diets are burdensome, and require the faithful cooperation of physician and patient. The rice-fruit-sugar diet is certainly no exception, but it must be repeated that "if there is a choice between an unpleasant diet on the one side and cardiac failure, uremia, encephalopathy or blindness on the other side, the diet is the lesser evil."[4b]

The rice-fruit-sugar diet, which, for the sake of brevity, will be referred to as "the rice diet," contains in 2000 calories about 20 Gm. of protein, 5 Gm. of fat, 460 Gm. of carbohydrate, 0.2 Gm. of sodium and 0.15 Gm. of chloride. Patients with marked hypochloremia, or with symptoms of salt deprivation, are given extra sodium chloride in small amounts, or hydrochloric acid. The fluid intake is usually limited to 700-1000 cc. of fruit juices per day (no water).

Dry rice contains about 350 calories per 100 Gm. The average patient can eat 200 to 300 Gm., or 6½ to 10 ounces daily, which will provide 700 to 1050 calories; the additional calories required must be supplied by the liberal use of sugar and fresh or preserved fruits. All fruits are allowed, with the exception of nuts, dates, avocados, and any dried or canned fruit, or fruit derivatives, to which substances other than sugar have been added. *No salt is permitted.* All fruit juices are allowed, but tomato or vegetable juices are not. Brown or white sugar may be used *ad libitum.* Any kind of rice is used. The rice is boiled or steamed in plain water or fruit juices, without salt, milk or fat.

The palatability of rice depends to some extent upon the way in which it is cooked. Patients, of course, vary in their tastes; some prefer it dry, each grain standing apart, while others prefer it rather wet. If ordinary white rice is used, it may be added slowly to boiling water and boiled for about twenty minutes, then drained in a colander, washed with hot water, and either served at once or steamed for fifteen or twenty minutes. If wet rice is preferred, the washing with hot water is omitted. A little ingenuity in the use of sugar, sliced and preserved fruits, and so forth, will be rewarded. Some patients who object to the sweet taste find the use of lemon juice helpful. Most patients accustom themselves to the rice diet, and some even like it.

3. Kempner, W.: Discussion note, Clinico-Pathological Conference, North Carolina M. J. 4:227-228 (June) 1943.
4. Kempner, W.: (a) Treatment of Kidney Disease and Hypertensive Vascular Disease with Rice Diet. North Carolina M. J. 5:125-133 (April); (b) 273-274 (July) 1944.

*The patient should receive daily as minimal doses: Vitamin A, 5000 units; vitamin D, 1000 units; thiamine chloride, 5 mg.; riboflavin, 5 mg.; niacinamide, 25 mg.; calcium pantothenate, 2 mg.; ferrous sulfate, 0.6 Gm.

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It is not unusual for the weight to decrease more or less markedly during the first twenty days. The reason for this weight loss may be that the amount of food given does not cover the caloric requirements; in such cases, the amount of food must be increased, unless reduction of weight is indicated. Another reason may be that the patient does not eat the full amount of his diet during the first period of adjustment. The most frequent cause is the loss of visible or invisible edema; one patient with marked edema, for example, lost 63 pounds within the first sixteen days on the diet.

During the first few weeks of the rice regime hospitalization greatly facilitates the study and treatment of the patient, but rest in bed, unless the severity of the disease demands it, is neither necessary nor desirable.

A great number of patients on the rice diet have experienced marked relief from giddiness, headache, mental sluggishness and depression, and easy fatigability. Such *subjective* improvement has not been accepted as evidence of successful therapy; only *objective* results, such as loss of edema and changes in urine and blood chemistry findings, in blood pressure, eyegrounds, heart size, and electrocardiograms, have been used to determine the effect of the treatment.

For some of the patients who had shown satisfactory improvement, the diet, after a time, was modified by the addition of nonleguminous vegetables or small amounts of potatoes, lean beef, chicken, fish, or eggs (everything prepared without salt or fat). This was usually done on the insistence of the patient. It must be borne in mind, however, that even these slight modifications change the character of the diet and may spoil the entire effect. Where a critical condition of kidney, heart or retina exists, any compromise may be too much, and the patient may have to pay for the few exceptions made with the reappearance of all the signs and symptoms of the disease. In such cases, the strict diet should be continued indefinitely, just as liver is continued in pernicious anemia and insulin in diabetes.

It must, however, be emphasized that even in the less serious cases the "modified" rice diet, though still preferable to other diets of low protein, fat and salt content, cannot replace in effectiveness the strict rice diet and should be used with caution. Each patient, preferably while in the hospital, should be individually "regulated" on the modified diet by being allowed only so much additional food as he can take without reacting unfavorably with changes in blood pressure, heart size, electrocardiogram, nonprotein nitrogen, and so forth. This will be further illustrated in the case histories and charts.

The diet was used in the treatment of 213 patients in whom *insufficiency of the metabolic function of the kidney* either was evident or could not be ruled out. Eighty-three patients had "primary" kidney disease (7 patients acute glomerulonephritis, 73 chronic glomerulonephritis, chronic pyelonephritis, or nephrolithiasis, 2 lupus erythematosus, and 1 polycystic kidney disease). One hundred and thirty patients were listed under the diagnosis of "hypertensive vascular disease"; 67 of them showed no conclusive evidence of renal *excretory* dysfunction, 63 had definite "secondary" kidney involvement—that is, one or several of the following findings: phenolsulfonphthalein excretion in two hours below 50 per cent, urea clearance below 50 per cent, nonprotein nitrogen above 40 mg. per 100 cc. of blood, more than 0.8 Gm. of albumin per 1000 cc. of urine, range in specific gravity (concentration-dilution test) of less than 0.012, 5 red blood cells or 3 granular casts per high power field. The diet was used for periods varying from four days to thirty-two months; after two to five months some of the modifications listed were permitted in most cases.

The diet has been ineffective in 75 of the 213 patients treated (35 per cent), if we judge according to rigid standards and include 27 patients who were in a critical condition when started on the diet and who died after an average period of twenty-five days. In 138 of the 213 patients (65 per cent) the diet has proved to be beneficial. In no instance has it been harmful; careful medical supervision, however, including control of blood and urine chemistry, is essential.

Protein Requirements of Patients on Rice Diet

We were afraid that the small amount of protein contained in the rice diet would lead to a depletion of the plasma proteins and to a decrease in hemoglobin; but we were willing to take these risks, since we thought that such deficiencies could be corrected at some later stage after the imminent danger of uremic or cardiac death or of blindness had been overcome. The determinations,

however, showed that the rice diet did not cause depletion of the plasma proteins or decrease in the hemoglobin.

Urinary nitrogen excretion

With the reduced protein and high carbohydrate intake of the rice diet, the total nitrogen excretion in the urine decreases to a level considerably below that found in complete fasting. Three hundred and three determinations of the total nitrogen excretion in the urine of 82 patients with kidney disease (whose nonprotein nitrogen was not above 50 mg. per 100 cc. of blood) or with "hypertensive vascular disease," before and after they had received the rice diet for varying periods of time, are summarized in table 1.

TABLE 1

Nitrogen Excretion in Urine

Period on rice diet	*Number of patients*	*Number of determinations*	*Gm. total nitrogen per 1000 cc. of urine (average)*	*Gm. total nitrogen excreted in 24 hours (average)*
0	55	64	7.09	7.60
1-14 days	52	90	5.10	4.83
15-30 days	46	55	3.59	3.60
1-2 months	26	33	3.12	2.93
Over 2 months	32	61	2.26	2.26

In many instances the protein intake before the beginning of the diet had been limited, either because the patients were too ill to eat the full amount of a mixed diet, or because they had received other low protein diets. (The regular hospital diet contains about 65 Gm. of protein.) Consequently, the nitrogen excretion in the urine before the beginning of the rice diet was relatively low, averaging 7.09 Gm. per 1000 cc., 7.6 Gm. in twenty-four hours.

After two months of rice diet, the nitrogen excretion in the urine averaged 2.26 Gm. per 1000 cc., 2.26 Gm. in twenty-four hours. If an allowance of 0.9 Gm. per twenty-four hours is made for the excretion of nitrogen other than that excreted in the urine, the total nitrogen loss in twenty-four hours is about 3.16 Gm. With a daily intake of $3.2 \times 6.25 = 20$ Gm. of protein, these patients are in protein equilibrium.

Plasma proteins

The rice diet does not cause depletion of the plasma proteins. The greatest decrease —from 7.7 to 5.9 Gm. of protein per 100 cc. of plasma—was found after twenty-four weeks of rice diet in a patient with chronic nephritis. This patient had had a number of gastro-intestinal upsets with diarrhea, during which he had been able to eat only part of the diet. (After three weeks of rice diet, the plasma proteins were 6.9 Gm. per 100 cc., after ten weeks 7.6 Gm., after eighteen weeks 6.35 Gm.) The greatest increase —from 5.4 to 7.2 Gm. of protein per 100 cc. of plasma—was found after twenty-two days of rice diet in a patient who was recovering from acute glomerulonephritis with marked edema. The average plasma protein concentration of 120 patients, many of whom were in a critical condition, was:

Before rice diet.....6.3 Gm. per 100 cc. of plasma
After 90 days (average) of rice diet .....6.3 Gm. per 100 cc. of plasma

Hemoglobin

The rice diet does not cause a decrease in the hemoglobin. The average hemoglobin value (per cent of 15.5 Gm.) in 165 patients, including 23 moribund patients with an average nonprotein nitrogen of 138 mg. per 100 cc. of blood, was:

Before rice diet .....79.9 per cent
After 75 days (average) of rice diet....80.1 per cent

The fact that the average values of the plasma proteins and hemoglobin do not decrease on the rice regime, but are maintained at a constant level, is in itself of positive significance when we consider how common progressive hypoproteinemia and progressive anemia are in kidney disease.

Urine Chlorides and Plasma Chlorides of Patients on Rice Diet

With the reduced chloride intake of the rice diet, the chloride excretion in the urine decreases. A typical example is given in table 2.

TABLE 2

Plasma and Urine Chlorides of a Patient on the Rice Diet

Period on rice diet (days)	*Plasma chlorides (milli-equivalents)*	*Urine chlorides (milli-equivalents)*
0 (regular hospital diet)	99	83
0 (regular hospital diet)		73
2		47
4		20.8
10		9
18	95	
21		2.7
26	95	3.2

The lowest urine chloride concentration found in this series (as compared to about 60 to 150 milli-equivalents in a person on a normal diet) was 1.35 milli-equivalents, with a total urinary excretion of 18 mg. of chloride per twenty-four hours, in a patient with "hypertensive vascular disease" without apparent renal excretory dysfunction

who had been on the rice diet for seventy days. The plasma chlorides were 93.1 milli-equivalents (as sodium chloride, 544 mg. per 100 cc. of plasma). The highest plasma chloride concentration found after more than two months of the rice regime was 102.3 milli-equivalents (as sodium chloride, 598 mg. per 100 cc. of plasma) in a patient with chronic nephritis in the nephrotic stage; the urine chloride concentration was about 5.2 milli-equivalents, the total urinary chloride excretion per twenty-four hours, 160 mg.

The average values of 381 determinations of the plasma chlorides in 91 non-uremic patients (nonprotein nitrogen below 75 mg. per 100 cc. of blood) were:

Before rice diet .....97.0 milli-equivalents (as sodium chloride, 567 mg. per 100 cc. of plasma)

After 44 days (average) of rice diet .....91.7 milli-equivalents (as sodium chloride, 536 mg. per 100 cc. of plasma)

The rice diet as such—within the periods studied—does not cause a reduction of the plasma chlorides below the critical level. Since critical hypochloremia, however, is frequent in patients with kidney disease, symptoms such as muscle cramps, increased nervousness, and anorexia must be watched for and the chloride concentration in the plasma must be checked frequently.

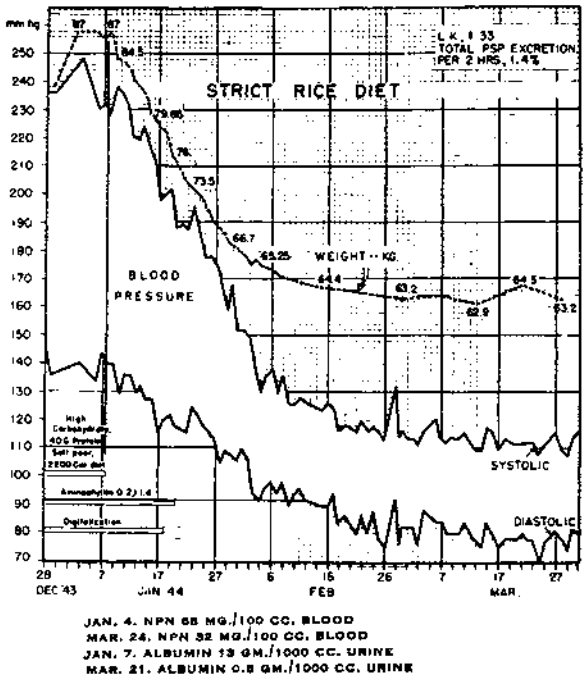

Fig. 1. L.K. (f., 33). Terminal stage of chronic nephritis with cardiorenal failure and uremic pericarditis. No decrease of hypertension and edema after ten days of high carbohydrate, 40 Gm. protein, salt-poor diet, with aminophylline and digitalis. Decrease of blood pressure to normal and loss of 50 pounds of edema on rice diet.

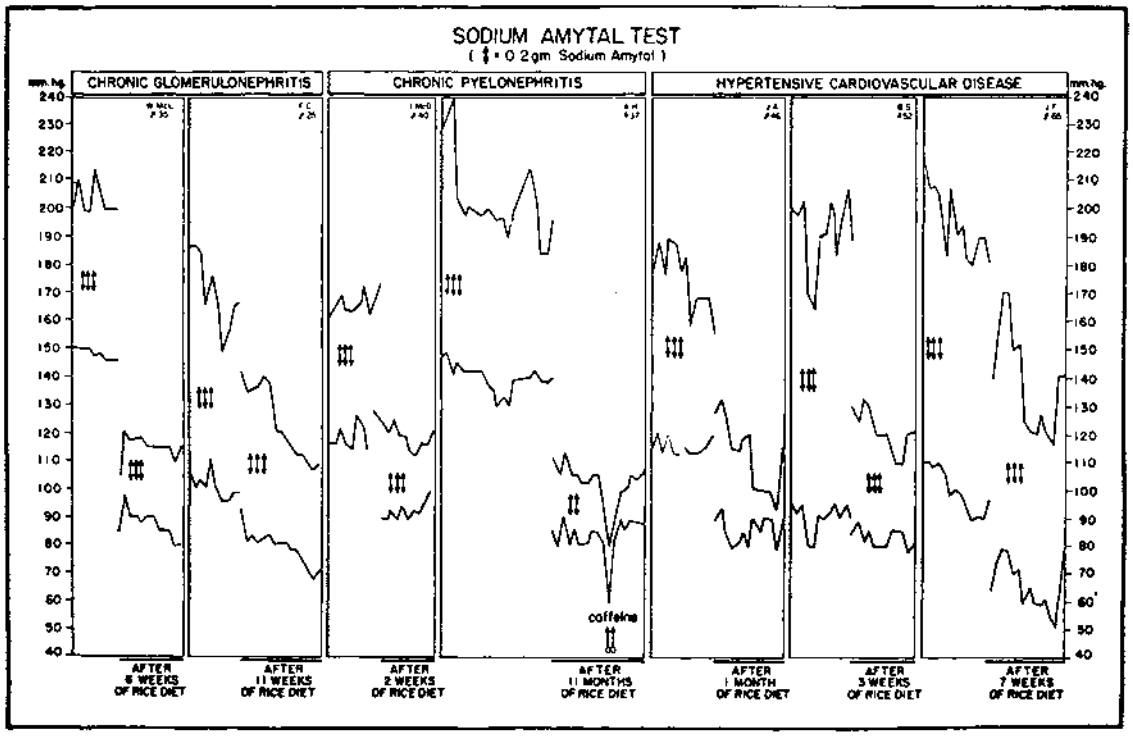

Fig. 2. Effect of 0.6 Gm. of sodium amytal on the blood pressure of patients with chronic nephritis and "hypertensive vascular disease" before and after rice diet.

6

Hypertension

One hundred and ninety-two patients[5] with hypertension (115 males, 77 females), aged 8 to 75 (average 41 years), were treated with the strict or modified rice diet. Five patients had acute glomerulonephritis, 57 patients chronic glomerulonephritis, chronic pyelonephritis, or nephrolithiasis, 1 patient polycystic kidney disease. In 129 patients, the diagnosis of "hypertensive vascular disease" was made; 63 of these patients showed signs of "secondary" kidney involvement; in 66, no conclusive evidence of kidney involvement was found.

Eleven patients were not hospitalized and were seen only in the out-patient clinic. One hundred and eighty-one patients received the rice diet in the hospital. A great number of patients were in a hopeless condition when they were started on the diet, and were given as much as they were able to take. Of these, 25 died after six to eighty-one days on the strict diet (average twenty-five days). Of the remaining 156 hospital patients, 42 were on the diet (first admission) for four to fourteen days (average ten days); 114 patients (first admission) for fifteen to eighty-four days (average thirty-one days). Sixty-three of the 156 patients were readmitted to the hospital for one to eight re-examinations and 13 patients were periodically re-examined in the clinic, after continuing the diet (more or less strictly) at home for periods varying from two weeks to five months.

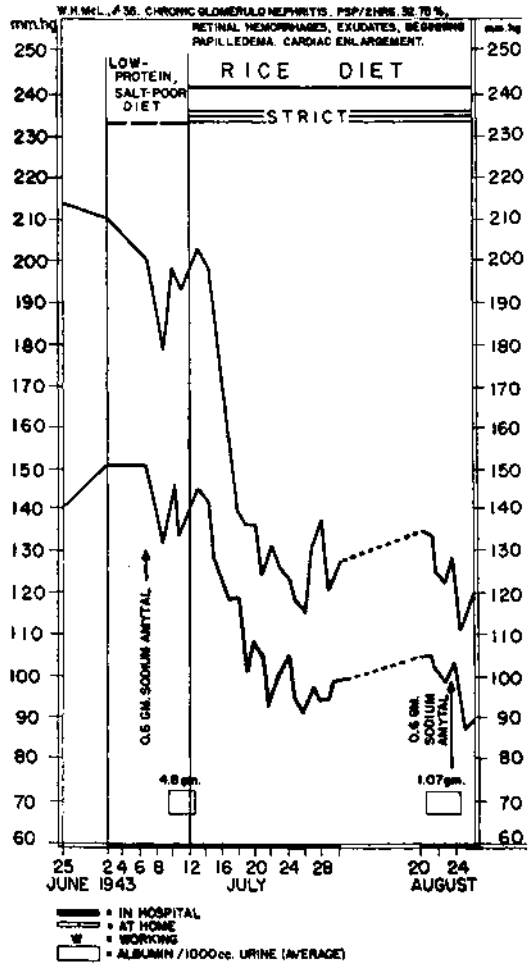

Fig. 3. W.H.McL. (m., 35). Chronic glomerulonephritis. No decrease of hypertension on high carbohydrate, low protein, salt-poor diet. Decrease of blood pressure to normal on rice diet.

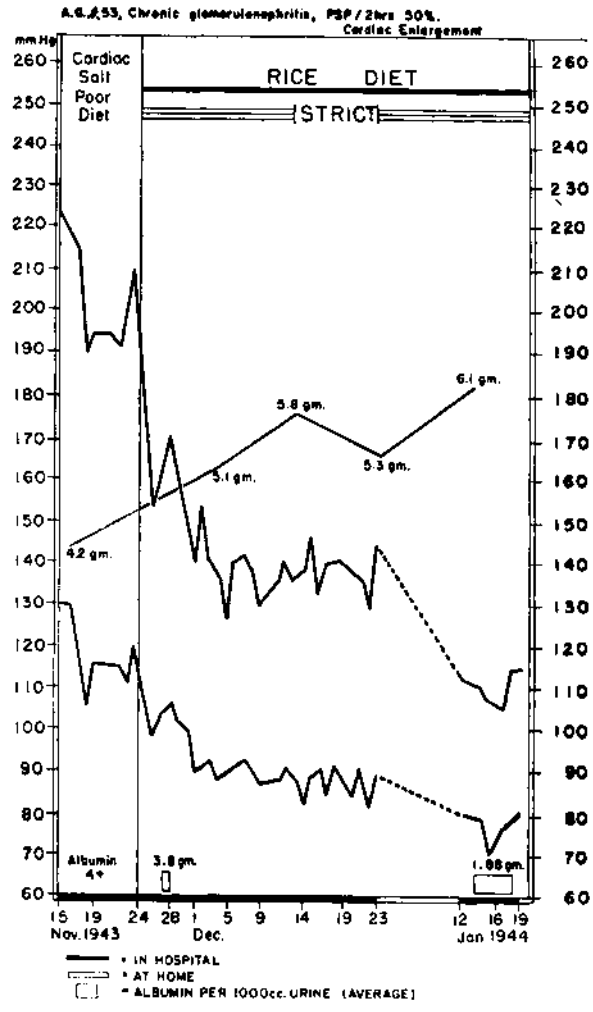

Fig. 4. A.G. (m., 53). Chronic nephritis. No decrease of hypertension after nine days of "cardiac salt-poor" diet. Decrease of blood pressure to normal on rice diet, with increase of plasma proteins.

5. One patient with "hypertensive vascular disease" is not included because the rice diet had been started at home several weeks before the first examination in this hospital.

7

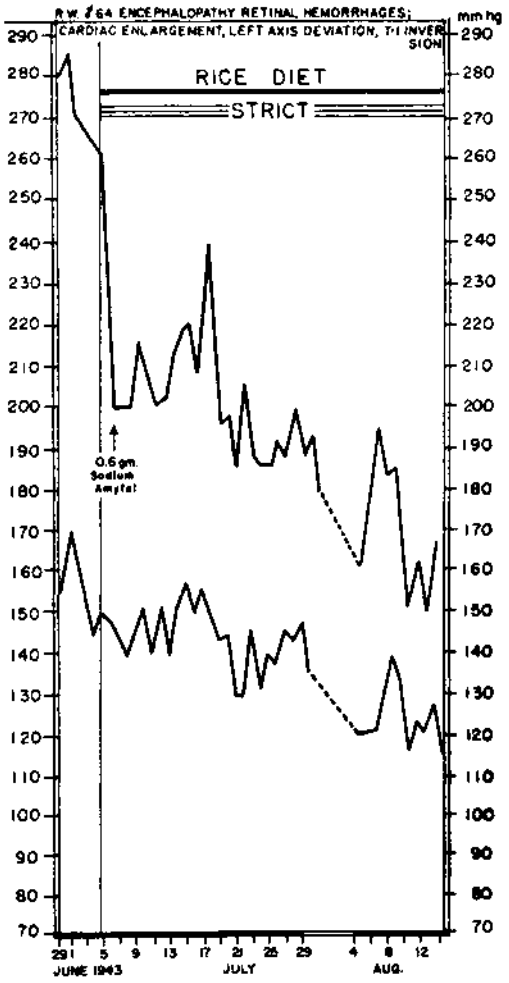

Fig. 5. R.W. (m., 64). "Hypertensive vascular disease." No decrease of hypertension after five days of 60 Gm. protein hospital diet. Decrease of blood pressure on rice diet.

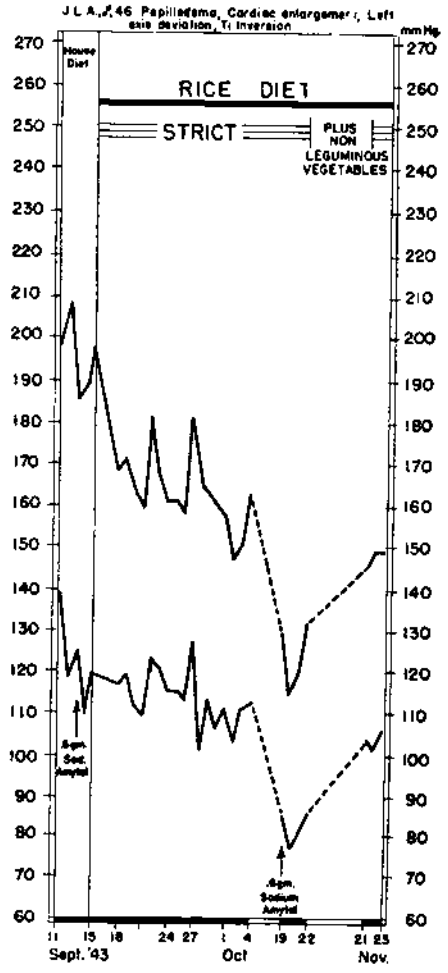

Fig. 6. J.L.A. (m., 46). "Hypertensive vascular disease." Decrease of blood pressure to normal on rice diet. Increase of blood pressure on addition of non-leguminous vegetables.

The routine blood pressure readings were taken at about the same time each day by the same examiner, with the patient in a recumbent position and after a period of about twenty minutes' rest. For the sodium amytal test, blood pressure readings were made every hour during the sodium amytal sleep, as well as during a six hour period both before and after it. Six-tenths of a gram of sodium amytal was used for the test.

In 5 patients with *acute glomerulonephritis* and hypertension, the blood pressure decreased from a level of 170 systolic, 109 diastolic (average) to 108 systolic, 66 diastolic (average), within an average period of fifteen days on the rice diet.

Of the 58 patients with hypertension and *chronic glomerulonephritis, chronic pyelonephritis, nephrolithiasis, or polycystic kidney disease,* 11 died after seven to fifty-one days (average thirty days) on the strict rice diet. The initial blood pressure readings in these patients averaged 208 systolic, 137 diastolic.

In 10 of the remaining 47 patients (21 per cent) the hypertension was not improved; the decrease in the mean arterial pressure was less than 20 mm. of mercury, the average blood pressure decreasing from a level of 208 systolic, 132 diastolic to a level of 192 systolic, 124 diastolic after sixty-seven days (average) on the rice diet.

In 37 of the 47 patients (79 per cent) the hypertension was improved, the average blood pressure decreasing from a level of 194 systolic, 124 diastolic to a level of 140 systolic, 96 diastolic after an average of seventy-seven days on the diet. (Table 3).

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TABLE 3

EFFECT OF RICE DIET ON BLOOD PRESSURE

	Blood Pressure before Rice Diet (mm. Hg.)	*Blood Pressure after Rice Diet (mm. Hg.)*	*Change in Systolic and Diastolic Blood Pressure (mm. Hg.)*	*Change in Mean Arterial Pressure (mm. Hg.)*	*Days on Rice Diet*
HYPERTENSION ON BASIS OF ACUTE GLOMERULONEPHRITIS					
1.	165/97	103/70	− 62/−27	−44.5	13
2.	167/112	120/55	−47/−57	−52	22
3.	182/107	108/78	− 74/−29	−51.5	23
4.	150/125	95/50	− 55/−75	−65	10
5.	184/104	114/76	− 70/−28	−49	6
Average	**170/109**	**108/66**	**− 62/−43**	**−52.5**	**15**
HYPERTENSION ON BASIS OF CHRONIC GLOMERULONEPHRITIS, CHRONIC PYELONEPHRITIS, NEPHROLITHIASIS, OR POLYCYSTIC KIDNEY DISEASE					
Hypertension not improved (Decrease of mean arterial pressure less than 20 mm. Hg.)					
1.	168/117	152/106	− 16/−11	−13.5	7
2.	202/117	187/112	− 15/− 5	−10	8
3.	209/137	191/130	− 18/− 7	−12.5	12
4.	169/98	148/91	− 21/− 7	−14	19
5.	244/144	210/150	− 34/+ 6	−14	7
6.	211/169	189/156	− 22/−13	−17.5	10
7.	185/115	165/98	− 20/−17	−18.5	7
8.	225/129	210/115	− 15/−14	−14.5	16
9.	240/150	(154/108	− 86/−42	−64	166)
		240/142	0/− 8	− 4	548
10.	228/143	225/139	− 3/− 4	− 3.5	36
Average	**208/132**	**192/124**	**− 16/− 8**	**−12**	**67**
Hypertension improved (Decrease of mean arterial pressure 20-96.5 mm. Hg.)					
1.	250/174	131/100	−119/−74	−96.5	90
2.	189/125	139/100	− 50/−25	−37.5	313
3.	193/118	150/107	− 43/−11	−27	34
4.	169/93	121/77	− 48/−16	−32	20
5.	218/146	125/89	− 93/−57	−75	29
6.	200/140	115/85	− 85/−55	−70	24
7.	167/120	115/81	− 52/−39	−45.5	63
8.	157/111	122/88	− 35/−23	−29	34
9.	171/105	131/72	− 40/−33	−36.5	77
10.	201/130	163/125	− 38/− 5	−21.5	24
11.	277/157	213/121	− 64/−36	−50	25
12.	222/148	179/127	− 43/−21	−32	11
13.	227/135	165/114	− 62/−21	−41.5	20
14.	155/98	128/74	− 27/−24	−25.5	135
15.	202/116	111/78	− 91/−38	−64.5	53
16.	188/111	124/85	− 64/−26	−45	412
17.	172/99	120/86	− 52/−13	−32.5	19
18.	158/107	122/79	− 36/−28	−32	95
19.	228/145	113/79	−115/−66	−90.5	180
20.	166/109	134/88	− 32/−21	−26.5	35
21.	169/110	114/82	− 55/−28	−41.5	55
22.	237/139	117/81	−120/−58	−89	48
23.	222/136	198/120	− 24/−16	−20	23
24.	160/94	120/80	− 40/−14	−27	30
25.	154/111	123/92	− 31/−19	−25	14
26.	200/120	165/112	− 35/− 8	−21.5	12
27.	190/139	120/94	− 70/−45	−57.5	43
28.	180/121	127/83	− 53/−38	−45.5	65
29.	189/136	161/116	− 28/−20	−24	21
30.	257/153	230/130	− 27/−23	−25	240
31.	189/147	161/103	− 28/−44	−36	25
32.	230/160	191/131	− 39/−29	−34	356
33.	165/108	122/92	− 43/−16	−29.5	95
34.	164/89	127/86	− 37/− 3	−20	14
35.	172/103	121/88	− 51/−15	−33	24
36.	210/127	147/97	− 63/−30	−46.5	80
37.	166/115	129/99	− 37/−16	−26.5	9
Average	**194/124**	**140/96.**	**− 54/−28**	**−41**	**77**

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TABLE 3—Continued

	Blood Pressure before Rice Diet (mm. Hg.)	*Blood Pressure after Rice Diet (mm. Hg.)*	*Change in Systolic and Diastolic Blood Pressure (mm. Hg.)*	*Change in Mean Arterial Pressure (mm. Hg.)*	*Days on Rice Diet*
"HYPERTENSIVE VASCULAR DISEASE" WITH "SECONDARY" RENAL INVOLVEMENT					
Hypertension not improved (Decrease of mean arterial pressure less than 20 mm. Hg.)					
1.	227/155	215/135	− 12/−20	− 16	64
2.	242/151	210/152	− 32/+ 1	−15.5	13
3.	223/130	222/118	− 1/−12	− 6.5	13
4.	229/113	207/102	− 22/−11	−16.5	216
5.	176/103	151/92	− 25/−11	−18	35
6.	240/159	230/159	− 10/ 0	− 5	12
7.	244/147	231/152	− 13/+ 5	− 4	28
8.	186/114	170/110	− 16/− 4	−10	25
9.	196/98	181/95	− 15/− 3	− 9	5
10.	194/133	175/117	− 19/−16	−17.5	32
11.	225/124	216/121	− 9/− 3	− 6	7
12.	211/126	222/134	+ 11/+ 8	+ 9.5	10
13.	233/140	216/144	− 17/+ 4	− 6.5	25
14.	170/110	167/112	− 3/+ 2	− 0.5	4
15.	240/150	225/145	− 15/− 5	−10	19
16.	236/134	206/128	− 30/− 6	−18	19
17.	200/126	194/130	− 6/+ 4	− 1	88
18.	199/148	206/154	+ 7/+ 6	+ 6.5	30
19.	183/94	161/93	− 22/− 1	−11.5	5
20.	222/134	229/145	+ 7/+11	+ 9	18
21.	226/156	209/141	− 17/−15	−16	126
22.	171/96	148/92	− 23/− 4	−13.5	68
Average	**212/129**	**200/126**	**− 12/− 3**	**− 7.5**	**39**
Hypertension improved (Decrease of mean arterial pressure 20-77 mm. Hg.)					
1.	195/121	147/102	− 48/−19	−33.5	67
2.	242/144	176/119	− 66/−25	−45.5	58
3.	179/136	148/114	− 31/−22	−26.5	9
4.	164/100	112/76	− 52/−24	−38	82
5.	240/128	168/91	− 72/−37	−54.5	82
6.	195/120	144/89	− 51/−31	−41	585
7.	210/120	186/101	− 24/−19	−21.5	8
8.	240/140	197/124	− 43/−16	−29.5	57
9.	225/130	153/93	− 72/−37	−54.5	38
10.	200/108	142/69	− 58/−39	−48.5	228
11.	236/156	203/141	− 33/−15	−24	19
12.	188/122	157/106	− 31/−16	−23.5	84
13.	236/120	190/85	− 46/−35	−40.5	59
14.	227/120	189/110	− 38/−10	−24	29
15.	214/138	151/109	− 63/−29	−46	53
16.	204/150	172/108	− 32/−42	−37	34
17.	184/102	136/87	− 48/−15	−31.5	60
18.	211/134	149/111	− 62/−23	−42.5	14
19.	233/138	190/106	− 43/−32	−37.5	79
20.	225/124	159/94	− 66/−30	−48	21
21.	245/139	171/107	− 74/−32	−53	30
22.	235/135	200/110	− 35/−25	−30	17
23.	211/94	128/76	− 83/−18	−50.5	80
24.	251/128	203/121	− 48/− 7	−27.5	81
25.	244/119	193/86	− 51/−33	−42	38
26.	200/129	125/88	− 75/−41	−58	60
27.	220/150	168/118	− 52/−32	−42	31
28.	275/156	155/122	−120/−34	−77	40
Average	**219/128**	**165/102**	**− 54/−26**	**−40**	**73**
"HYPERTENSIVE VASCULAR DISEASE" WITHOUT CONCLUSIVE EVIDENCE OF "SECONDARY" RENAL INVOLVEMENT					
Hypertension not improved (Decrease of mean arterial pressure less than 20 mm. Hg.)					
1.	183/122	171/120	− 12/− 2	− 7	25
2.	200/104	172/101	− 28/− 3	−15.5	21
3.	177/115	166/109	− 11/− 6	− 8.5	12
4.	165/108	148/92	− 17/−16	−16.5	38
5.	203/127	188/115	− 15/−12	−13.5	72
6.	165/107	146/107	− 19/ 0	− 9.5	60
7.	215/124	192/115	− 23/− 9	−16	34

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TABLE 3—Continued

	Blood Pressure before Rice Diet (mm. Hg.)	Blood Pressure after Rice Diet (mm. Hg.)	Change in Systolic and Diastolic Blood Pressure (mm. Hg.)	Change in Mean Arterial Pressure (mm. Hg.)	Days on Rice Diet
8.	163/106	149/99	— 14/— 7	—10.5	65
9.	225/93	194/86	— 31/— 7	—19	70
10.	190/115	166/104	— 24/—11	—17.5	16
11.	171/107	153/96	— 18/—11	—14.5	134
12.	182/121	154/113	— 28/— 8	—18	10
13.	170/96	158/96	— 12/— 0	— 6	17
14.	163/95	154/92	— 9/— 3	— 6	17
15.	177/96	154/80	— 23/—16	—19.5	18
16.	179/114	158/106	— 21/— 8	—14.5	41
17.	178/104	189/115	+ 11/+11	+11	24
18.	156/103	132/92	— 24/—11	—17.5	8
19.	172/100	146/93	— 26/— 7	—16.5	16
20.	190/107	157/103	— 33/— 4	—18.5	20
21.	185/109	155/100	— 30/— 9	—19.5	4
22.	188/110	168/99	— 20/—11	—15.5	16
23.	163/110	141/100	— 22/—10	—16	24
24.	170/93	150/87	— 20/— 6	—13	4
25.	160/90	138/89	— 22/— 1	—11.5	5
26.	164/118	176/140	+ 12/+22	+17	22
27.	168/92	149/85	— 19/— 7	—13	24
28.	187/128	159/118	— 28/—10	—19	20
Average	**179/108**	**160/102**	**— 19/— 6**	**—12.5**	**30**
Hypertension improved (Decrease of mean arterial pressure 20-66 mm. Hg.)					
1.	171/116	130/84	— 41/—32	—36.5	240
2.	200/155	170/128	— 30/—27	—28.5	26
3.	200/92	148/76	— 52/—16	—34	61
4.	214/118	174/96	— 40/—22	—31	27
5.	235/148	168/118	— 67/—30	—48.5	19
6.	188/114	142/93	— 46/—21	—33.5	56
7.	188/112	158/95	— 30/—17	—23.5	38
8.	207/123	162/96	— 45/—27	—36	19
9.	260/138	204/140	— 56/+ 2	—27	69
10.	214/110	162/96	— 52/—14	—33	20
11.	225/124	162/96	— 63/—28	—45.5	33
12.	158/98	125/82	— 33/—16	—24.5	9
13.	201/129	168/112	— 33/—17	—25	50
14.	215/134	175/134	— 40/— 0	—20	15
15.	246/136	165/97	— 81/—39	—60	38
16.	201/110	145/99	— 56/—11	—33.5	43
17.	165/89	129/79	— 36/—10	—23	256
18.	169/110	132/95	— 37/—15	—26	21
19.	171/95	131/85	— 40/—10	—25	118
20.	154/102	121/83	— 33/—19	—26	14
21.	233/123	177/110	— 56/—13	—34.5	4
22.	165/101	130/84	— 35/—17	—26	51
23.	190/88	145/74	— 45/—14	—29.5	48
24.	215/130	183/114	— 32/—16	—24	32
25.	196/127	164/115	— 32/—12	—22	28
26.	194/112	155/89	— 39/—23	—31	79
27.	194/144	124/82	— 70/—62	—66	21
28.	180/100	126/83	— 54/—17	—35.5	26
29.	200/100	120/84	— 80/—16	—48	4
30.	240/120	200/110	— 40/—10	—25	105
31.	173/103	140/94	— 33/— 9	—21	16
32.	176/112	155/92	— 21/—20	—20.5	29
33.	212/110	142/93	— 70/—17	—43.5	84
34.	162/98	126/81	— 36/—17	—26.5	10
35.	198/122	153/108	— 45/—14	—29.5	22
36.	193/125	139/95	— 54/—30	—42	33
37.	180/99	143/94	— 37/— 5	—21	14
Average	**197/115**	**151/97**	**— 46/—18**	**—32**	**48**

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Some results that were important to the individual patient necessarily fail to appear in such a summary. In one patient with chronic nephritis and almost complete blindness, who was moribund when he was started on the diet, the blood pressure decreased from 240 systolic, 150 diastolic to 160 systolic, 110 diastolic within forty days. After five and one half months of diet, the blood pressure was 154 systolic, 108 diastolic, and after fourteen months 155 systolic, 110 diastolic. The eyesight improved so much that the patient could read fine print and was able to resume his work. One would be justified in the conclusion that the diet had a beneficial effect on the course of this patient's nephritis. In the blood pressure and nonprotein nitrogen tables, however, this case had to be listed as a negative result, because at the time of the last examinations (after fifteen to eighteen months of rice diet), following a number of intercurrent infections and an automobile accident which resulted in a fractured pelvis, the blood pressure had again risen to the initial level.

Of the 63 patients on whom the diagnosis of *"hypertensive vascular disease" with "secondary" kidney involvement* was made, 13 died after six to eighty-one days (average twenty days) on the strict rice diet. The initial blood pressure readings in these patients averaged 226 systolic, 150 diastolic.

In 22 of the remaining 50 patients (44 per cent), the hypertension was not improved; the decrease in the mean arterial pressure was less than 20 mm. of mercury, the average blood pressure decreasing from a level of 212 systolic, 129 diastolic to a level of 200 systolic, 126 diastolic in an average time of thirty-nine days.

In 28 of the 50 patients (56 per cent) the hypertension was improved, the average blood pressure decreasing from a level of 219 systolic, 128 diastolic to a level of 165 systolic, 102 diastolic after seventy-three days (average) on the rice diet.

Of 66 patients whose condition was diagnosed as *"hypertensive vascular disease," without conclusive evidence of renal excretory dysfunction,* 1 patient died after thirty-six days on the strict diet. His initial blood pressure average was 248 systolic, 138 diastolic.

In 28 of the remaining 65 patients (43 per cent), the hypertension was not improved; the decrease in the mean arterial pressure was less than 20 mm. of mercury, the average blood pressure decreasing from a level of 179 systolic, 108 diastolic to a level of 160 systolic, 102 diastolic after an average of thirty days on the rice diet.

In 37 of the 65 patients (57 per cent) the hypertension was improved, the average blood pressure decreasing from a level of 197 systolic, 115 diastolic to a level of 151 systolic, 97 diastolic in an average time of forty-eight days.

Since, according to our hypothesis, the rice diet acts by compensating renal metabolic dysfunction, one may assume that in those cases in which the blood pressure decreased under treatment the hypertension was not "essential," but was due to some impairment of the metabolic function of the kidney, even though no conclusive sign of kidney disease could be demonstrated. On the other hand, in the patients who did not respond to the diet (exclusive of those with a too rapid down-hill course and those in whom irreversible anatomical lesions had already taken place), one may assume that the hypertension must have originated not from any renal dysfunction, but from some extra-renal condition. On this premise, it would be advisable (for instance, if sympathectomy is being considered) to use the rice diet as a therapeutic test which, if negative, may help to confirm the diagnosis of "neurogenic" or "essential" hypertension.

Histories 1-10 and figures 1-6, 14, 15, 19-23, 25-30, 33-35, 37-40, 42-44, 46-49, 51-58 illustrate the response of patients with various types of hypertension to the diet.

Electrocardiogram and Heart Size

Cardiac enlargement, inversion of T_1, and left axis deviation are reversible in patients with *acute* nephritis. In patients with *chronic* nephritis and hypertensive vascular disease we expected that the rice regime, at best, might prevent the usual progressive course of the disease, the further increase in heart size, the deeper inversion of T_1, and the greater deviation of the electrical axis.

However, the chest films and electrocardiograms show that, even in chronic nephritis and hypertensive vascular disease, the rice diet may lead to such an improvement of the heart that it may become normal in size and that the inverted T_1 may become upright, and the left axis deviation may disappear. Since we did not anticipate these findings, it is only recently that chest films

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and electrocardiograms of every patient have been repeated after treatment, but electrocardiograms of 82 patients and chest films of 72 patients are available for study. None of these patients whose electrocardiograms and chest films are under consideration received digitalis or any other medication.

The 82 patients on whom the electrocardiograms were made received the strict or modified rice diet for one to thirty-two months. All electrocardiograms were made with the patient in a recumbent position.

Electrical axis

In 76 patients, the electrical axis could be evaluated. In the remaining 6 patients $R_1 + S_1$, plus the absolute value of $R_3 + S_3$, was less than 10 mm. An angle of the electrical axis of more than +30 degrees was found:

Before the diet .....in 19 patients
After the diet .....in 31 patients

An angle of the electrical axis of 0 to +30 degrees was found:

Before the diet .....in 29 patients
After the diet .....in 27 patients

An angle of the electrical axis of less than 0 degrees was found:

Before the diet .....in 28 patients
After the diet .....in 18 patients

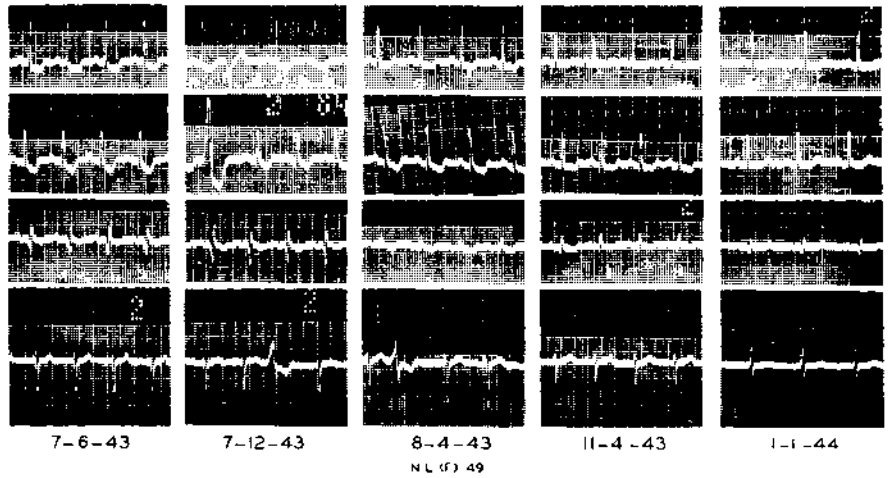

Fig. 7. N.L. (f., 49). "Hypertensive vascular disease." Rice diet since June 29, 1943. No bedrest after September, 1943. No digitalis. Depressed S-T segments have become normal; inverted T_1 has become upright.

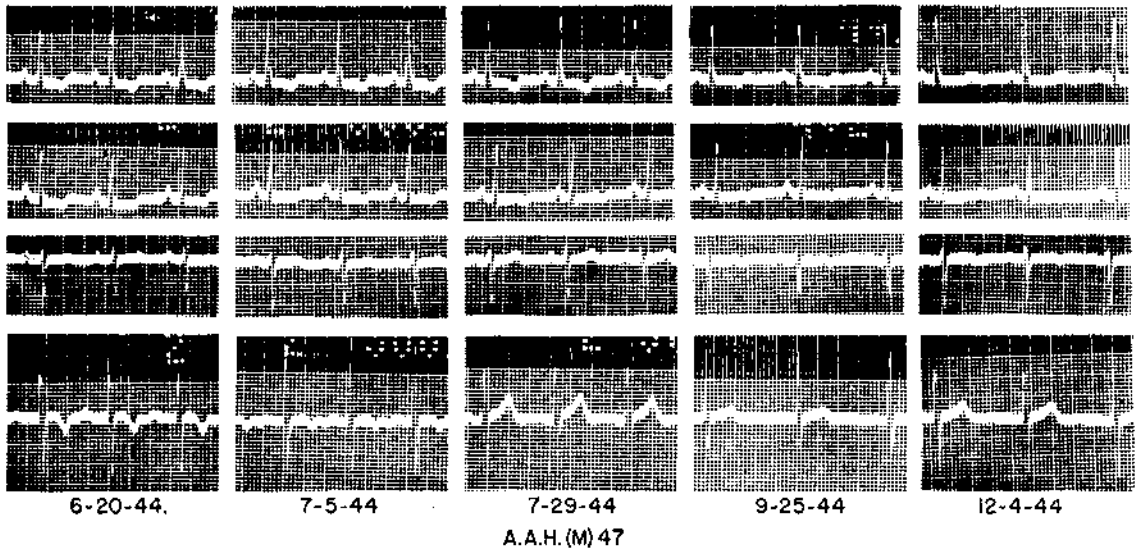

Fig. 8. A.A.H. (m., 47). "Hypertensive vascular disease." Retinopathy with papilledema and exudates. Rice diet since July 4, 1944. Bedrest part of the time. No digitalis. Inverted T_1 has become upright.

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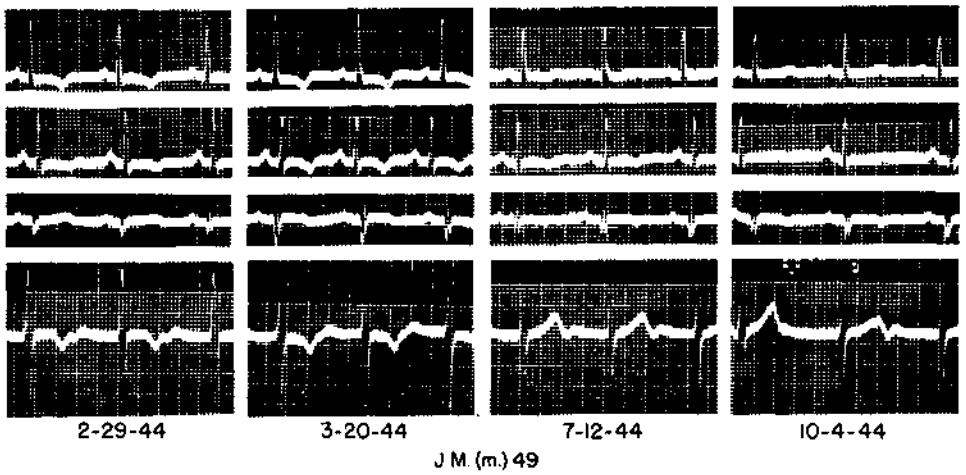

Fig. 9. J.M. (m., 49). "Hypertensive vascular disease." Rice diet since March 10, 1944. No bedrest. No digitalis. Inverted T_1 has become upright.

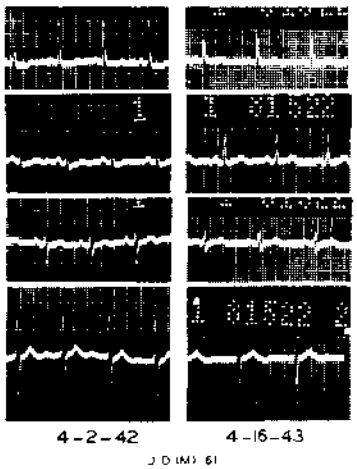

Fig. 10. J.D. (m., 61). "Hypertensive vascular disease." Rice diet since April 13, 1942. No digitalis. No bedrest. Angle of electrical axis has increased from +12° to +40°. Diphasic T_1 has become upright.

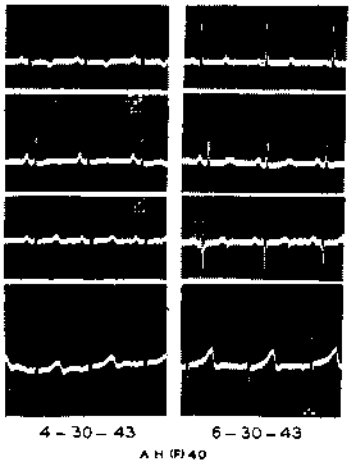

Fig. 11. A.H. (f., 40). "Hypertensive vascular disease." Rice diet since April 28, 1943. No digitalis. Bedrest part of the time. Inverted T_1 has become upright.

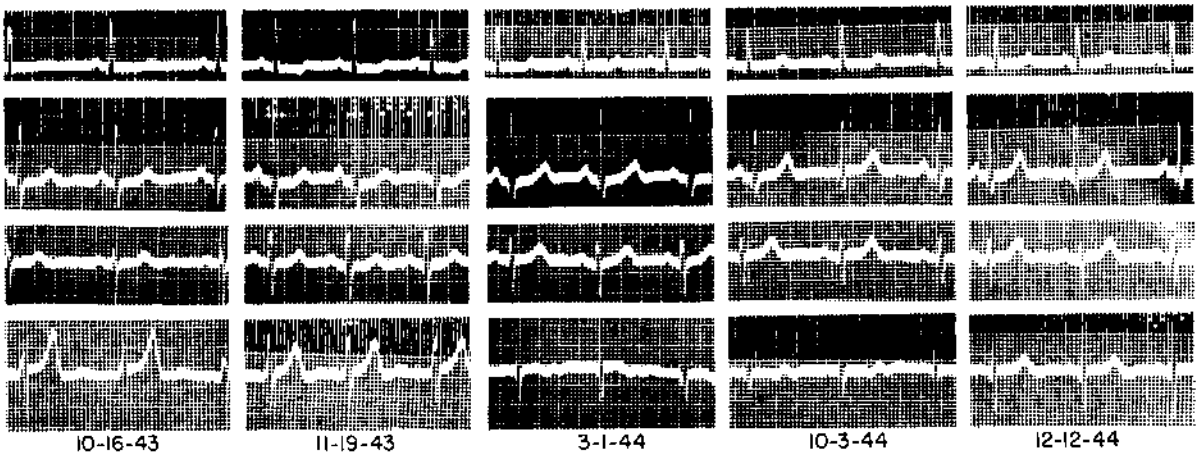

Fig. 12. J.S. (m., 55). "Hypertensive vascular disease." Retinopathy with exudates. Rice diet since October 27, 1943. No bedrest. No digitalis. T_1 flat, then diphasic; has become upright.

In 43 of the 76 patients there were no changes, or only minor changes (less than ±15 degrees) in the electrical axis. In 20 of the 76 patients there was a change in the angle of the electrical axis in the range of +15 to +25 degrees or −15 to −25 degrees. In 13 of the 76 patients there was a change in the angle of the electrical axis of ±26 or more degrees.

TABLE 4

Change in Electrical Axis

Number of patients	Angle of electrical axis (degrees)				Period on rice diet (months)
	Range of change	Before Diet	After Diet	Change	
1	more than −25	+37.0	+ 2.0	−35.0	4
5	−15 to −25	+14.8	− 2.4	−17.2	5
18	− 1 to −14	+19.4	+12.8	− 6.6	5
3	± 0	−25.3	−25.3	± 0	2
22	+ 1 to +14	+19.9	+27.8	+ 7.9	6
15	+15 to +25	+ 7.4	+26.1	+18.7	5
12	more than +25	− 6.1	+30.0	+36.1	7

Of the 33 patients with definite changes in the electrical axis during the rice diet, 6 showed a decrease, 27 an increase in the angle of the electrical axis.

The T wave in lead I

In 82 patients the T_1 waves could be evaluated.

In 59 patients, there was no change in T_1 during the period of treatment with the rice diet (average four months).

In 28 of the 59 patients, T_1 was normally upright.

In 31 of them, T_1 or ST_1 was abnormal.

In 8 of the 31 patients T_1 was low upright.
In 1 diphasic.
In 20 inverted.
In 2 ST_1 was depressed, with upright T_1.

In 23 patients there was a change in T_1 during the period of treatment (average four months); in 3 the change was in the direction from upright to inverted, in 20 in the direction from inverted to upright.

In 2 patients, the upright T_1 became flat.
In 1 patient, the upright T_1 became diphasic.

In 8 patients, the flat T_1 became upright.
In 4 patients, the diphasic T_1 became upright.
In 2 patients, the inverted T_1 became diphasic.
In 6 patients, the inverted T_1 became upright.

(Fig. 7-13, 36, 41, 50)

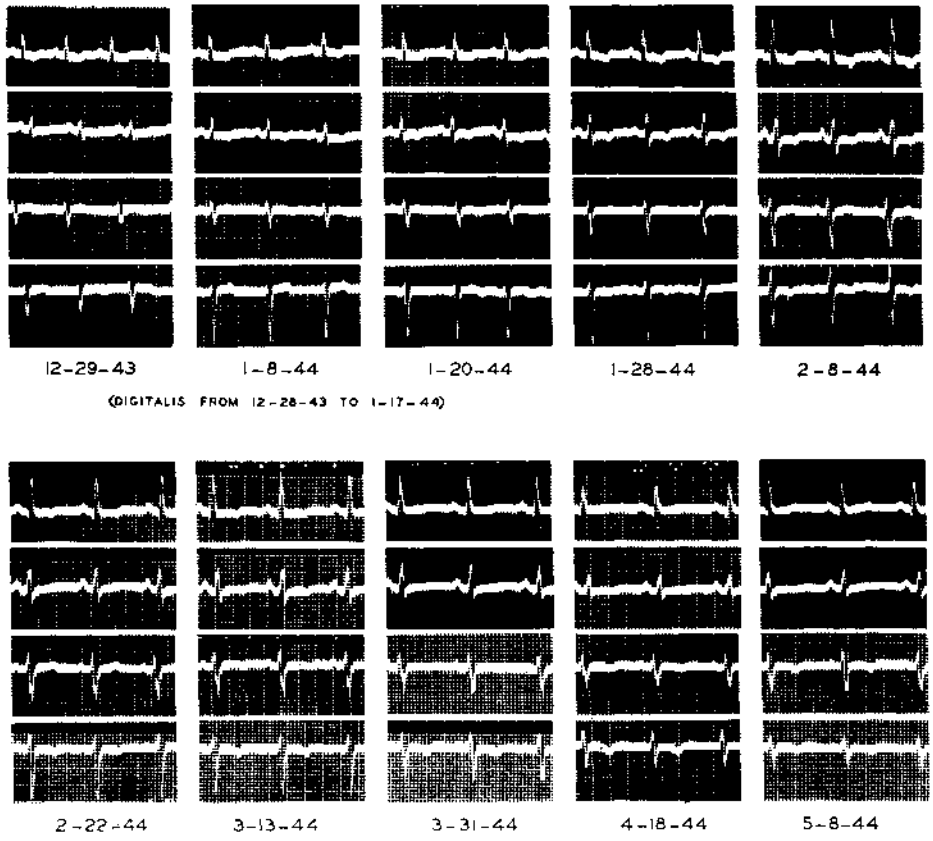

Fig. 13. L.K. (f., 33). Terminal stage of chronic nephritis. Retinopathy with papilledema, hemorrhages, exudates. Rice diet since January 7, 1944. Bedrest until March 1, 1944. No digitalis after January 17, 1944. Inverted T_1 has become upright.

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Heart size

Table 5 lists the measurements of the transverse diameter of the heart in 25 patients with chronic glomerulonephritis, chronic pyelonephritis, or nephrolithiasis, 1 patient with lupus erythematosus disseminatus, and 46 patients with "hypertensive vascular disease," who received the strict or modified rice diet for periods varying from eleven days to twenty-two months.

In 6 of the 72 patients the heart became larger. In these the transverse diameter of the heart increased by 0.9 to 4.9 per cent, the average increase being 3.2 per cent. The average chest diameter increased by 1.5 per cent.

In 66 of the 72 patients the heart became smaller in size with a change in the transverse diameter of the heart of 1.8 per cent to 51.8 per cent, the average change being 13.3 per cent. The average chest diameter decreased by less than 0.4 per cent. (Fig. 14-23, 33, 35, 40, 46, 49, 53, 57)

TABLE 5

EFFECT OF RICE DIET ON HEART SIZE

	Period of Rice Diet (Days)	Diameter of Chest (Cm.)		Transverse Diameter of Heart (Cm.)		Change in Transverse Diameter of Heart	
		Before Diet	After Diet	Before Diet	After Diet	Cm.	Per Cent (Transverse diameter of smaller heart = 100%)
CHRONIC GLOMERULONEPHRITIS, CHRONIC PYELONEPHRITIS, OR NEPHROLITHIASIS							
1.	312	30.1	29.8	15.9	12.35	−3.55	−28.8
2.	22	31.25	31.75	14.0	13.75	−0.25	− 1.8
3.	48	32.0	32.0	16.5	14.2	−2.3	−16.2
4.	65	25.35	25.75	10.8	9.8	−1.0	−10.2
5.	234	30.0	29.9	14.4	12.6	−1.8	−14.3
6.	19	32.4	32.7	14.2	13.8	−0.4	− 2.9
7.	28	23.2	25.4	10.6	10.9	+0.3	+ 2.8
8.	99	30.2	31.1	13.6	12.3	−1.3	−10.6
9.	50	29.3	29.3	10.35	7.9	−2.45	−31.0
10.	677	28.5	28.5	16.7	12.6	−4.1	−32.5
11.	336	27.4	28.3	11.95	10.15	−1.8	−17.7
12.	24	29.95	29.45	17.45	16.0	−1.45	− 9.1
13.	483	27.1	26.25	9.4	9.15	−0.25	− 2.7
14.	122	28.7	28.3	15.8	13.9	−1.9	−14.3
15.	119	30.8	29.9	15.8	11.8	−4.0	−33.9
16.	40	31.2	31.6	14.5	12.5	−2.0	−16.0
17.	534	30.0	27.9	16.7	11.0	−5.7	−51.8
18.	61	32.2	32.0	14.0	11.5	−2.5	−21.7
19.	58	27.65	26.9	11.4	10.85	−0.55	− 5.1
20.	67	28.6	28.0	13.05	12.0	−1.05	− 8.7
21.	95	31.2	31.2	12.9	10.3	−2.6	−25.2
22.	27	29.9	29.0	17.7	14.1	−3.6	−25.5
23.	94	28.9	28.6	12.4	11.9	−0.5	− 4.2
24.	68	28.0	28.45	11.95	11.6	−0.35	− 3.0
25.	155	31.4	31.3	12.3	12.75	+0.45	+ 3.7
Average	**153**	**29.41**	**29.33**	**13.77**	**11.99**	**−1.78**	**−15.23**
LUPUS ERYTHEMATOSUS DISSEMINATUS							
1.	165	26.8	25.5	12.8	9.9	−2.9	−29.3
"HYPERTENSIVE VASCULAR DISEASE"							
1.	67	33.8	33.8	15.0	12.8	−2.2	−17.2
2.	100	31.2	30.6	13.4	12.2	−1.2	− 9.8
3.	20	31.3	29.8	13.5	11.75	−1.75	−14.9
4.	66	28.2	27.55	15.9	14.4	−1.5	−10.4
5.	43	30.9	29.95	16.2	14.6	−1.6	−10.9
6.	71	31.9	31.9	16.4	14.0	−2.4	−17.1
7.	64	28.6	28.4	14.3	15.0	+0.7	+ 4.9
8.	215	24.7	24.45	12.25	11.15	−1.1	− 9.9
9.	174	31.8	31.4	16.7	15.5	−1.2	− 7.7
10.	32	29.1	29.3	19.1	17.8	−1.3	− 7.3
11.	588	30.0	29.2	11.9	10.9	−1.0	− 9.2
12.	50	28.4	29.9	16.3	15.3	−1.0	− 6.5
13.	32	29.8	29.3	15.4	14.2	−1.2	− 8.0
14.	62	28.3	30.3	18.0	13.4	−4.6	−34.3
15.	55	33.85	33.3	14.0	13.25	−0.75	− 5.7
16.	178	30.5	30.1	14.85	14.1	−0.75	− 5.3
17.	117	31.25	30.6	18.0	14.6	−3.4	−23.3

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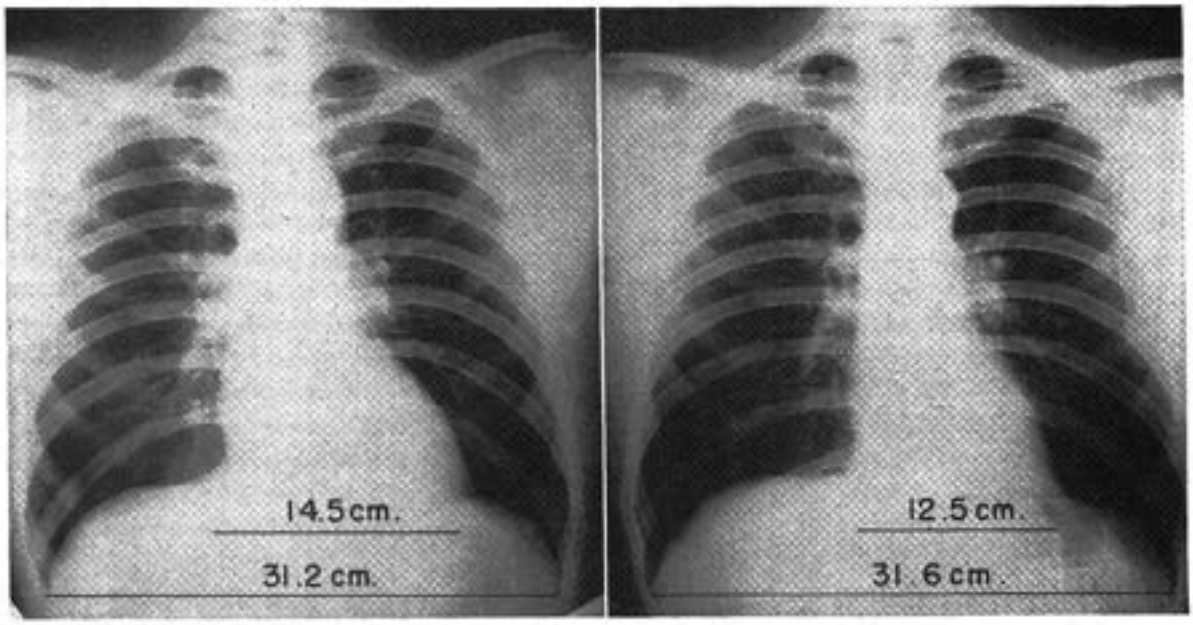
TABLE 5—Continued

	Period of Rice Diet (Days)	Diameter of Chest (Cm.) Before Diet	Diameter of Chest (Cm.) After Diet	Transverse Diameter of Heart (Cm.) Before Diet	Transverse Diameter of Heart (Cm.) After Diet	Change in Transverse Diameter of Heart Cm.	Change in Transverse Diameter of Heart Per Cent (Transverse diameter of smaller heart = 100%)
18.	37	31.8	32.0	16.8	15.7	−1.1	− 7.0
19.	54	24.05	24.25	14.0	12.65	−1.35	−10.7
20.	25	26.55	26.8	17.15	15.2	−1.95	−12.8
21.	129	32.3	31.8	15.4	14.1	−1.3	− 9.2
22.	125	31.7	31.8	15.3	13.4	−1.9	−14.2
23.	43	32.4	32.8	16.5	13.8	−2.7	−19.6
24.	253	28.4	27.5	10.75	10.5	−0.25	− 2.4
25.	32	23.95	24.75	13.85	13.5	−0.35	− 2.6
26.	86	26.0	25.6	13.8	12.6	−1.2	− 9.5
27.	173	26.5	26.25	13.9	12.8	−1.1	− 8.6
28.	32	31.1	31.9	15.6	14.4	−1.2	− 8.3
29.	116	24.85	25.45	10.6	10.7	+0.1	+ 0.9
30.	55	30.2	30.4	14.2	12.4	−1.8	−14.4
31.	18	32.2	32.6	16.2	15.5	−0.7	− 4.5
32.	34	24.75	24.5	12.25	11.75	−0.5	− 4.3
33.	24	32.7	32.4	14.6	13.25	−1.35	−10.2
34.	30	30.7	30.2	15.7	14.6	−1.1	− 7.5
35.	53	26.1	25.95	11.55	10.35	−1.2	−11.6
36.	36	25.1	24.8	12.5	11.2	−1.3	−11.6
37.	43	26.8	26.2	13.8	14.4	+0.6	+ 4.3
38.	28	27.0	27.3	11.7	12.0	+0.3	+ 2.6
39.	115	29.8	30.25	14.9	13.25	−1.65	−12.5
40.	20	26.4	25.15	12.7	11.3	−1.4	−12.4
41.	412	29.0	29.1	14.0	13.2	−0.8	− 6.1
42.	40	26.9	27.0	15.9	14.0	−1.9	−13.6
43.	98	22.05	22.05	12.10	10.75	−1.35	−12.6
44.	22	34.65	33.7	17.6	16.35	−1.25	− 7.6
45.	21	28.4	31.45	15.65	14.1	−1.55	−11.0
46.	174	29.7	31.1	14.7	12.7	−2.0	−15.8
Average	**93**	**29.04**	**29.02**	**14.67**	**13.38**	**−1.29**	**− 9.68**



7-12-43 197/139 mm. Hg. 8-21-43 134/104 mm. Hg.

Fig. 14. W.McL. (m., 35). Chronic glomerulonephritis. Retinopathy with hemorrhages and exudates. Phenolsulfonphthalein excretion in two hours, 31 per cent. Rice diet since July 12, 1943. Bedrest. No digitalis. Reduction in heart size with change in transverse diameter of 16 per cent.

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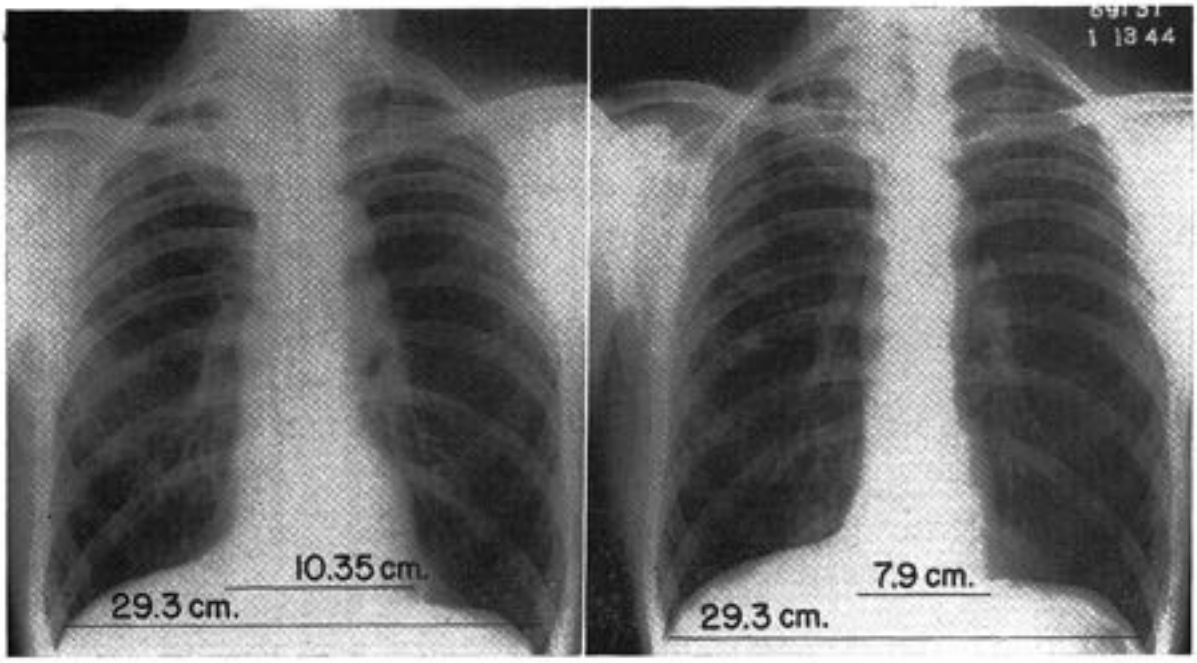
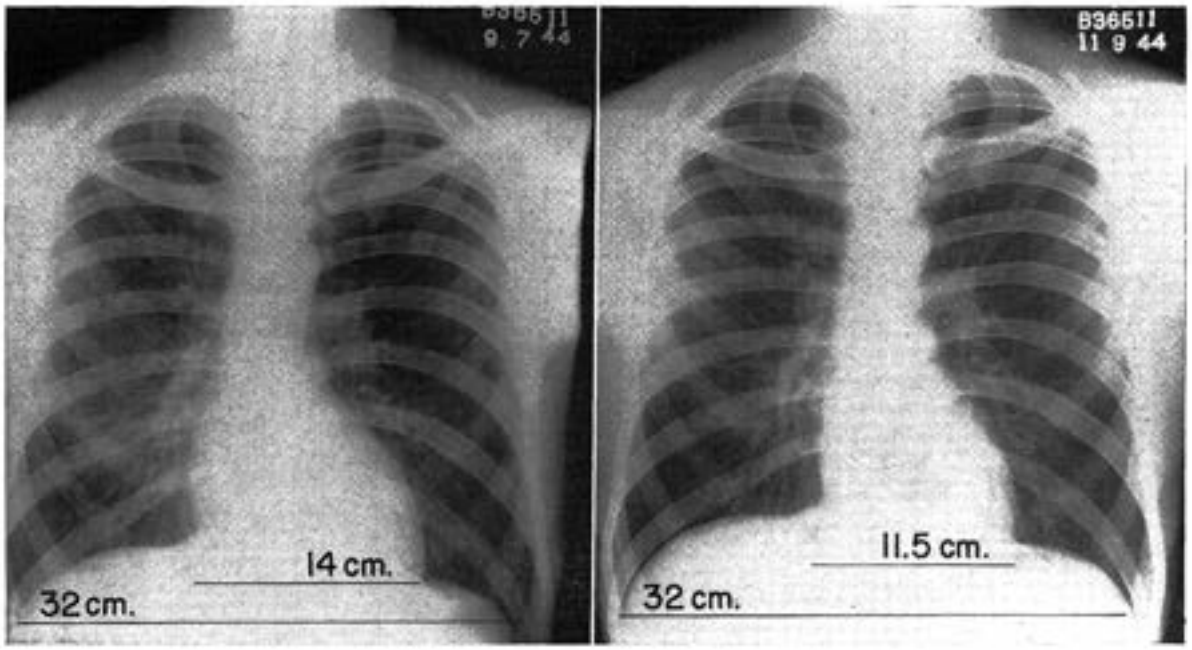


11-16-43 220/130 mm. Hg. 1-13-44 111/79 mm. Hg.

Fig. 15. A.G. (m., 53). Chronic glomerulonephritis. Phenolsulfonphthalein excretion in two hours, 50 per cent. Rice diet since November 24, 1943. Bedrest part of the time. No digitalis. Reduction in heart size with change in transverse diameter of 31 per cent.



9-7-44 140/96 mm. Hg. 11-9-44 146/80 mm. Hg.

Fig. 16. B.M. (m., 31). Chronic nephritis. Phenolsulfonphthalein excretion in two hours, 7 per cent. Rice diet since September 9, 1944. No bedrest. No digitalis. Reduction in heart size with change in transverse diameter of 21 per cent.

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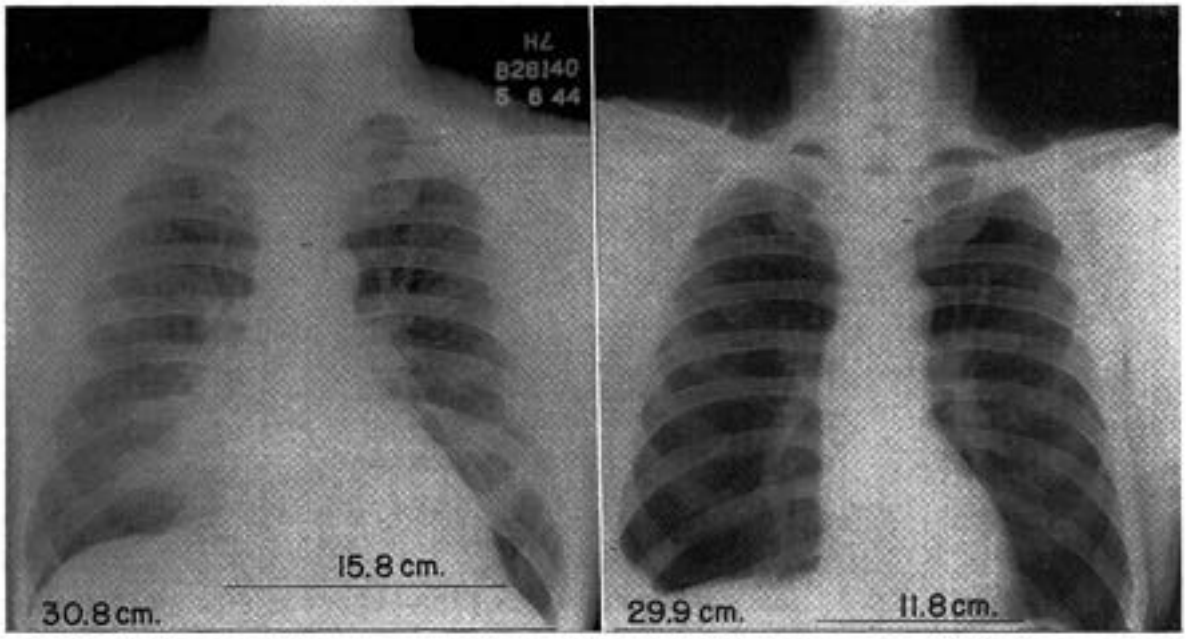
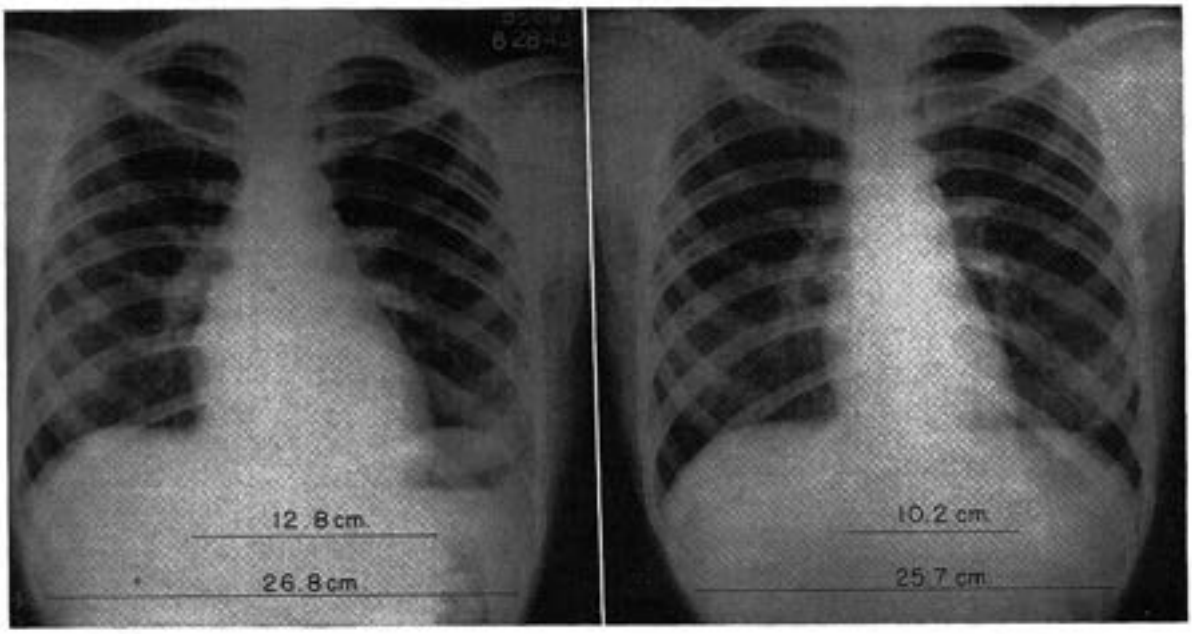


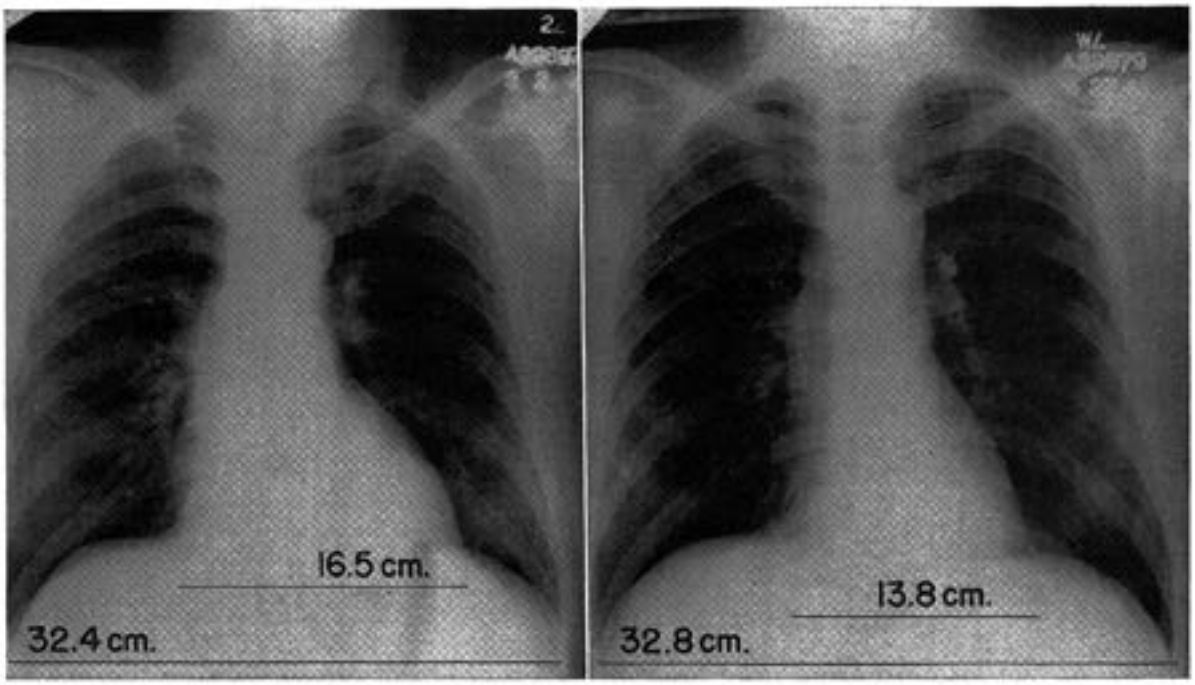
5-6-44 144/84 mm. Hg. 9-9-44 130/80 mm. Hg.

Fig. 17. B.K. (m., 43). Terminal stage of chronic nephritis. Phenolsulfonphthalein excretion in two hours, 0.56 per cent. Rice diet since May 13, 1944. No digitalis. Bedrest part of the time. Reduction in heart size with change in transverse diameter of 34 per cent.



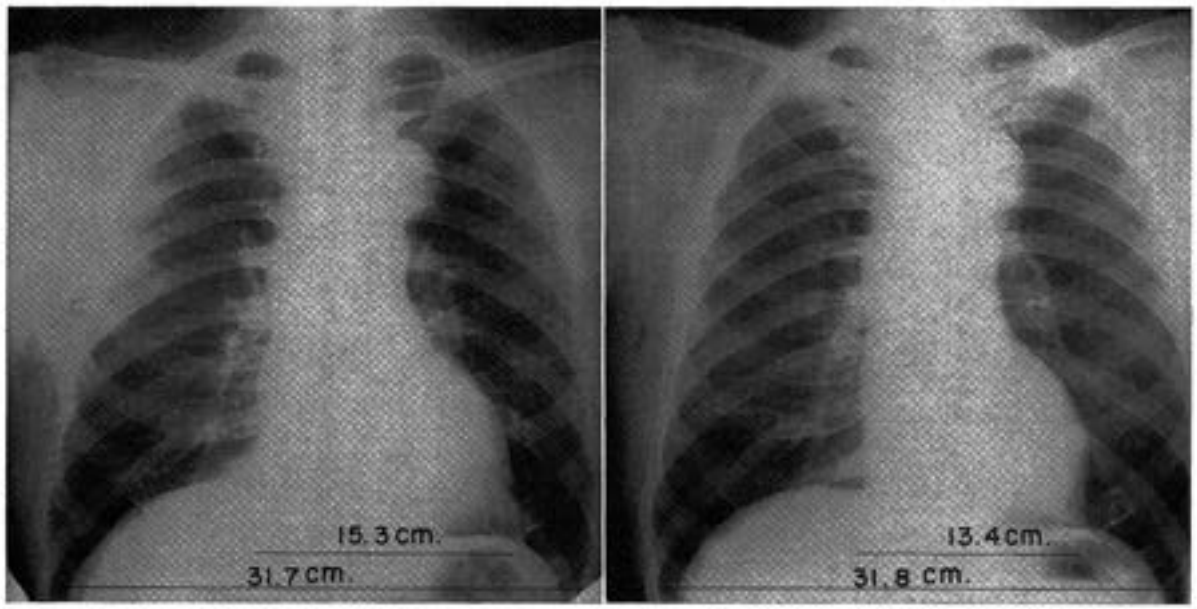
6-28-43 110/60 mm. Hg. 9-3-43 94/60 mm. Hg.

Fig. 18. T.A. (f., 20). Lupus erythematosus disseminatus. Exudative retinopathy. Phenolsulfonphthalein excretion in two hours, 75 per cent. Rice diet since July 19, 1943. Bedrest. No digitalis. Reduction in heart size with change in transverse diameter of 25 per cent.



3-2-44 220/124 mm. Hg. 4-27-44 140/97 mm. Hg.

Fig. 19. J.K. (m., 48). "Hypertensive vascular disease." Phenolsulfonphthalein excretion in two hours, 63 per cent. Rice diet since March 14, 1944. No digitalis. No bedrest. Reduction in heart size with change in transverse diameter of 20 per cent.



9-28-43 220/150 mm. Hg. 2-1-44 152/110 mm. Hg.

Fig. 20. J.L. (m., 54). "Hypertensive vascular disease." Phenolsulfonphthalein excretion in two hours, 50 per cent. Rice diet since October 3, 1943. No digitalis. No bedrest (three months of bedrest before admission because of coronary infarction). Reduction in heart size with change in transverse diameter of 14 per cent.

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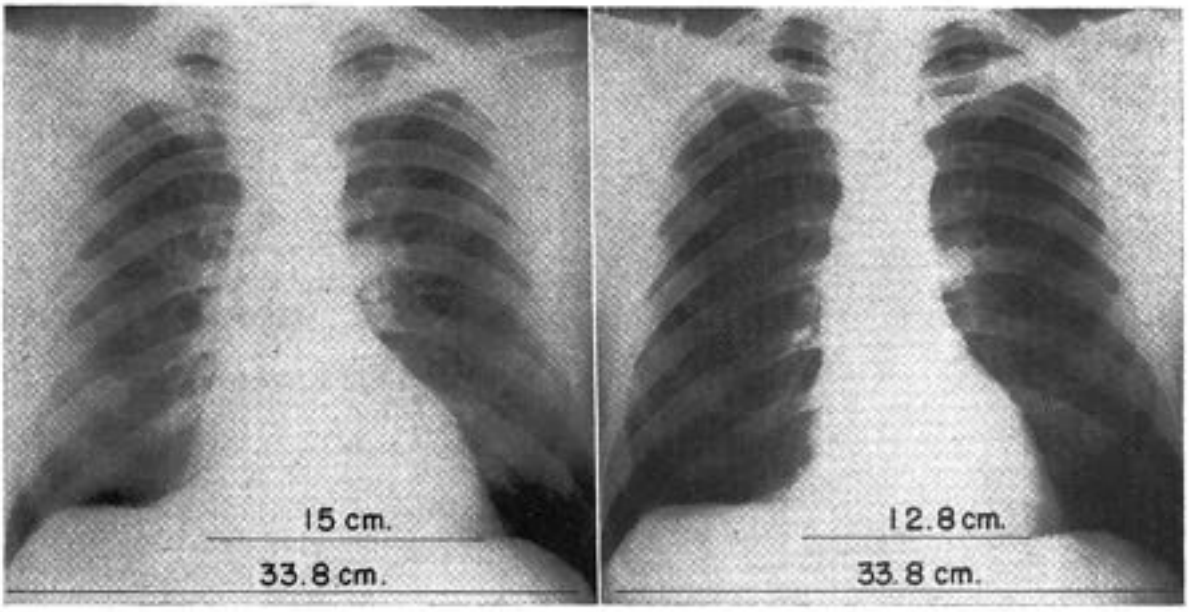
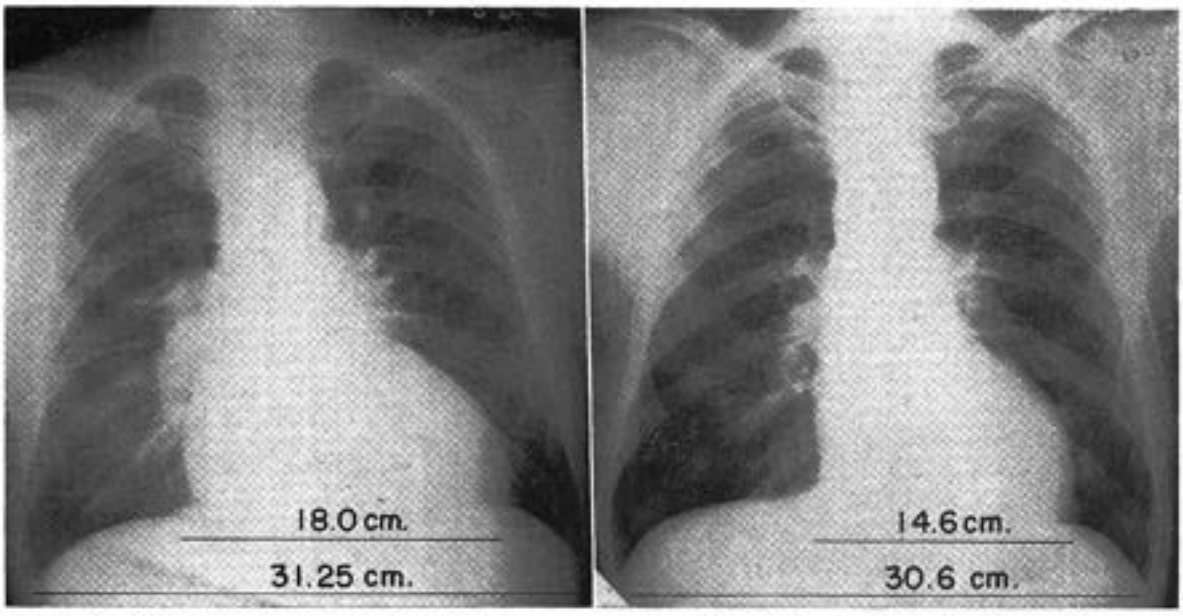


9-13-43 208/118 mm. Hg. 11-22-43 148/100 mm. Hg.

Fig. 21. J.L.A. (m., 46). "Hypertensive vascular disease." Retinopathy with papilledema. Phenolsulfonphthalein excretion in two hours, 54 per cent. Rice diet since September 16, 1943. Bedrest. No digitalis. Reduction in heart size with change in transverse diameter of 17 per cent.



3-24-43 212/110 mm. Hg. 7-28-43 137/63 mm. Hg.

Fig. 22. J.F. (m., 65). "Hypertensive vascular disease." Phenolsulfonphthalein excretion in two hours, 43 per cent. Rice diet since April 2, 1943. No bedrest. No digitalis. Reduction in heart size with change in transverse diameter of 23 per cent.

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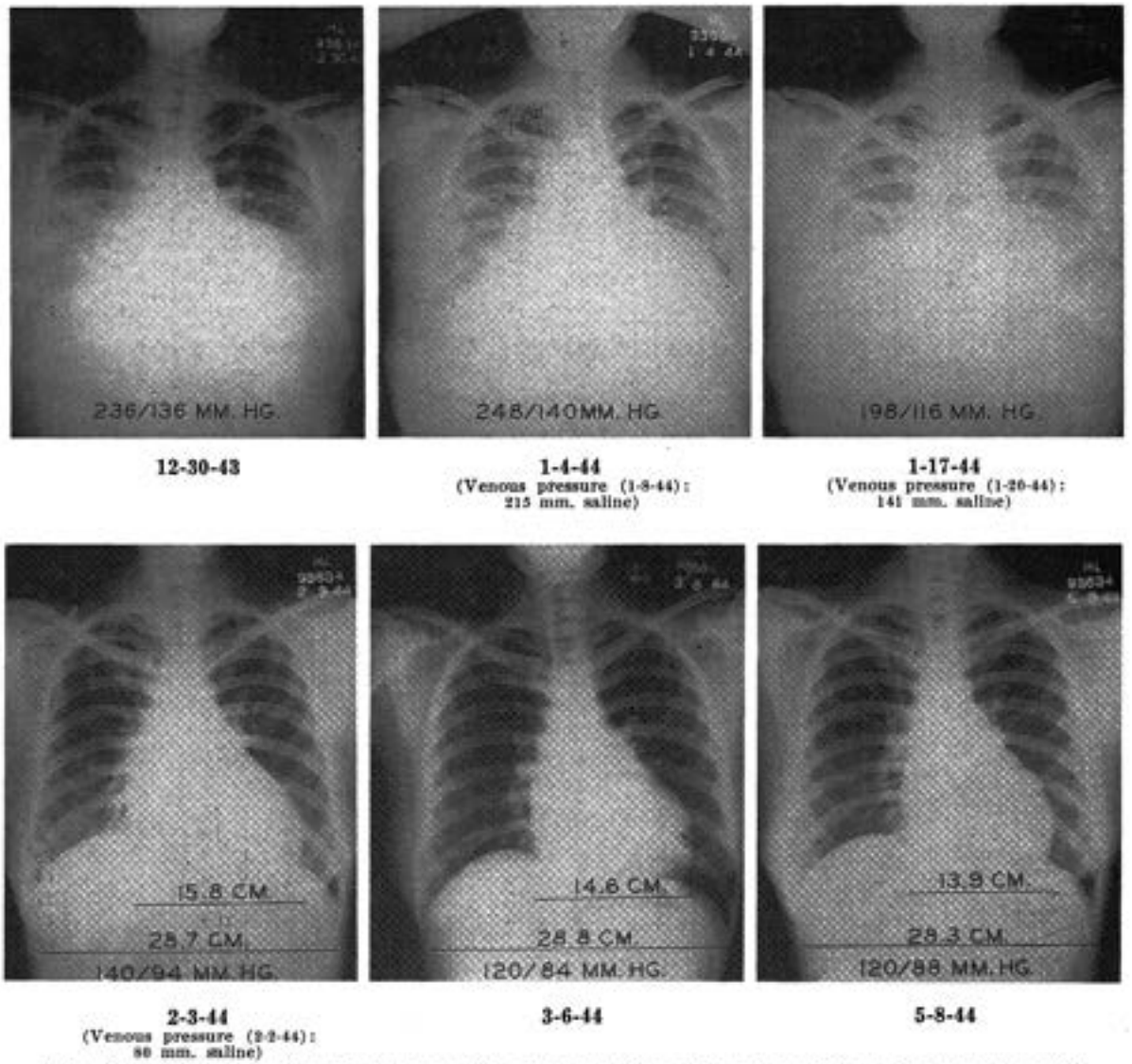

12-30-43

1-4-44
(Venous pressure (1-8-44): 215 mm. saline)

1-17-44
(Venous pressure (1-20-44): 141 mm. saline)

2-3-44
(Venous pressure (2-2-44): 80 mm. saline)

3-6-44

5-8-44

Fig. 23. L.K. (f., 33). Terminal stage of chronic nephritis, with pericarditis and retinopathy with papilledema, hemorrhages, exudates. Phenolsulfonphthalein excretion in two hours, 1.4 per cent. Rice diet since January 7, 1944. Bedrest until March 1, 1944. No digitalis after January 17, 1944. After the pericarditis cleared up, the heart size was reduced, with a change in the transverse diameter of 14 per cent.

Nonprotein Nitrogen

Table 6 shows the effect of the rice diet on the nonprotein nitrogen of 171 patients who received the strict or modified diet for periods varying from four days to thirty-two months. Five patients had acute glomerulonephritis, 66 patients chronic glomerulonephritis, chronic pyelonephritis, nephrolithiasis, or polycystic kidney disease, 2 patients lupus erythematosus, 55 patients "hypertensive vascular disease" with "secondary" renal involvement, 43 patients "hypertensive vascular disease" without conclusive evidence of renal excretory dysfunction.

Twenty-two patients died after six to eighty-one days (average twenty-five); 1 patient died after twenty months:

Average nonprotein nitrogen:
Before diet .....115 mg. per 100 cc. of blood
Before death .....186 mg. per 100 cc. of blood

The nonprotein nitrogen of 35 patients increased or did not decrease during the period of rice diet:

Average nonprotein nitrogen:
Before diet .....42.7 mg. per 100 cc. of blood
After 63 days of diet 50.2 mg. per 100 cc. of blood

The nonprotein nitrogen of 113 patients decreased during the period of diet:

Average nonprotein nitrogen:
Before diet .....53.1 mg. per 100 cc. of blood
After 78 days of diet 36.0 mg. per 100 cc. of blood

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TABLE 6

EFFECT OF RICE DIET ON NONPROTEIN NITROGEN

	Phenolsulfonphthalein Test (Total Excretion in 2 Hours) Per Cent	Nonprotein Nitrogen (mg. per 100 cc. blood) Before Rice Diet	After Rice Diet	Change	Days on Rice Diet
ACUTE GLOMERULONEPHRITIS					
1.	75, 60	73	31	−42	153
2.	55, 61	37	28	− 9	11
3.	78	54	26	−28	32
4.	78, 85, 71	33	27	− 6	180
5.	40, 50	32	28	− 4	83
Average		**46**	**28**	**−18**	**92**
CHRONIC GLOMERULONEPHRITIS, CHRONIC PYELONEPHRITIS, NEPHROLITHIASIS, OR POLYCYSTIC KIDNEY DISEASE					
NPN Increased or Unchanged					
Initial NPN 39-238 mg. per 100 cc. blood					
1.*	30	174	360	+186	37
2.*	2	90	138	+ 48	9
3.*		132	375	+243	38
4.*	less than 9	78	203	+125	50
5.	2, 1.2	138	170	+ 32	36
6.	3, 7, 14.5, 12, 10, 9, 1	77	78	+ 1	710
7.*	less than 3	190	355	+165	16
8.	5, 10	132	150	+ 18	27
9.*	19, 33, 24	42	145	+103	595
10.*	less than 5	190	208	+ 18	30
11.*	20	87	143	+ 56	10
12.*	0	238	300	+ 62	32
13.	51, 51	43	46	+ 3	210
14.	54, 57.5	39	46	+ 7	8
Average		**118**	**194**	**+ 76**	**129**
Initial NPN 22-35 mg. per 100 cc. blood					
15.*	45	28	76	+ 48	35
16.	80	22	32	+ 10	20
17.	62.5	30	32	+ 2	19
18.	55, 50	33	42	+ 9	14
19.	45, 39, 38	35	35	0	21
20.*	55, 43,	35	204	+169	42
Average		**30**	**70**	**+ 40**	**25**
NPN Decreased					
Initial NPN 39-242 mg. per 100 cc. blood					
1.	17.5	87	38	− 49	90
2.	50, 33	43	31	− 12	62
3.	77	41	28	− 13	70
4.	15	118	108	− 10	16
5.	20, 12	60	44	− 16	65
6.	30, 22	42	29	− 13	30
7.	22.5, 27.5, 30, 22.5, 25	72	33	− 39	160
8.	4.5, 4, 4.3, 5	143	46	− 97	252
9.	20, 22.5, 35, 21, 25, 22, 23	58	32	− 26	406
10.	12.5, less than 22.5, 25, 9, 18, 19	46	32	− 14	198
11.	less than 2, 1.4, 3.2, 3.3, less than 1	68	47	− 21	137
12.	Faint trace	156	84	− 72	27
13.		175	102	− 73	29
14.	40, 38, 17.5, 27.5	85	80	− 5	45
15.	25, 27.5, 16, 15, 18.5, 23, 21	54	36	− 18	236
16.	8	78	63	− 15	7
17.	5, 10, 7, 10	73	41	− 32	240
18.*	0, less than 1, less than 1	138	104	− 34	42
19.	25, 20, 18, 30, 25, 12, 16	66	62	− 4	348
20.	47, 55, 40	55	31	− 24	72
21.	40, 40	53	48	− 5	67
22.	70	175	35	−140	38
23.	22	44	27	− 17	80
24.	55	46	26	− 20	14
25.	0.1	168	102	− 66	42
26.	65	48	27	− 21	17

* Death after 6-595 days.

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TABLE 6—Continued

	Phenolsulfonphthalein Test (Total Excretion in 2 Hours) Per Cent	*Nonprotein Nitrogen (mg. per 100 cc. blood)*			
		Before Rice Diet	*After Rice Diet*	*Change*	*Days on Rice Diet*
27.	less than 1, less than 1, less than 1, 0	125	84	— 41	119
28.	5.5, 2.2	82	60	— 22	21
29.	70	39	32	— 7	6
30.	4, 7, 10.5	87	46	— 41	59
31.		93	71	— 22	31
32.	3	71	46	— 25	7
33.	71, 68	42	34	— 8	58
34.	10.2, 4.7	140	87	— 53	49
35.	less than 1	242	84	—158	51
Average		**89**	**54**	**— 35**	**91.5**
Initial NPN 27-38 mg. per 100 cc. blood					
36.	70	27	23	— 4	7
37.	72	31	29	— 2	24
38.	65	33	31	— 2	28
39.	64	30	25	— 5	15
40.	55	34	30	— 4	22
41.	38, 19, 24	36	34	— 2	190
42.	49, 52	32	27	— 5	19
43.		31	24	— 7	25
44.	67	29	25	— 4	98
45.	45	38	28	— 10	16
46.	75, 69, 77	33	28	— 5	215
Average		**32**	**28**	**— 4**	**60**
LUPUS ERYTHEMATOSUS					
1.	65, 85	55	45	— 10	91
2.	65, 57	69	34	— 35	27
Average		**62**	**39.5**	**— 22.5**	**59**
"HYPERTENSIVE VASCULAR DISEASE" WITH "SECONDARY" RENAL INVOLVEMENT					
NPN Unchanged or Increased					
Initial NPN 42-277 mg. per 100 cc. blood					
1.*	0	230	260	+ 30	22
2.	2.3	67	108	+ 41	8
3.*	18	80	111	+ 31	81
4.*	15.5	61	108	+ 47	27
5.*		202	252	+ 50	10
6.	5	51	75	+ 24	18
7.*	11, 7	54	102	+ 48	15
8.*		110	198	+ 88	14
9.	25	42	46	+ 4	25
10.	30	42	44	+ 2	32
11.		78	109	+ 31	22
12.*	60	48	74	+ 26	6
13.*		66	104	+ 38	17
14.*		277	292	+ 15	7
15.*	28, 32	57	126	+ 69	7
16.	45	48	54	+ 6	48
Average		**95**	**129**	**+ 34**	**22.5**
Initial NPN 27-37 mg. per 100 cc. blood					
17.	70, 45, 48	35	35	0	66
18.*		36	45	+ 9	10
19.	47, 65	29	49	+ 20	78
20.	20	34	37	+ 3	29
21.	42, 43, 51	33	33	0	86
22.	70, 85	27	40	+ 13	30
23.	46	37	40	+ 3	15
Average		**33**	**40**	**+ 7**	**45**
NPN Decreased					
Initial NPN 39-63 mg. per 100 cc. blood					
1.	75	57	41	— 16	68
2.	45, 42.5	40	21	— 19	9
3.	67, 75, 48, 51	44	24	— 20	209
4.	47, 69.5	40	25	— 15	32
5.	40	40	30	— 10	82

* Death after 6-595 days.

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TABLE 6—Continued

		Phenolsulfonphthalein Test (Total Excretion in 2 Hours) Per Cent	Nonprotein Nitrogen (mg. per 100 cc. blood) Before Rice Diet	After Rice Diet	Change	Days on Rice Diet
6.	49		58	38	— 20	10
7.	44		42	32	— 10	35
8.	40, 45		49	44	— 5	103
9.	44, 48, 54		39	24	— 15	121
10.	50		50	37	— 13	28
11.	45		52	38	— 14	32
12.	64		51	32	— 19	7
13.	28		50	33	— 17	32
14.			57	34	— 23	9
15.	45		58	44	— 14	13
16.			48	41	— 7	7
17.	45		53	24	— 29	6
18.	55, 50		46	31	— 15	79
19.	45, 68		47	34	— 13	77
20.			63	44	— 19	40
21.	50, 65		40	37	— 3	22
Average			**49**	**34**	**— 15**	**49**
Initial NPN 28-38 mg. per 100 cc. blood						
22.	57		33	28	— 5	47
23.	57, 28, 30		36	34	— 2	15
24.	58, 54, 65, 53		29	18	— 11	970
25.	32		35	32	— 3	60
26.	60, 60, 55		29	26	— 3	90
27.	47		38	33	— 5	20
28.	32, 52, 67		35	23	— 12	113
29.	37, 64		33	24	— 9	198
30.	30		36	28	— 8	15
31.	66, 64, 47, 58		33	25	— 8	177
32.	59, 44		28	25	— 3	127
Average			**33**	**27**	**— 6**	**167**
"HYPERTENSIVE VASCULAR DISEASE" WITHOUT CONCLUSIVE EVIDENCE OF RENAL INVOLVEMENT						
NPN Unchanged or Increased						
Initial NPN 23-40 mg. per 100 cc. blood						
1.	65		35	40	+ 5	13
2.	83, 60		26	28	+ 2	61
3.	53		33	34	+ 1	26
4.			26	28	+ 2	11
5.	69		35	35	0	13
6.	55, 49		34	36	+ 2	132
7.	69, 87, 91		27	28	+ 1	252
8.	61		23	25	+ 2	14
9.	63		32	38	+ 6	12
10.			31	36	+ 5	7
11.	52		28	28	0	36
12.	64		26	32	+ 6	4
13.	55		40	41	+ 1	4
14.	57		28	28	0	86
Average			**30**	**32.5**	**+ 2.5**	**48**
NPN Decreased						
Initial NPN 25-40 mg. per 100 cc. blood						
1.	74, 71, 72		33	27	— 6	239
2.	97		34	32	— 2	16
3.			37	26	— 11	48
4.	67, 75		34	25	— 9	72
5.	59		31	24	— 7	57
6.	92		30	28	— 2	60
7.	59		34	29	— 5	112
8.	52		37	33	— 4	32
9.	65		25	23	— 2	21
10.	62, 69		29	21	— 8	55
11.	53		27	20	— 7	38
12.	70		30	28	— 2	22
13.	55, 55		30	29	— 1	65
14.	58		40	30	— 10	82
15.	69		26	25	— 1	28

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TABLE 6—Continued

	Phenolsulfonphthalein Test (Total Excretion in 2 Hours) Per Cent	Nonprotein Nitrogen (mg. per 100 cc. blood) Before Rice Diet	After Rice Diet	Change	Days on Rice Diet
16.	67	28	24	— 4	18
17.	82, 90, 71	30	26	— 4	22
18.	64, 86	30	24	— 6	113
19.	72	31	26	— 5	20
20.	53	31	29	— 2	18
21.	55	35	27	— 8	45
22.	72, 63	36	32	— 4	26
23.	73	35	25	— 10	149
24.	88	30	24	— 6	34
25.	70	39	27	— 12	4
26.	78	28	22	— 6	17
27.	63, 87	29	24	— 5	96
28.	81	30	25	— 5	23
29.	69	39	30	— 9	18
Average		**32**	**26**	**— 6**	**53**

An erroneous impression might be conveyed by the figures in table 6, because only the nonprotein nitrogen values before the start of treatment and the last ones recorded after treatment are compared. Since many patients with chronic kidney disease, however, do not realize the seriousness of their condition before manifestations of terminal renal failure become apparent, they frequently come to the hospital at a time when the nonprotein nitrogen is no longer at a constant level, but is rising rapidly. The effect of the diet in such instances might therefore be seen more correctly in the difference between the patient's nonprotein nitrogen at the end of the treatment and his highest nonprotein nitrogen value, even if this value was found after he was already on the diet (fig. 24).

The lowering of the nonprotein nitrogen in the greater number of patients is not the only point of significance in table 6; the length of time on the rice diet is also important, for it shows that in spite of even critical decrease in renal excretory function, as indicated by the low phenolsulfonphthalein excretion, the usually progressive increase of the nonprotein nitrogen and actual uremia may be prevented for years.

Histories 1-3, 5-7 and figures 24, 34, 38, 45, 47 illustrate the response of the nonprotein nitrogen to the diet.

Urea

Table 7 shows the effect of the strict or modified rice diet on the blood urea nitrogen concentration and on the urea nitrogen-nonprotein nitrogen ratio in 63 patients.

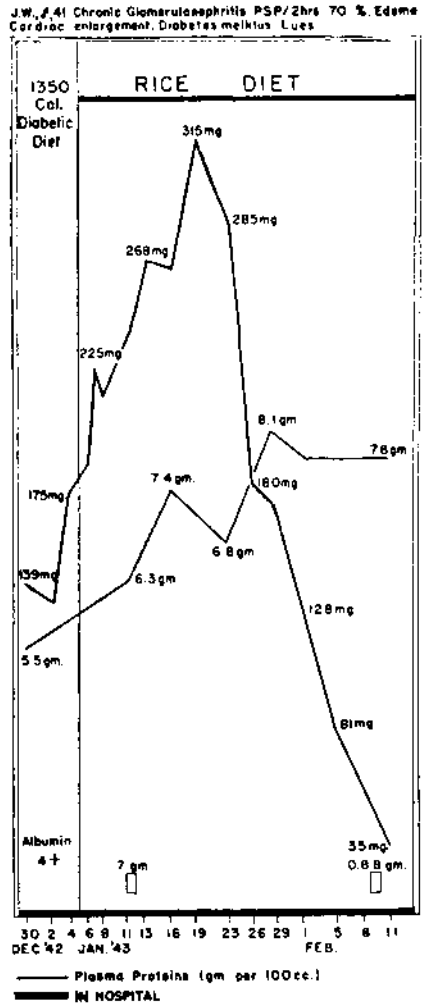

Fig. 24. J.W. (m., 41). Blood nonprotein nitrogen (mg. per 100 cc.) of nephritic patient with rapidly developing uremia.

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TABLE 7

EFFECT OF RICE DIET ON BLOOD UREA NITROGEN

	UREA NITROGEN (mg. per 100 cc. blood)		*NONPROTEIN NITROGEN (mg. per 100 cc. blood)*		*UREA RATIO %*		
	Before Rice Diet	*After Rice Diet*	*Before Rice Diet*	*After Rice Diet*	*Before Rice Diet*	*After Rice Diet*	*Days on Rice Diet*
I. Urea Nitrogen Increased							
Initial urea nitrogen 32-116 mg. per 100 cc. blood							
1.	116	130.8	138	163	84.1	80.2	28
2.	47.4	56.8	90	93	52.7	61.1	53
3.	32.7	77.4	61	108	53.6	71.7	27
4.	50	51.8	70	114	71	45.4	15
5.	89.1	181.7	110	198	81	91.8	14
Average	**67**	**99.7**	**94**	**135**	**68.5**	**70**	**27**
Initial urea nitrogen 10 mg. per 100 cc. blood							
6.	10.1	14.9	30	40	34	37.2	14
II. Urea Nitrogen Decreased							
Initial urea nitrogen 33-110 mg. per 100 cc. blood							
1.	36.8	27.3	60	44	61.3	62.5	62
2.	108	70.3	168	102	64.3	68.9	47
3.	42.3	24.2	68	47	62.2	51.5	166
4.	105	48.4	156	84	67.3	57.6	27
5.	109.6	42.4	148	84	74.1	50.5	118
6.	49.9	26.4	87	48	57.4	55	42
7.	34	14.9	50	31	68	48.1	92
8.	91.5	61.6	140	87	65	70.8	48
9.	43.5	22.8	80	48	54.4	47.5	42
10.	33	10.7	50	33	66	32.4	32
Average	**65.4**	**34.9**	**100.7**	**60.8**	**64**	**54.5**	**68**
Initial urea nitrogen 7-29 mg. per 100 cc. blood							
11.	20.4	4.2	44	31	46.4	13.5	131
12.	12.6	6.2	31	29	40.6	22.8	23
13.	21	9.1	36	34	58.3	27	190
14.	15.2	4.2	41	26	37.1	16.2	190
15.	28.9	12.6	55	31	52.5	40.6	70
16.	25.7	12.4	42	34	61.2	36.5	57
17.	10.8	4.2	34	28	31.8	15	210
18.	21.4	14.4	42	30	51	48	189
19.	21.2	7.8	35	35	60.6	22.3	36
20.	18.4	9	36	36	51.1	25	146
21.	15.6	7.8	33	25	47.3	31.2	32
22.	18.1	3.6	36	18	50.3	20	970
23.	19.2	12.7	37	38	51.9	33.4	46
24.	24.2	14.4	51	32	47.5	45	224
25.	18	4.3	39	24	46.2	17.9	153
26.	8.9	7.8	29	26	30.7	30	79
27.	17.2	10	38	33	45.3	30.3	20
28.	10.8	8.3	35	24	30.9	34.6	200
29.	10.2	2.3	33	18	30.9	12.8	460
30.	16.5	6	46	31	36	19.7	77
31.	20	14.9	47	35	42.6	42.6	240
32.	14	4.2	37	21	37.8	20	20
33.	9.9	5	29	25	34.1	20	72
34.	11.3	6.6	30	25	37.7	26.4	125
35.	15.8	6.1	34	29	46.5	21	112
36.	13.8	6.6	36	21	38.3	31.4	55
37.	10.2	1.8	26	25	39.2	7.2	191
38.	11.9	6	27	20	44.1	30	38
39.	14.2	4.5	40	30	35.5	15	82
40.	11.8	7.2	34	36	34.7	20	129
41.	7.7	1.8	26	29	29.6	6.2	172
42.	10.4	3.6	28	24	37.1	15	81
43.	8.1	5.5	32	30	25.3	18	68
44.	11.9	7.8	32	38	37.2	20.5	11
45.	10.9	6.6	31	30	35.2	22	120
46.	11.4	7.7	31	29	36.8	26.6	18
47.	12.6	6.6	35	27	36.1	24.4	45
48.	14	5.4	28	28	50	19.3	36
49.	13.8	2.4	36	32	38.3	7.5	26
50.	10.8	5.4	30	25	36	21.6	10

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TABLE 7—Continued

	UREA NITROGEN (mg. per 100 cc. blood)		NONPROTEIN NITROGEN (mg. per 100 cc. blood)		UREA RATIO %		
	Before Rice Diet	After Rice Diet	Before Rice Diet	After Rice Diet	Before Rice Diet	After Rice Diet	Days on Rice Diet
51.	9.5	4.8	28	30	33.9	16	85
52.	9.1	4.2	30	25	30	16.8	23
53.	12.6	7.8	28	24	44.1	32.5	26
54.	16.8	4.2	36	30	46.7	14	35
55.	12.6	2.4	33	26	38.2	9.2	251
56.	13.7	9	36	34	38.1	26.5	23
57.	7.1	1.2	28	25	25.4	4.8	127
Average	**14.5**	**6.6**	**35**	**28**	**40.8**	**22.9**	**122**

In 6 of the 63 patients the blood urea nitrogen increased (group I). Two of these died after fourteen and twenty-seven days.

	Urea N (average) (mg. per 100 cc. of blood)	Urea N-NPN ratio (average) (per cent)
Initial urea nitrogen 32-116 mg. per 100 cc. of blood (I, patients 1-5)		
Before diet	67	68.5
After 27 days of diet	99.7	70.0
Initial urea nitrogen 10 mg. per 100 cc. of blood (I, patient 6)		
Before diet	10.1	34
After 14 days of diet	14.9	37.2

In 57 of the 63 patients the blood urea nitrogen decreased (group II).

	Urea N (average) (mg. per 100 cc. of blood)	Urea N-NPN ratio (average) (per cent)
Initial urea nitrogen 33-110 mg. per 100 cc. of blood (II, patients 1-10)		
Before diet	65.4	64
After 68 days of diet	34.9	54.5
Initial urea nitrogen 7-29 mg. per 100 cc. of blood (II, patients 11-57)		
Before diet	14.5	40.8
After 122 days of diet	6.6	22.9

Of 48 patients whose initial urea nitrogen concentration was normal or almost normal (7-29 mg. per 100 cc. of blood), only 1 patient had an increase of the blood urea nitrogen concentration, whereas 47 patients had an average decrease of the blood urea nitrogen concentration of 55 per cent.

The lowest urea nitrogen values we found were 1.2 mg. per 100 cc. of blood in 1 patient, and 1.8-2.4 mg. per 100 cc. of blood in 4 patients. The urea nitrogen-nonprotein nitrogen ratio in these 5 patients ranged from 4.8 to 12.4 per cent[6].

This finding again shows that patients on the rice diet are in protein equilibrium, since in fasting and inanition the urea nitrogen concentration of the blood is increased.

6. Dr. Haywood Taylor of the Department of Biochemistry is engaged in a study to determine the nature of those nonprotein nitrogen substances, the increase of which makes up for the decreased urea ratio in the blood of patients on the rice diet.

Two hundred and eighty-one determinations of the urea nitrogen excretion per twenty-four hours in the urine of 96 patients with kidney disease (with a nonprotein nitrogen not above 50 mg. per 100 cc. of blood), or with "hypertensive vascular disease," before and after they had received the rice diet for varying periods of time, are summarized in table 8.

TABLE 8

Urea Excretion in Urine

Period on rice diet	Number of patients	Number of determinations	Gm. urea nitrogen excreted in 24 hours (average)
0*	49	60	5.4
1-14 days	46	73	2.9
15-30 days	36	47	1.9
1-2 months	22	35	1.6
Over 2 months	30	66	1.1

* In many instances the protein intake before the beginning of the rice diet had been limited, either because the patients were too ill to eat the full amount of a mixed diet, or because they had received other low protein diets. The regular hospital diet contains about 65 Gm. of protein.

The twenty-four hour urinary urea nitrogen excretion on a 100 Gm. protein diet is about 12 Gm., in complete starvation about 6 Gm., after an average period of two or more months on the rice diet about 1.1 Gm.

The excretion of urea constitutes one of the main tasks of the kidney. According to Addis[7], the excretion of 10 Gm. of urea nitrogen requires 677 gram calories of work from the kidney. Borsook[8] has calculated that ordinarily 76 per cent of all the work of the kidney is spent on urea excretion. The fact that the rice diet causes an 80 or 90 per cent reduction in urinary urea excretion may not be without effect upon the "metabolic situation" of the kidney cells.

This article will be concluded in the March issue of the JOURNAL.

7. Addis, T.: Theory and Practice in Dietetic Treatment of Glomerular Nephritis, J. Am. Dietet. A. 16:306-312 (April) 1940.
8. Borsook, H., and Winegarden, H. M.: The Work of the Kidney in the Production of Urine, Proc. Nat. Acad. Sc. 17:3-18, 1931.

Compensation of Renal Metabolic Dysfunction:
Treatment of Kidney Disease and Hypertensive Vascular Disease
with Rice Diet, III. Part 2

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FROM NORTH CAROLINA MEDICAL JOURNAL, MARCH, 1945, VOL. 6, NO. 3

Compensation of Renal Metabolic Dysfunction

Treatment of Kidney Disease and Hypertensive Vascular Disease With Rice Diet, III

PART 2

Cholesterol

The relation of hypercholesterolemia to generalized arteriosclerosis, coronary disease, and vascular retinopathy has been a subject of extensive study. High carbohydrate—low calorie diets have been shown to reduce the serum cholesterol level in patients with diabetes mellitus[12].

The effect of the strict or modified rice diet on the serum total cholesterol concentration was determined in 82 patients (table 9). Three of the patients had acute glomerulonephritis; 32 patients had chronic glomerulonephritis, chronic pyelonephritis, or nephrolithiasis; 47 patients had "hypertensive vascular disease" with or without apparent renal excretory dysfunction. Hypercholesterolemia (220 to 840 mg. of cholesterol per 100 cc. of serum) was present in 53 of the 82 patients before the rice diet was started, the average cholesterol concentration in these 53 patients being

Before rice diet .....294 mg. per 100 cc. of serum
After 91 days (average)
of rice diet .....198 mg. per 100 cc. of serum

In the remaining 29 patients the serum cholesterol concentration ranged from 135 to 218 mg. per 100 cc. before the rice diet was started, the average concentration being

Before rice diet .....185 mg. per 100 cc. of serum
After 89 days (average)
of rice diet .....158 mg. per 100 cc. of serum

In 9 of the 82 patients there was an *increase* in the cholesterol concentration of from 2 to 38 mg. per 100 cc. of serum, the average cholesterol concentration being

Before rice diet .....173 mg. per 100 cc. of serum
After 91 days (average)
of rice diet .....190 mg. per 100 cc. of serum

TABLE 9

SERUM CHOLESTEROL OF PATIENTS ON RICE DIET

(Mg. per 100 cc. of serum)

Acute glomerulonephritis

Case	*Before*	*After*	*Days*
1.	168	100	150
2.	220	176	300
3.	142	155	180
Aver.	**177**	**144**	**210**

Chronic glomerulonephritis, chronic pyelonephritis, nephrolithiasis.

Case	*Before*	*After*	*Days*	*Case*	*Before*	*After*	*Days*
1.	220	185	24	18.	176	150	77
2.	210	186	28	19.	151	110	169
3.	236	152	34	20.	160	172	10
4.	338	244	18	21.	440	285	71
5.	158	145	16	22.	212	110	240
6.	368	230	167	23.	208	162	42
7.	840	410	14	24.	237	185	28
8.	230	150	31	25.	640	225	212
9.	180	205	40	26.	211	93	74
10.	310	142	309	27.	185	170	350
11.	296	148	50	28.	240	177	288
12.	225	156	346	29.	178	180	9
13.	150	142	42	30.	315	185	78
14.	135	160	18	31.	320	260	150
15.	270	140	180	32.	315	190	83
16.	272	210	21				
17.	274	183	202	**Aver.**	**272**	**183**	**107**

12. Rabinowitch, I. M.: Experiences with a High Carbohydrate—Low Calorie Diet for the Treatment of Diabetes Mellitus, Canad. M. A. J. 23:489-493 (Oct.) 1930.

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"Hypertensive vascular disease"

Case	Before	After	Days	Case	Before	After	Days
1.	205	178	67	26.	137	175	28
2.	168	175	240	27.	238	210	84
3.	225	177	143	28.	333	270	28
4.	238	200	61	29.	266	154	112
5.	255	215	47	30.	345	258	74
6.	354	275	134	31.	293	200	20
7.	242	172	72	32.	222	70	99
8.	292	237	212	33.	210	190	109
9.	234	173	73	34.	300	225	166
10.	325	226	31	35.	318	235	9
11.	217	190	125	36.	220	187	53
12.	317	186	52	37.	210	205	24
13.	224	155	32	38.	225	200	16
14.	172	160	35	39.	273	230	9
15.	218	135	90	40.	292	168	78
16.	255	146	139	41.	215	110	76
17.	210	225	228	42.	239	149	60
18.	230	164	35	43.	258	175	41
19.	300	198	6	44.	193	153	16
20.	250	260	65	45.	260	170	178
21.	252	161	14	46.	200	175	6
22.	185	108	14	47.	304	169	66
23.	188	150	83				
24.	284	235	18				
25.	332	246	14	Aver.	249	188	72

In the remaining 73 patients there was a *decrease* of from 5 to 430 mg. per 100 cc. of serum, the average cholesterol concentration being

Before rice diet .....266 mg. per 100 cc. of serum
After 91 days (average) of rice diet .....183 mg. per 100 cc. of serum

Vascular Retinopathy

Recovery from advanced vascular retinopathy requires a period of months. Thirty-three patients with papilledema, hemorrhages, or exudates followed the rice diet for a period of at least eight weeks. In 30 of these patients eyeground photographs were taken before and after treatment; in 3, only after treatment.

In 1 patient, the retinopathy became worse. In 11 patients, the retinopathy not only came to a standstill, but papilledema, hemorrhages, and exudates partially cleared up. In 21 of the 33 patients, the retinopathy improved greatly or even cleared up completely under the rice regime. Five patients who had not been able to recognize objects regained their eyesight to such an extent that they were able to read fine print. As the photographs of the eyegrounds show, papilledema, hemorrhages, and exudates disappeared, arteriovenous compression decreased, the arterioles became less tortuous, and the previously engorged and tortuous veins became delicate and straight.

Histories 2-7, 9-10 and figures 25-32, 39, 43-44, 48, 54, and 56 illustrate the response of vascular retinopathy to the diet.

HISTORIES OF PATIENTS TREATED WITH THE RICE DIET*

PATIENT 1. *Acute glomerulonephritis. Example of decrease of high blood pressure and nonprotein nitrogen to normal and of disappearance of generalized edema and heart enlargement.*

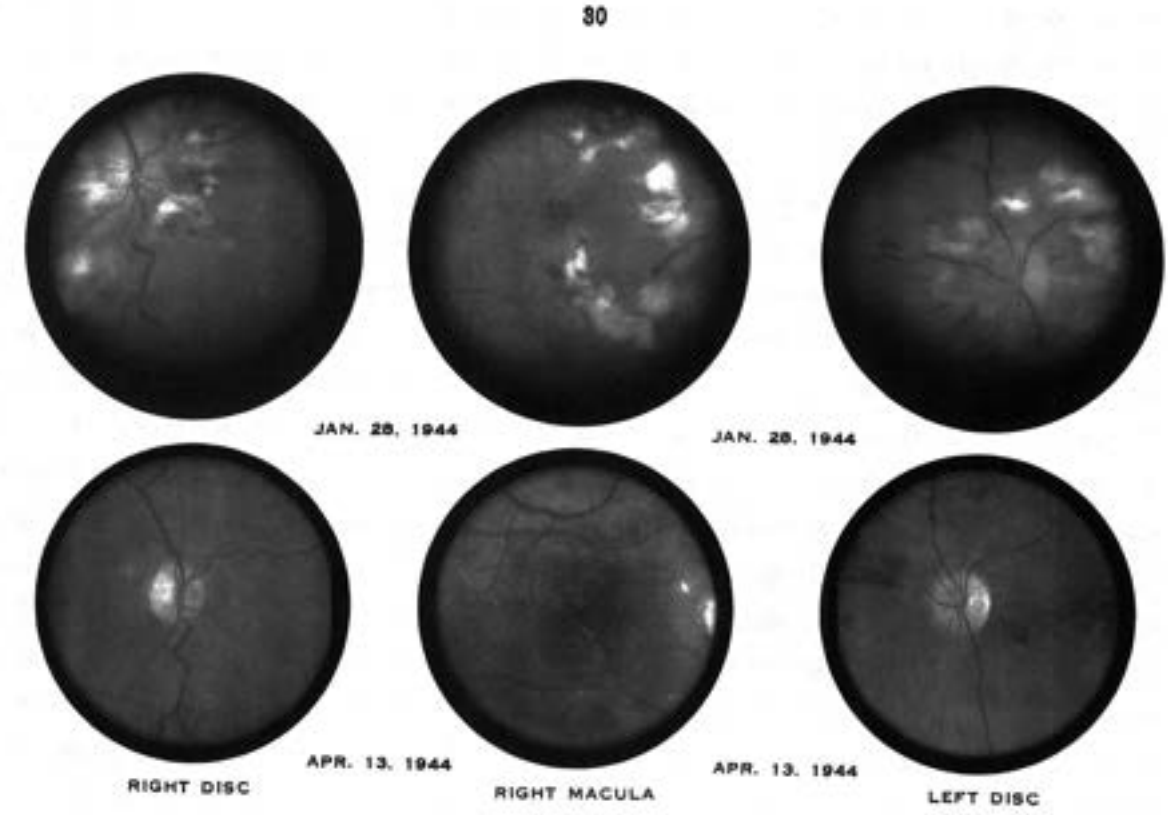
W.B. (B4700), a 17 year old farm boy, came to the outpatient clinic on May 5, 1943, complaining of edema, headache, and backache. He was admitted to the hospital on May 6 at 2 a.m.

History: The patient had had measles, whooping cough, chickenpox, and pneumonia in early childhood, mumps at the age of 7, diphtheria at 12, malaria at 13. He had colds two or three times a year, associated with frontal headaches and sometimes with cough productive of yellow mucoid sputum.

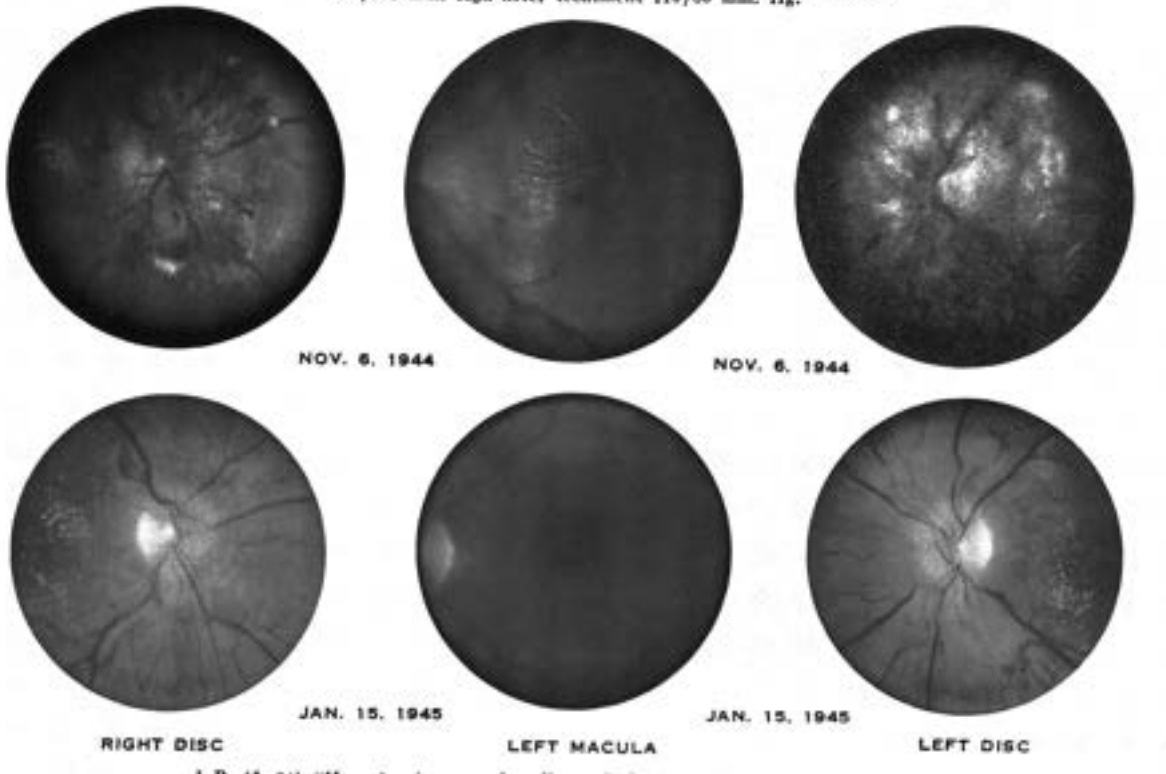
About April 15, 1943, the patient developed a sore throat, night sweats, dysphagia, and swelling under the right jaw; his urine became dark and smoky. On May 2, he went on a fishing trip and got his "legs wet up to the thighs." The following morning, he noticed fatigue and puffiness of the face, but in spite of this, took part in a ball game. Next day the edema was worse, his back ached from the hips to the shoulders, and he had a feeling of tightness in the abdomen, and marked fatigue (he fell asleep in class). He complained of nocturia and generalized muscular aching.

Examination: The patient's height was 168 cm., his weight 73.1 Kg., his temperature 37 C., pulse 50, respiration 16, blood pressure 176 systolic, 101 diastolic. Generalized pitting edema, especially of the face and extremities, was present; the knuckles of the hands were almost invisible. There was generalized lymph node enlargement. The eyelids were puffy. The pupils reacted well to light and accommodation, and there were no pathological findings in the eyegrounds. The teeth were in good repair. The tonsils were red, moderately large and cryptic. The lungs were clear to percussion and auscultation. The heart was markedly enlarged, the rhythm regular; the aortic second sound was louder than the pulmonic second sound; no murmurs were heard. The liver was not enlarged and the spleen was not palpable; there was no tenderness in

* The histories of 2 other patients, a 25 year old man with chronic nephritis, and a 36 year old man with "hypertensive vascular disease," were previously published in this **Journal**[4a].



L.K. (f. 33) Terminal Stage of chronic nephritis. BP before treatment 238/139 mm. Hg., after treatment 110/80 mm. Hg.



L.B. (f. 24) "Hypertensive vascular disease," first noted in pregnancy. BP before treatment 233/157 mm. Hg., after treatment 120/87 mm. Hg.

Fig. 25. Improvement of advanced vascular retinopathy with disappearance of papilledema, hemorrhages, and exudates.

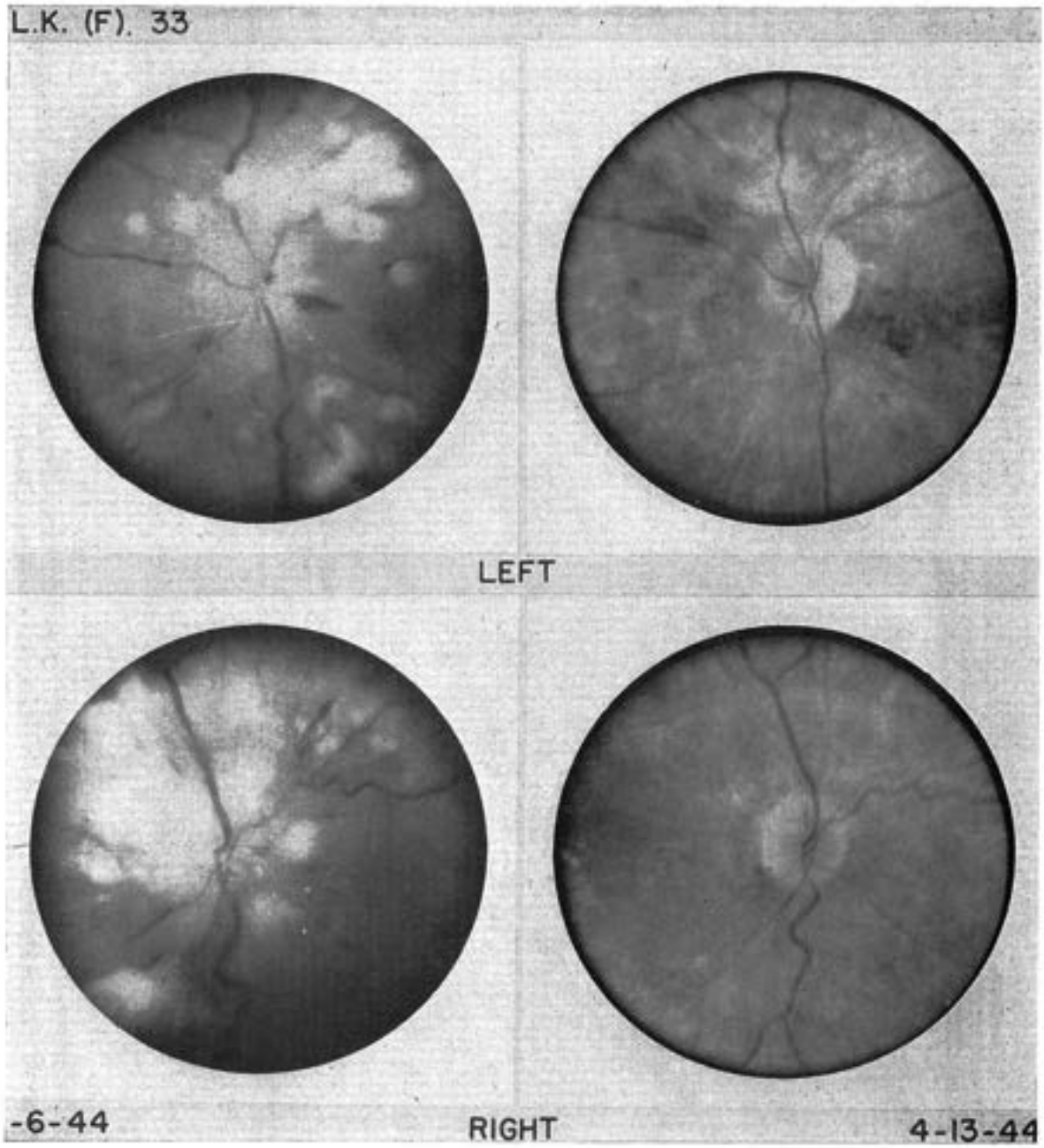


Fig. 26. L. K. (f., 33). Terminal uremic stage of chronic nephritis. Phenolsulfonphthalein excretion in two hours, 1.4 per cent. Rice diet started January 6, 1944. See figures 1, 13, 23, 25. Disappearance of papilledema, hemorrhages, exudates, venous engorgement, both eyes.

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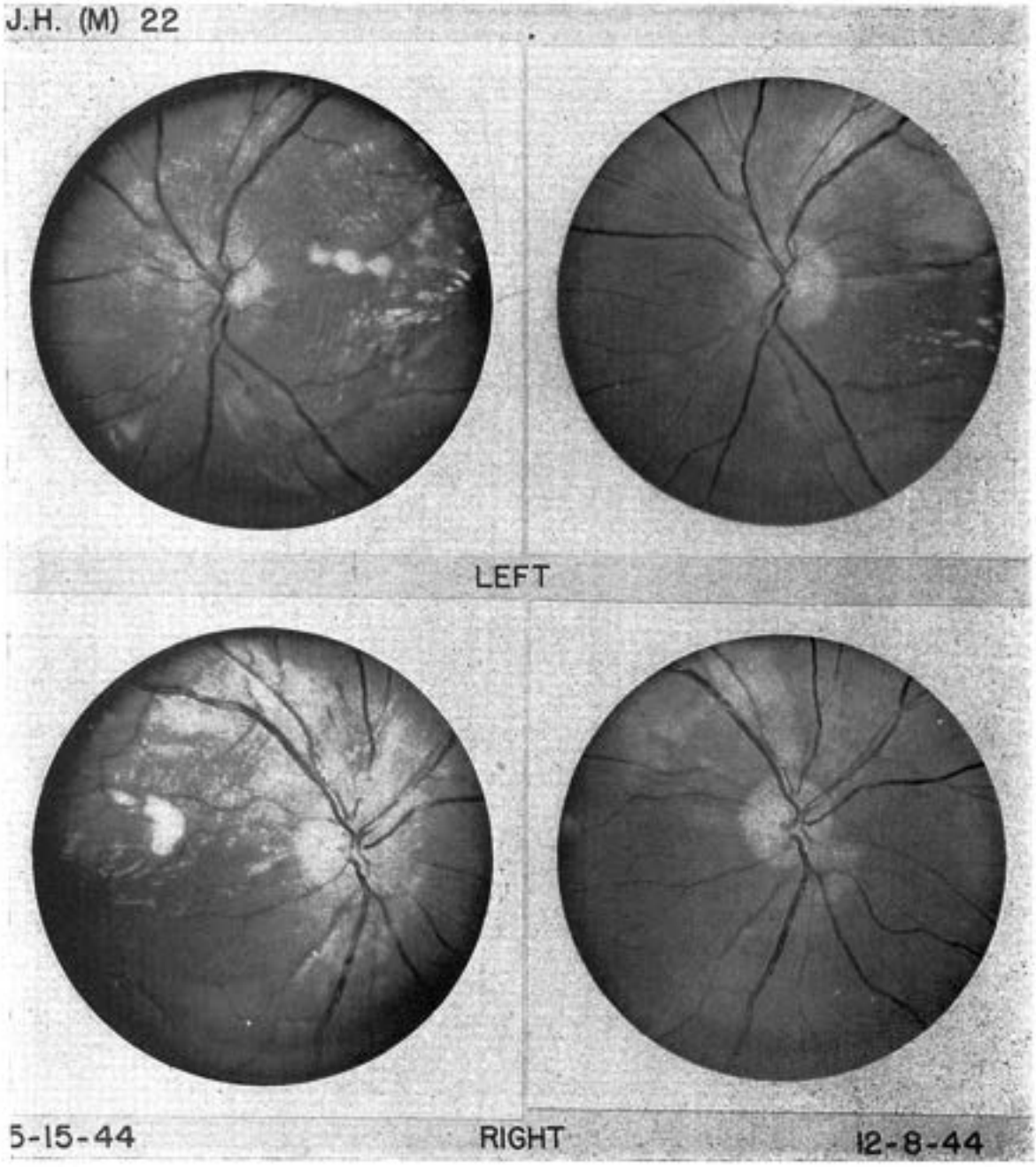

Fig. 27. J.H. (m., 22). Chronic glomerulonephritis. Phenolsulfonphthalein excretion in two hours, 27 per cent. Rice diet from May 14 to August 30, 1944. Blood pressure on May 15, 1944, 164 systolic, 108 diastolic; on December 8, 1944, 134 systolic, 80 diastolic. Disappearance of hemorrhages, right eye. Disappearance of papilledema, marked decrease of exudates, both eyes.

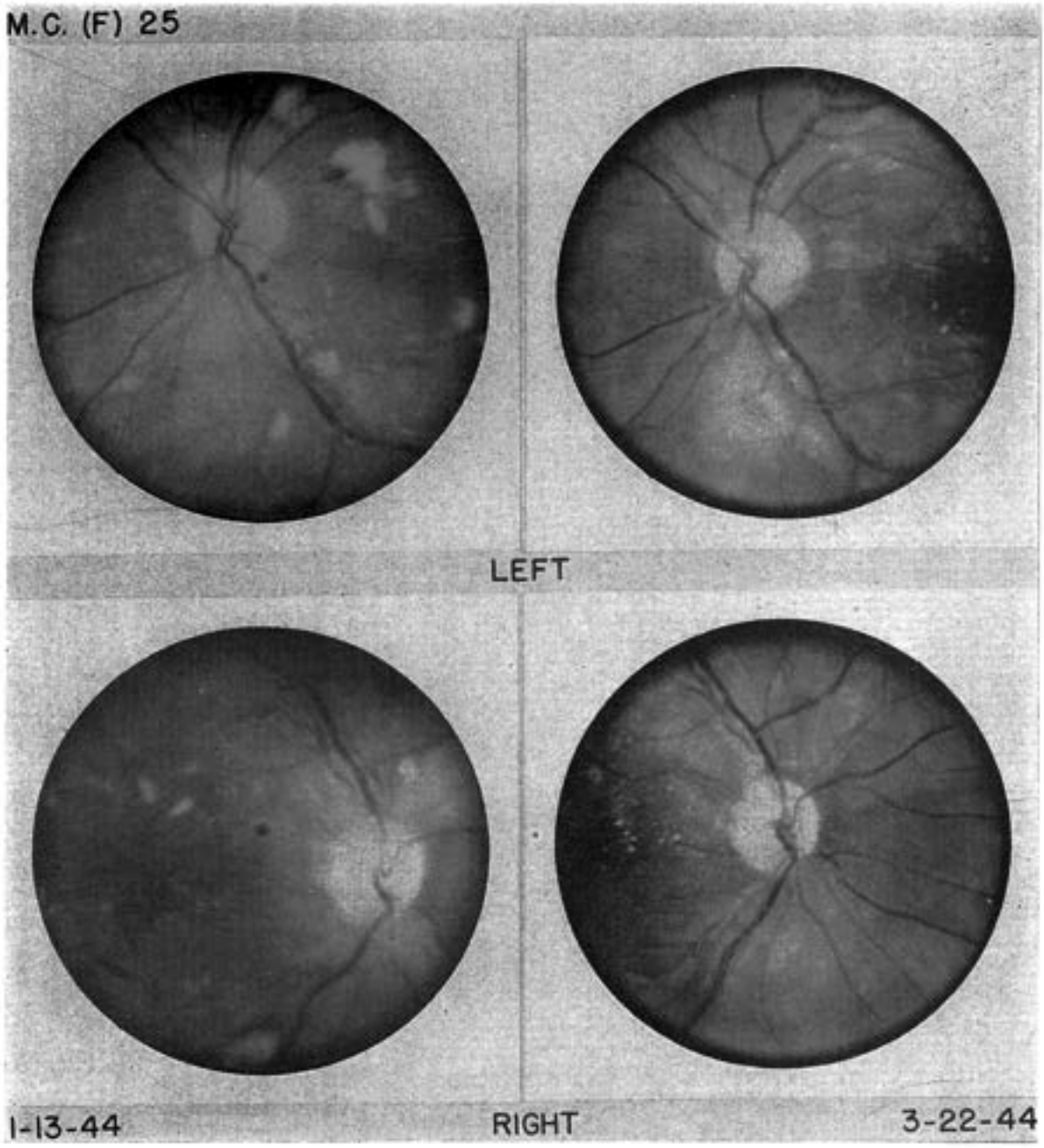

Fig. 28. M.C. (f., 25). Chronic pyelonephritis. Phenolsulfonphthalein excretion in two hours, 12 per cent. Rice diet started January 18, 1944. Before rice diet: Blood pressure 181 systolic, 131 diastolic. Transverse diameter of heart 10.3 cm., nonprotein nitrogen 60 mg. per 100 cc. of blood, albumin 5.5 Gm. per 1000 cc. of urine. After 2½ months of rice diet: Blood pressure 114 systolic, 80 diastolic. Transverse diameter of heart 9.3 cm., nonprotein nitrogen 40 mg. per 100 cc. of blood, albumin 1.1 Gm. per 1000 cc. of urine. **Disappearance of hemorrhages, left eye. Marked decrease of exudates, both eyes.**

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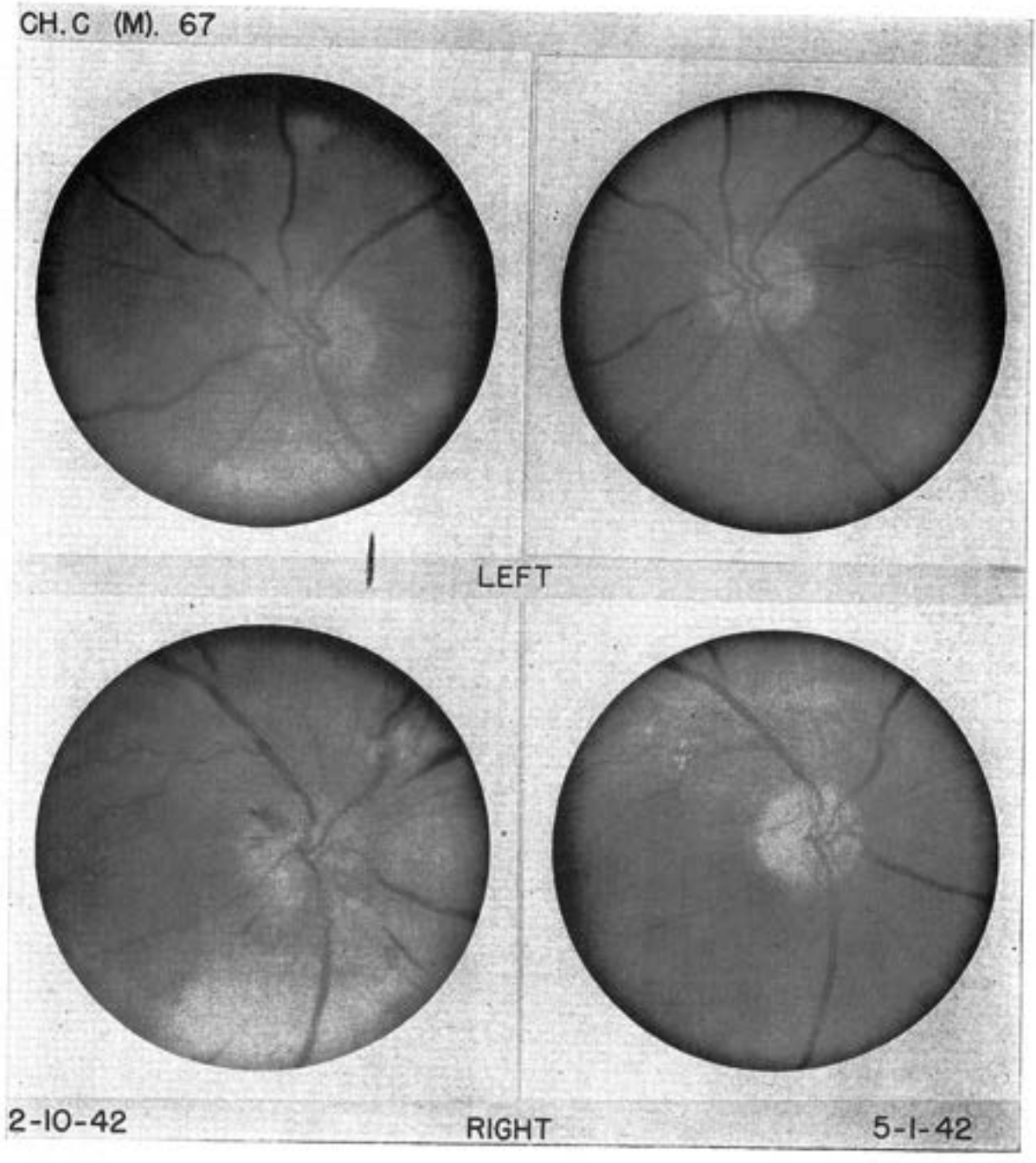

Fig. 29. Ch.C. (m., 67). Arteriosclerosis, "hypertensive vascular disease." Phenolsulfonphthalein excretion in two hours, 40 per cent. Rice diet started February 9, 1942. Before rice diet: Blood pressure 218 systolic, 112 diastolic, nonprotein nitrogen 40 mg. per 100 cc. of blood. After 2½ months of rice diet: Blood pressure 168 systolic, 91 diastolic, nonprotein nitrogen 30 mg. per 100 cc. of blood. **Disappearance of exudates, left eye; of papilledema, hemorrhages, exudates, right eye.**

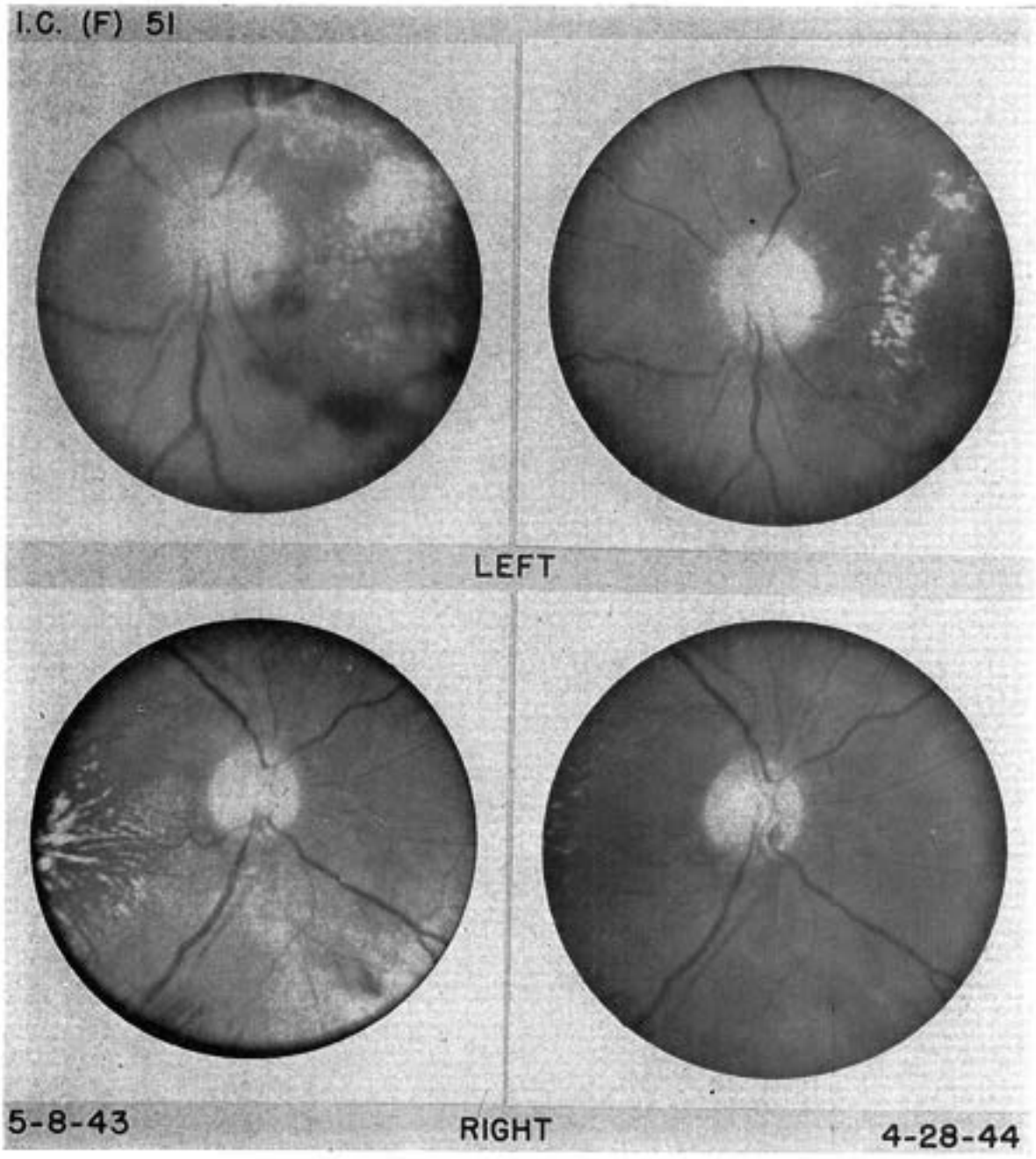

Fig. 30. I.C. (f., 51). "Hypertensive vascular disease." Phenolsulfonphthalein excretion in two hours 59 per cent. Rice diet started April 21, 1943. Before rice diet: Blood pressure 248 systolic, 125 diastolic, nonprotein nitrogen 44 mg. per 100 cc. of blood, cholesterol 292 mg. per 100 cc. of serum, albumin 0.6 Gm. per 1000 cc. of urine. After 11½ months of rice diet: Blood pressure 176 systolic, 100 diastolic, nonprotein nitrogen 30 mg. per 100 cc. of blood, cholesterol 178 mg. per 100 cc. of serum, albumin 0.08 Gm. per 1000 cc. of urine. **Disappearance of edema, hemorrhages, decrease of exudate, left eye. Disappearance of "star figure," right eye.**

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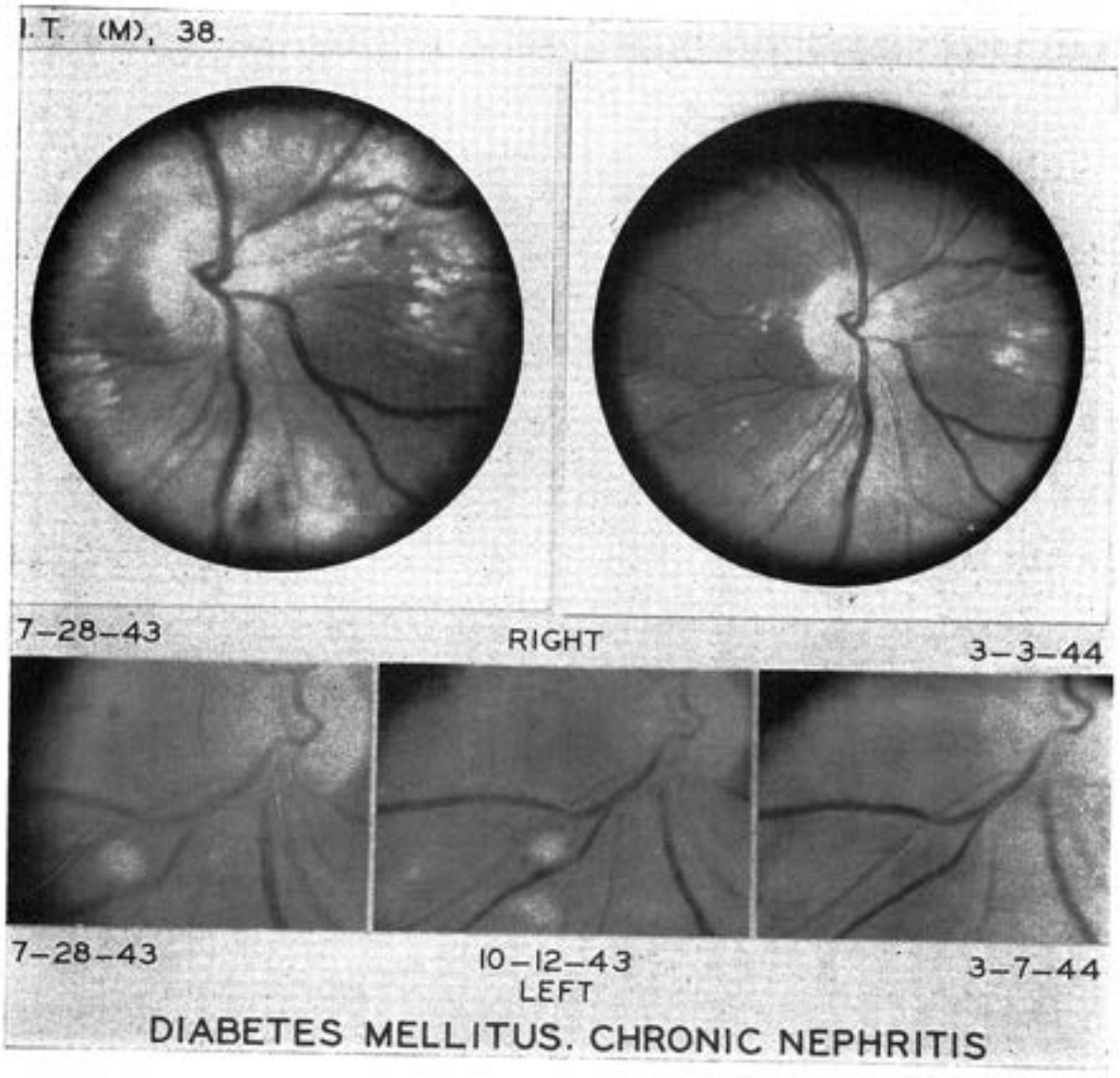

Fig. 31. I.T. (m., 38). Diabetes mellitus, chronic nephritis. Phenolsulfonphthalein excretion in two hours, 50 per cent. Rice diet started April 23, 1943. Before rice diet: Blood pressure 130 systolic, 76 diastolic, nonprotein nitrogen 55 mg. per 100 cc. of blood; total proteins 4.9 Gm. per 100 cc. of plasma; cholesterol 315 mg. per 100 cc. of serum; blood sugar 196 mg. per 100 cc. (35 units of insulin); albumin 3 Gm. per 1000 cc. of urine. After 7 months of rice diet: Blood pressure 130 systolic, 80 diastolic, nonprotein nitrogen 31 mg. per 100 cc. of blood; total proteins 5.8 Gm. per 100 cc. of plasma; cholesterol 230 mg. per 100 cc. of serum; blood sugar 120 mg. per 100 cc. (40 units of insulin); albumin 0.5 Gm. per 1000 cc. of urine. **Disappearance of exudate, left eye; of exudates, hemorrhages, right eye.**

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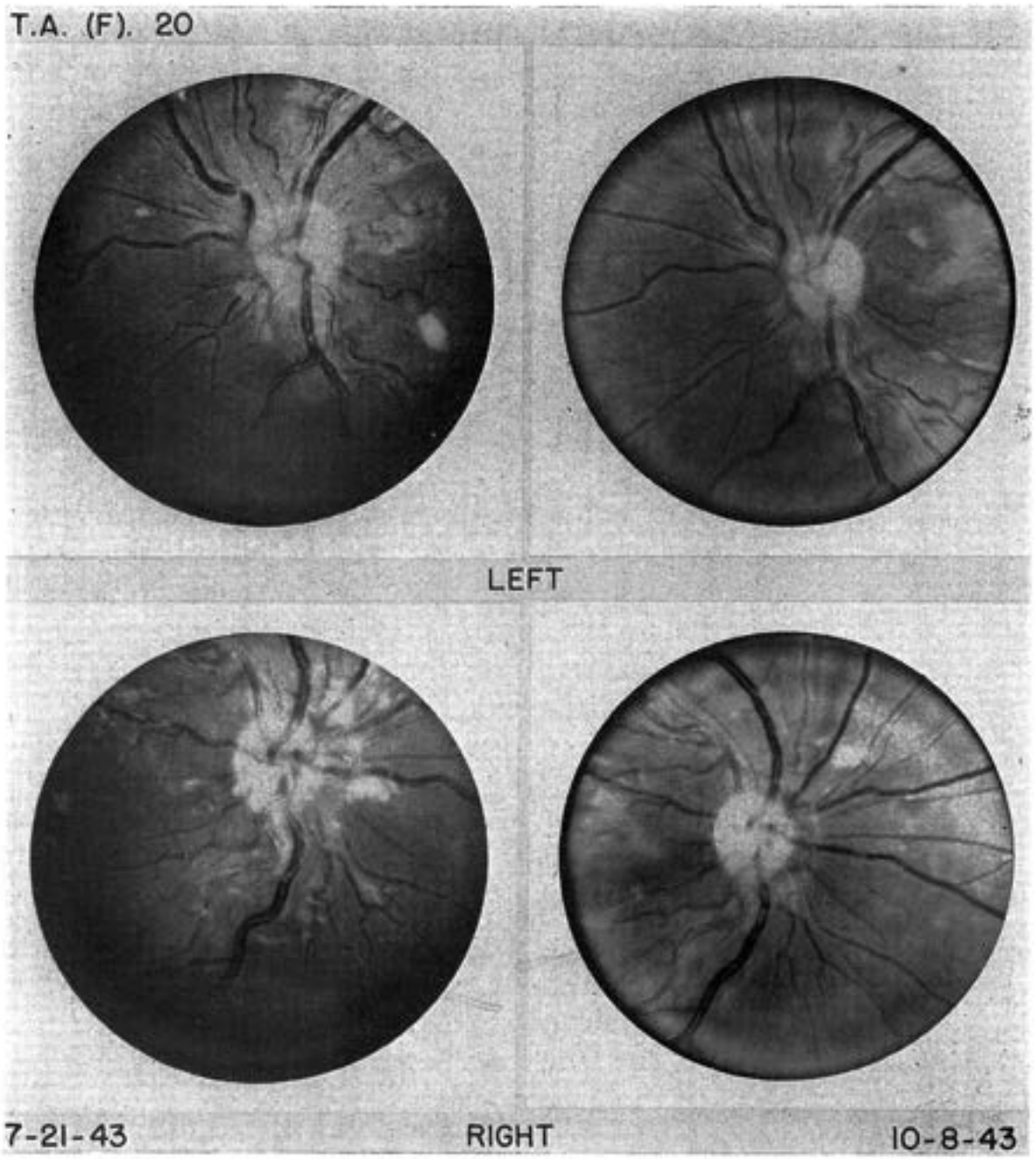

Fig. 32. T.A. (f., 20). Lupus erythematosus disseminatus. Phenolsulfonphthalein excretion in two hours, 85 per cent. Rice diet started July 19, 1943. Before rice diet: Albumin 2 Gm. per 1000 cc. of urine. After 2½ months of rice diet: Albumin 0.4 Gm. per 1000 cc. of urine. See fig. 18. Marked decrease of exudates and venous tortuosity, both eyes.

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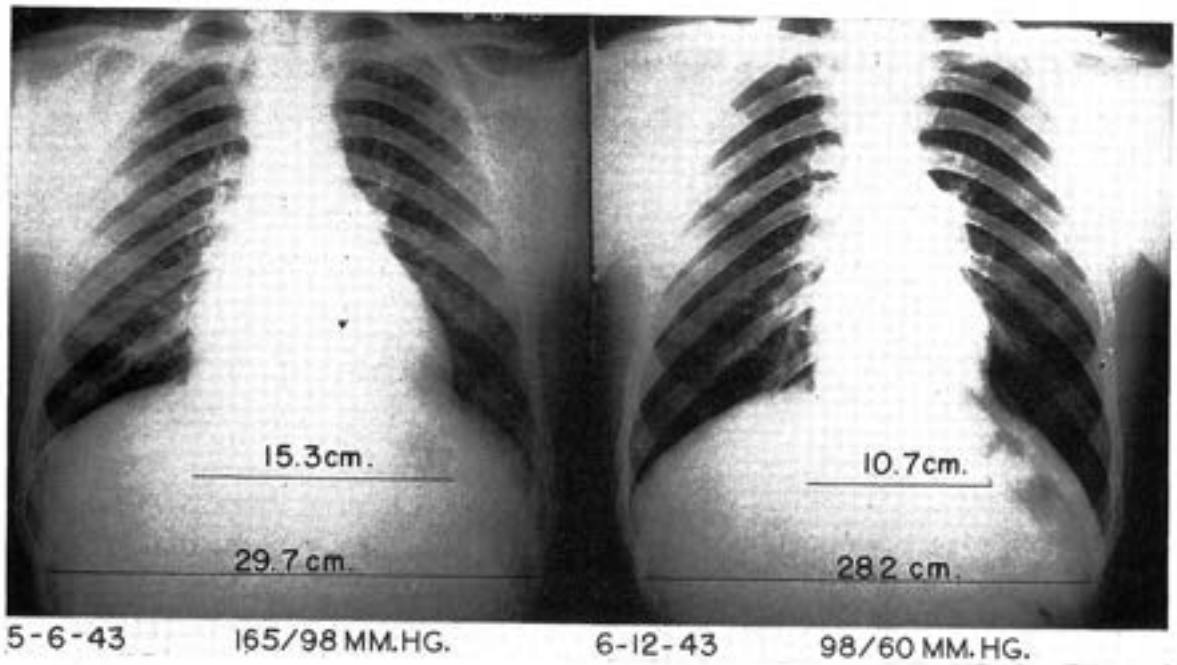

Fig. 33. W.B. Acute glomerulonephritis. Rice diet started May 6, 1943. No digitalis. Reduction in heart size with change in transverse diameter of 43 per cent.

either kidney region. An indirect inguinal hernia, descending into the scrotum, was present on the right side. The prostate was small. Neurological examination showed left lower facial paralysis ("birth injury").

A chest film showed the lungs clear, the heart considerably enlarged (fig. 33). A flat plate of the abdomen showed advanced arthritic changes in both sacro-iliac joints; the kidneys were not distinctly seen; the liver was not enlarged. A sinus plate showed old infection in both antra. The electrocardiogram showed upright T-waves in leads 1, 2, and 3, a diphasic T-wave in lead 4, and no axis deviation.

Accessory clinical findings: The hemoglobin was 91 per cent; there were 4,900,000 red blood cells, and 11,900 white blood cells with 2 per cent non-segmented polymorphonuclears, 68 per cent segmented polymorphonuclears, 2 per cent eosinophils, 3 per cent monocytes, 12 per cent large lymphocytes, and 13 per cent small lymphocytes; the corrected sedimentation rate was 5 mm. in one hour. The serological tests for syphilis were negative. The nonprotein nitrogen was 73 mg. per 100 cc. of blood. The total proteins were 6.1 Gm. per 100 cc. of plasma: albumin 2 Gm., globulin 4.1 Gm., albumin-globulin ratio 0.49. Chlorides (as sodium chloride) were 570 mg. per 100 cc. of plasma. The serum cholesterol concentration was 168 mg. per 100 cc. The urine had a specific gravity of 1.010, no sugar; there were 4.5 Gm. of albumin per 1000 cc. (6.3 Gm. in twenty-four hours), 30-35 red blood cells, 4-5 white blood cells per high power field, occasional hyaline and granular casts, and a 4 plus benzidine reaction. The urinary total nitrogen excretion was 15.6 Gm. in twenty-four hours, the urea excretion 18.4 Gm. in twenty-four hours. The results of the phenolsulfonphthalein test were as follows: Appearance time, ten minutes; excretion at the end of the first half hour 25 per cent, at one hour 20 per cent, at one and a half hours 18 per cent, at two hours 12 per cent; total excretion in two hours 75 per cent. Hookworm eggs were found in the stool. A culture from the nose and throat showed Micrococcus catarrhalis and alpha hemolytic organisms.

Impression: Acute glomerulonephritis with edema, hypertension, cardiac enlargement, and azotemia.

Course: The patient was afebrile except from the eighth to the eleventh hospital day, when his temperature went up to 38 C. The rice diet (1800 calories) was started on the first hospital day; fluid intake was limited to 400 cc. of fruit juices daily. During the first week, the weight fell from 73.1 Kg. to 63.25 Kg. (fig. 34), the blood pressure decreased from 176 systolic, 101 diastolic to 120 systolic, 80 diastolic, remaining at a level

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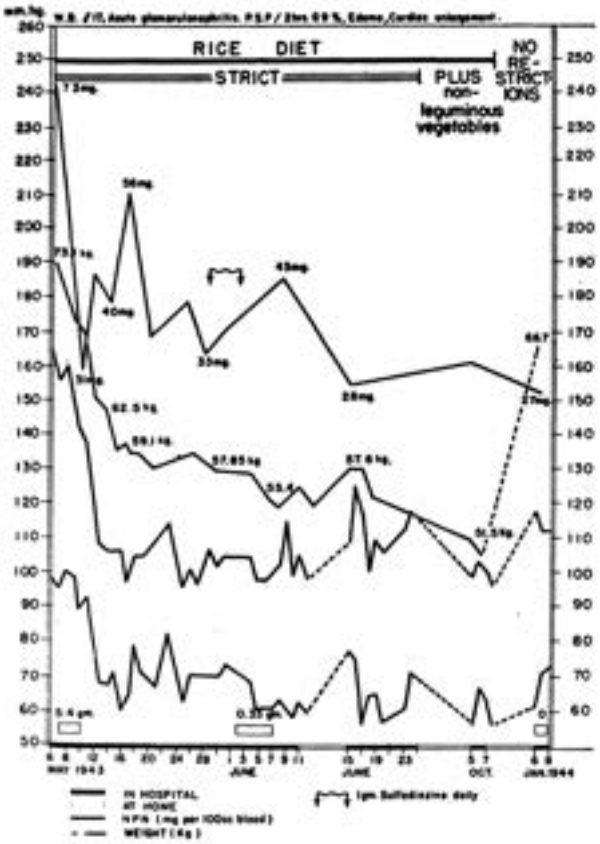

Fig. 34. W.B. Acute glomerulonephritis. Decrease of blood pressure to normal in 6 days on rice diet. Thirty pound weight loss (edema) in 10 days. Disappearance of albuminuria. Decrease of elevated nonprotein nitrogen to normal.

of 105 systolic, 68 diastolic from the second week on (fig. 34). The headache and backache disappeared. On the sixth hospital day the right antrum was irrigated. After fourteen days on the rice diet, the patient's nonprotein nitrogen was 35 mg. per 100 cc. of blood (fig. 34), his weight 58.3 Kg. There were many red blood cells in the urine during the first four weeks. Average albumin excretion during the third week was 1 Gm. per 1000 cc. (1.31 Gm. per twenty-four hours), as compared to an average excretion of 4.5 Gm. per 1000 cc. (6.49 Gm. per twenty-four hours) during the first week. During the fourth and fifth hospital weeks, the albumin excretion decreased to an average of 0.4 Gm. per 1000 cc. of urine (0.51 Gm. per twenty-four hours). Sulfadiazine (0.5 Gm. twice daily) was given for five days in the fourth week. When the patient was discharged in the sixth week, his hemoglobin was 91 per cent, total proteins per 100 cc. of plasma were 5.8 Gm. (albumin 3.0 Gm., globulin 2.8 Gm., albumin-globulin ratio 1.1). His nonprotein nitrogen was 38 mg. per 100 cc. of blood, his weight 56 Kg. He had lost 37 pounds of edema fluid and his heart size had decreased to normal (fig. 33).

The patient continued the strict rice diet at home and was readmitted to the hospital one month later. His blood pressure at that time was 107 systolic, 72 diastolic, his nonprotein nitrogen 28 mg. per 100 cc of blood, urea nitrogen 5.5 mg., urea ratio 20. The total proteins were 5.8 Gm. per 100 cc. of plasma: albumin 3.2 Gm., globulin 2.6 Gm., albumin-globulin ratio 1.2. Chlorides (as sodium chloride) were 512 mg., calcium was 9.6 mg., phosphorus 3.4 mg., cholesterol 80-115 mg. per 100 cc. of serum. The patient's tonsils and adenoids were removed. For the next two and a half months he remained on the rice diet, modified by the addition of nonleguminous vegetables. The urinary total nitrogen excretion at the end of this time was 1.66 Gm. in twenty-four hours, urea excretion 1.7 Gm. in twenty-four hours (1160 cc. of urine). There was no albuminuria, and the patient was completely asymptomatic. The rice diet was discontinued.

Eight months after his first hospitalization, the patient's blood pressure was 114 systolic, 67 diastolic, and his heart size was normal. The nonprotein nitrogen was 27 mg. per 100 cc. of blood, the urea nitrogen 10.2 mg.; chlorides (as sodium chloride) were 604 mg. per 100 cc. of serum. No albumin or red blood cells were present in the urine. Urea clearance was 86 per cent of normal (on a diet containing 50 Gm. of protein). Phenolsulfonphthalein excretion was 60 per cent in one hour. When he was last examined on July 24-27, 1944, he was again completely asymptomatic. There was no indication of any previous kidney disease. The blood pressure was 110 systolic, 70 diastolic; phenolsulfonphthalein excretion was 85 per cent in one hour.

PATIENT 2. *Chronic glomerulonephritis (total phenolsulfonphthalein excretion in two hours 15-35 per cent); hypertension (182 systolic, 117 diastolic); vascular retinopathy. Example of decrease of high blood pressure to normal, and disappearance of retinopathy, heart enlargement, and depression of RT-1.*

N. McL. (A90726), a 33 year old white farmer's widow, was admitted to the hospital on September 17, 1942, complaining of giddiness, failing vision, substernal oppression, and exertional dyspnea.

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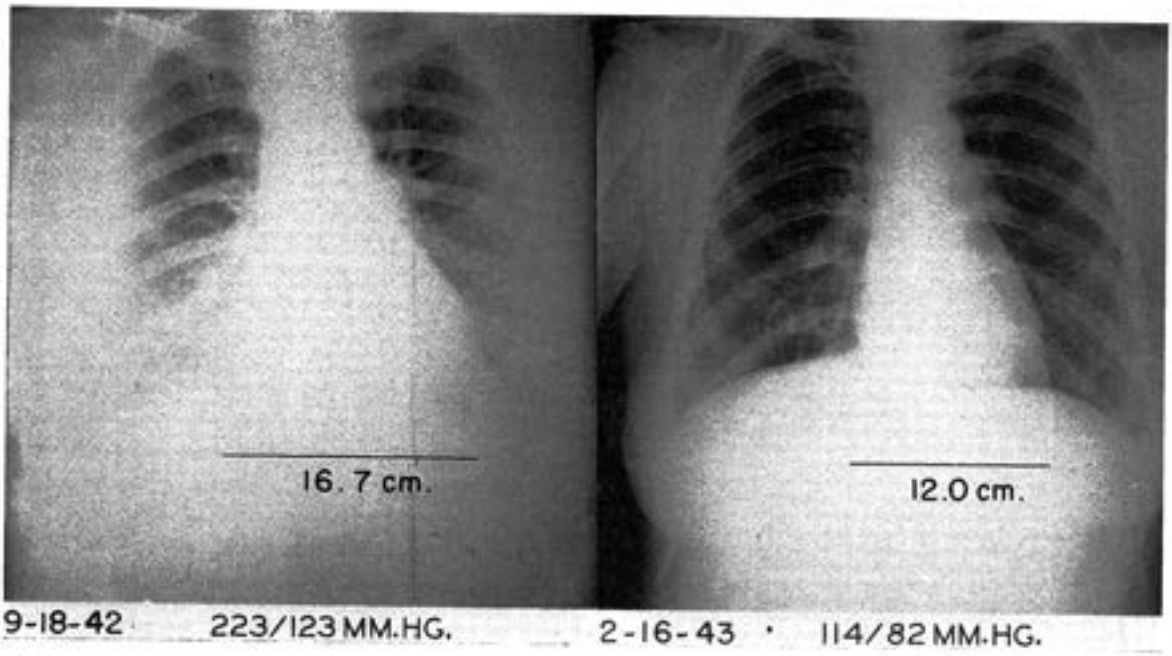

Fig. 35. N. McL. Chronic glomerulonephritis. Rice diet started September 28, 1942. No digitalis. Reduction in heart size with change in transverse diameter of 39 per cent.

History: The patient had had measles and pellagra in childhood, and "kidney trouble" at 17. She had received blood transfusions for anemia in the following years. At 22, she was treated for oliguria and dysuria; at 25-26, she had edema of the ankles and face. She had malaria and erysipelas of the leg when she was 27. Between 28 and 29, her vision began to fail; her physician told her that this was due to kidney disease. At 30, she had "something like a stroke," which cleared up after two or three weeks of bed rest. The patient had never been pregnant.

One year before admission, she was treated with "injections" and blood transfusions for anemia, and with diuretics and other medication for hypertension and "kidney trouble." Her vision was poor; she complained of diplopia and scotomata. There was edema of the feet and legs. She had dyspnea on exertion, paroxysmal nocturnal dyspnea, a feeling of substernal oppression, tachycardia and palpitation.

On *examination*, her height was 156 cm., her weight 82.2 Kg., temperature 37.5 C., pulse 88, respiration 20, blood pressure 190 systolic, 120 diastolic. Slight edema of the ankles and lower legs was noted. Extraocular movements were normal; the pupils were equal and reacted well to light and accommodation. Both discs were blurred on the nasal and temporal sides; the arterioles were silverish and moderately tortuous. A hemorrhage was present in the lower nasal region of the left eye. The teeth were carious, the tonsils enlarged. The lungs showed no pathological findings on percussion and auscultation. The heart was enlarged to the left and right; a soft systolic aortic murmur was heard. The abdomen was obese; no masses were felt, the liver was not enlarged, the spleen was not palpable, and no tenderness was present in either kidney region. The uterus was of normal size with a second degree retroversion. Neurological examination did not show any pathological findings.

A chest film (fig. 35) was read: "Lungs clear. Heart enlarged." The transverse diameter of the heart was 16.7 cm. A flat plate of the abdomen and a retrograde pyelogram were reported as follows: "Kidney normal in outline, no stones seen. Calices and pelves on both sides normal. Spleen slightly enlarged." The electrocardiogram (fig. 36) showed a depressed RT segment in lead 1, diphasic T_1, and a normal sinus rhythm. The basal metabolic rate was −11 per cent.

Accessory clinical findings: The hemoglobin was 92 per cent, red blood cells 4,410,000, white blood cells 6,400 with 1 per cent non-segmented polymorphonuclears, 60 per cent segmented polymorphonuclears, 1 per cent basophils, 5 per cent monocytes, 6 per cent large lymphocytes, 27 per cent small lymphocytes; the corrected sedimentation rate was 18 mm. in one hour. Serological

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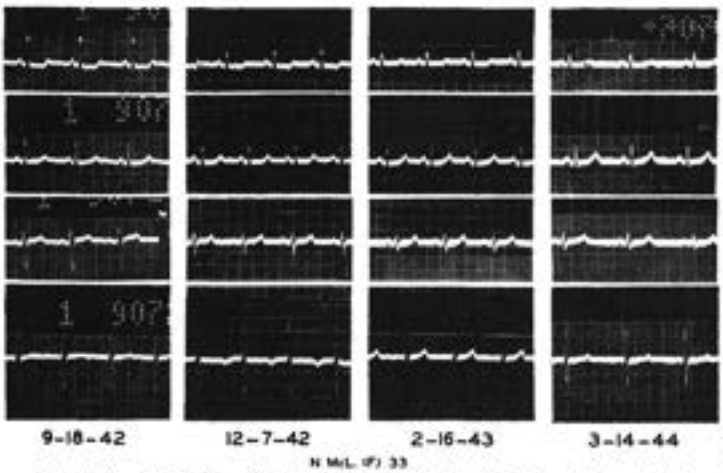

Fig. 36. N. McL. Chronic glomerulonephritis. Rice diet started September 28, 1942. No digitalis. **Increase in angle of electrical axis. Diphasic T_1 has become upright.**

tests for syphilis were negative. The nonprotein nitrogen was 54 mg. per 100 cc. of blood. Total proteins were 6.4 Gm. per 100 cc. of plasma: albumin 3.6 Gm., globulin 2.8 Gm., albumin-globulin ratio 1.3. The urine had a specific gravity of 1.012, no sugar, a 3 plus reaction for albumin, 10-15 white blood cells per high power field, no red blood cells, no casts, a negative benzidine reaction. The results of a phenolsulfonphthalein test were as follows: Appearance time five minutes; excretion at the end of the first half hour 10 per cent, at one hour 7.5 per cent, at one and a half hours 5 per cent, at two hours 2.5 per cent; total excretion in two hours was 25 per cent.

Impression: Chronic glomerulonephritis with hypertension, heart enlargement, diphasic T_1, vascular retinopathy.

Course: For the first eleven days, the patient received a 1500 calorie, salt-poor diet containing 30 Gm. of protein and 2000 cc. of fluids. Her blood pressure during this time averaged 182 systolic, 117 diastolic. The nonprotein nitrogen remained at 54 mg. per 100 cc. of blood. On the twelfth day, the rice diet was started (800-1500 calories, 900-1000 cc. of fruit juices). After six days, the nonprotein nitrogen had decreased to 42 mg. per 100 cc. of blood. The blood pressure at discharge after eleven days of rice diet was 162 systolic, 116 diastolic (fig. 37). The weight was 77.7 Kg., hemoglobin 101 per cent, red blood cells 5,100,000, white blood cells 5,150; the urine gave a 1 to 2 plus reaction for albumin. The patient continued the diet strictly at home, lying down most of the time. She returned to the hospital after eight weeks, feeling much improved. Her blood pressure then was 124 systolic, 84 diastolic, her weight 68.3 Kg., hemoglobin 84 per cent, red blood cells 4,000,000, white blood cells 7,100. The total plasma proteins were 6.8 Gm. per 100 cc. of plasma: albumin 3.6 Gm., globulin 3.2 Gm., albumin-globulin ratio 1.1. The nonprotein nitrogen was 51-64 mg. per 100 cc. of blood. Chlorides (as sodium chloride) were 516 mg. per 100 cc. of serum, calcium was 10.2 mg., phosphorus 4.3 mg., cholesterol 208 mg. There was a 2 plus reaction for albumin in the urine and 10-15 white blood cells per high power field. The results of a phenolsulfonphthalein test were as follows: Appearance time sixteen minutes; excretion at the end of the first half hour 5 per cent, at one hour 4 per cent, at one and a half hours 4 per cent, at two hours 3 per cent; total excretion in two hours 16 per cent. The electrocardiogram (fig. 36) showed a diphasic T_1, upright T_2 and T_3. Examination of the eyegrounds showed the discs more sharply outlined; the hemorrhage in the left eye had been absorbed, leaving a small area of pigmentation.

The patient was readmitted on February 16, 1943, after another two months of strict rice diet at home (1200 calories, 1000 cc. of fruit juices). She felt very well and had no complaints. Her nonprotein nitrogen was 69 mg. per 100 cc. of blood, her blood pressure 120 systolic, 84 diastolic, her weight 66.4 Kg., hemoglobin 78 per cent, total proteins 6.7 Gm. per 100 cc. of plasma, albumin-globulin ratio 0.81; chlorides (as sodium chloride) 528 mg. per 100 cc. of serum, calcium 9.4 mg., phosphorus 3.2 mg., cholesterol 121 mg. The albumin excretion in the urine was 1.52 Gm. in twenty-four hours (675 cc.), the total nitrogen excretion 1.82 Gm. and the urea excretion 2.52 Gm. The total phenolsulfonphthalein excretion in two hours was 15 per cent. There was marked reduction in the size of the heart (fig. 35); the transverse diameter was 12.0 cm. The electrocardiogram (fig. 36) showed the RT_1 segment to be less depressed. The basal metabolic rate was −12 per cent. After twelve days in the hospital, the nonprotein nitrogen was 40 mg. per 100 cc. of blood.

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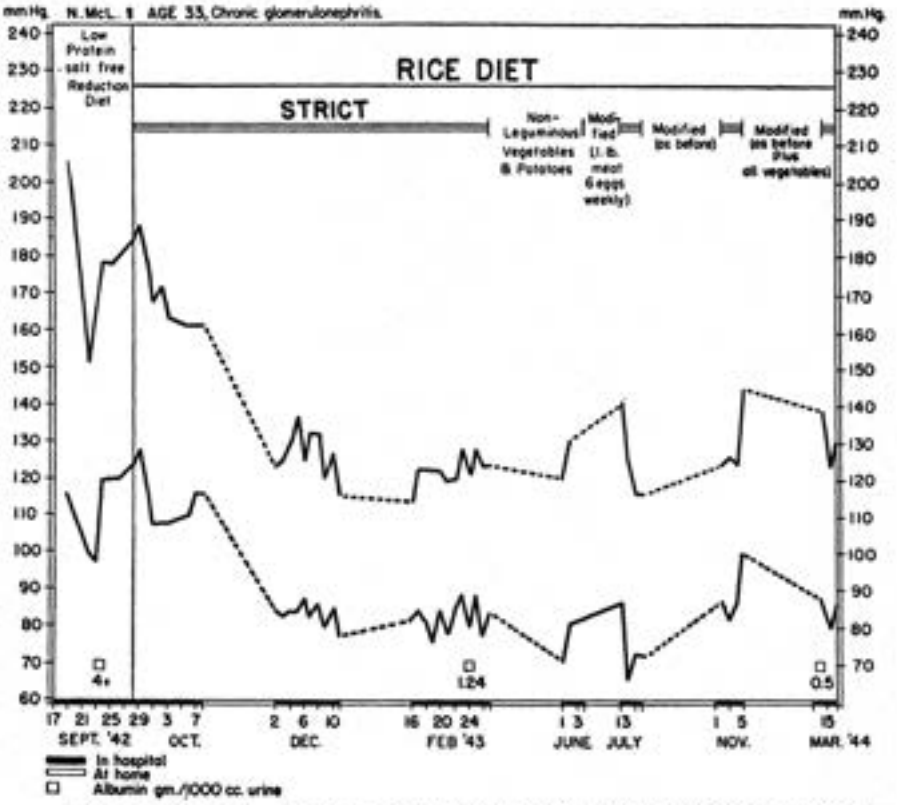

Fig. 37. N. McL. Chronic glomerulonephritis. Decrease of blood pressure to normal in two months on rice diet.

The hemoglobin at discharge was 84 per cent. The urine contained 10-12 white blood cells per high power field, but no red blood cells and no casts. The weight was 60.2 Kg. Non-leguminous vegetables and small amounts of Irish and sweet potatoes were added to the strict rice diet.

The patient stayed on this diet for the following three months and was up part of the day. When she was again seen in the hospital on June 1, 1943, she said that she had had no complaints except minimal ankle edema. Her blood pressure was 120 systolic, 70 diastolic, her weight 62.5 Kg. The nonprotein nitrogen was 36 mg. per 100 cc. of blood. Total proteins were 5.8 Gm. per 100 cc. of plasma; the albumin-globulin ratio was 1.2. Chlorides (as sodium chloride) were 592 mg. per 100 cc. of serum, calcium was 8.7 mg., phosphorus 3.4 mg., cholesterol 110 mg. The hemoglobin was 48 per cent, red blood cells 2,200,000, white blood cells 5,440. After five days in the hospital she was discharged on the diet which was started February 27, further modified by the addition of one egg six times a week and ¼ pound of liver, chicken, or lean beef four times a week.

Examination on November 1-5, 1943, gave the following findings: Blood pressure 124 systolic, 86 diastolic; hemoglobin 97 per cent, red blood cells 4,200,000; nonprotein nitrogen 43 mg., urea nitrogen 18 mg. per 100 cc. of blood; total proteins 6.2 Gm. per 100 cc. of plasma (albumin-globulin ratio 2.0); cholesterol 140 mg. per 100 cc. of serum. The urinary total nitrogen excretion was 3.4 Gm., the urea excretion 5.03 Gm. in twenty-four hours (580 cc.). The urea clearance was 46.2 per cent of normal. Phenolsulfonphthalein excretion in two hours was 21 per cent. The transverse diameter of the heart was 10.7 cm. The patient was feeling very well and had been doing light housework. Her diet was further modified to include corn, beans, and peas, besides the eggs, meat, and vegetables allowed before.

On March 13-16, 1944, the blood pressure averaged 131 systolic, 85 diastolic; the weight was 61.5 Kg. The transverse diameter of the heart was 11.0 cm., that of the great vessels 5.3 cm. The nonprotein nitrogen was 46 mg. per 100 cc. of blood; total proteins were 6.1 Gm. per 100 cc. of plasma (albumin 3.2 Gm., globulin 2.9 Gm.). Two phenolsulfonphthalein tests showed a total

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excretion in two hours of 35 and 28 per cent. The patient had been completely asymptomatic and was feeling perfectly well.

When last seen, September 4-8, 1944, the patient was still following the liberally modified rice diet and feeling "young and strong." She had married again in April and was doing her housework without noticing any fatigue. She was advised, however, to wait for another year before considering having a child.

The findings on the latest examination, compared with those on the first hospitalization, were:

	September, 1943	*September, 1944*
Blood pressure (mm. Hg.)	182/117	126/82
Hemoglobin (% of 15.5 Gm.)	92	85
RBC (per cubic mm.)	4,410,000	3,900,000
NPN (mg. per 100 cc. of blood)	54	38
Total proteins (Gm. per 100 cc. of plasma)	6.4	6.5
PSP (% excreted in two hours)	25	25
Weight (Kg.)	82.2	58.7
Transverse diameter of heart (cm.)	16.7	11.1
Diameter of great vessels (cm.)	6.8	5.3
T wave in lead 1	Diphasic	Upright
Retinal hemorrhages	+	0

PATIENT 3. *Chronic glomerulonephritis (total phenolsulfonphthalein excretion in two hours 17.5 per cent); hypertension (250 systolic, 174 diastolic); uremia (nonprotein nitrogen 87-153 mg. per 100 cc. of blood). Example of decrease of high blood pressure and nonprotein nitrogen to normal and of recovery of eyesight with disappearance of papilledema, retinal hemorrhages, and exudates.*

C.A. (A99483), a 32 year old white farmer's wife, was admitted to the hospital in a semi-comatose condition, very acutely ill. The *history* was obtained from the husband and, after recovery, from the patient. She had had ten children, of whom six were living. Her blood pressure had been high before delivery of the ninth child. One week before delivery of the tenth child—in February, 1942—she developed ankle edema and headache. She had had high blood pressure "ever since." Attacks of pain in both flanks, radiating into the lower part of the back, had occurred about every four to five weeks since July, 1942. Her vision had been failing since August. Since Christmas, 1942, she had had increasing weakness, intense headache, and vomiting; she had become completely blind, except for light perception. For a few days before admission she had been "out of her mind," and unconscious part of the time. During momentary lucid intervals, she complained of headache and vague abdominal pain.

Upon *examination* on February 2, 1943, her temperature was 36.5 C., pulse 120, respiration 22, blood pressure 250 systolic, 174 diastolic. She was pale and stuporous. There was no edema. She had a marked nephritic stare and mydriasis. The eyegrounds showed bilateral papilledema, engorgement and tortuosity of the veins, and numerous large hemorrhages and exudates; the arterioles were partly invisible. A few small blood clots were seen in the nose. The breath was uremic. She had moderate gingivitis. The neck showed no venous distention; the thyroid was slightly enlarged. There were no pathological findings in the lungs. The heart was enlarged to the left, the point of maximum impulse being 10 cm. from the midsternal line. The sounds were loud, and a slapping aortic second sound, a soft apical systolic murmur, and a loud, harsh aortic systolic murmur were heard. The rhythm was regular, and there was no friction rub. Moderate tenderness was present in the

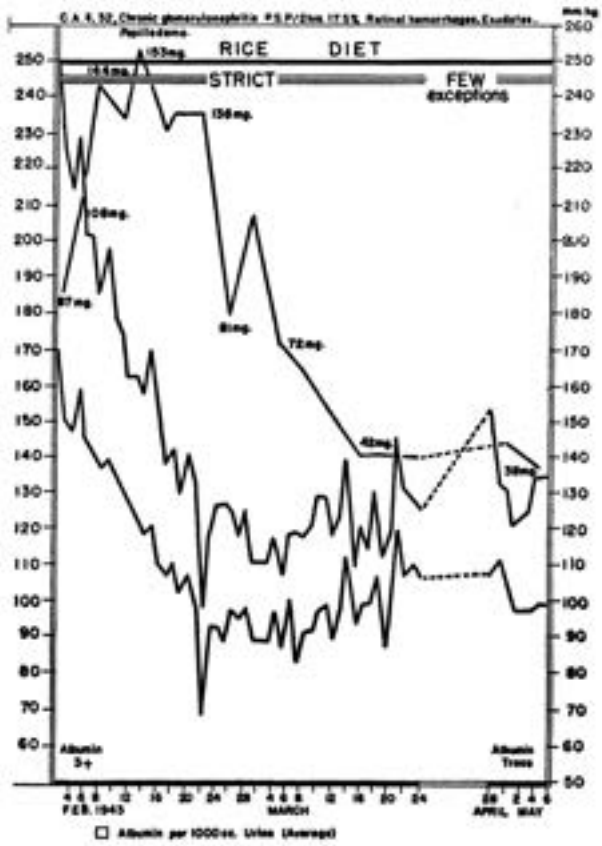

Fig. 38. C.A. Chronic glomerulonephritis. Decrease of blood pressure to normal in 3 weeks on rice diet. Decrease of nonprotein nitrogen and albuminuria.

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right lower quadrant. The liver was not enlarged.

Accessory clinical findings: The hemoglobin was 80 per cent, red blood cells 4,000,000, white blood cells 14,350, with 4 per cent juveniles, 10 per cent non-segmented polymorphonuclears, 78 per cent segmented polymorphonuclears, 2 per cent eosinophils, 3 per cent monocytes, 2 per cent large lymphocytes, 1 per cent small lymphocytes. The corrected sedimentation rate was 40 mm. in one hour. Serological tests for syphilis were negative. The nonprotein nitrogen was 87 mg. per 100 cc. of blood. The carbon dioxide combining power of the plasma was 41 volumes per cent. Total proteins were 6.9 Gm. per 100 cc. of plasma: albumin 4.0 Gm., globulin 2.9 Gm., albumin-globulin ratio 1.4. Chlorides (as sodium chloride) were 414 mg. per 100 cc. of serum, calcium 9.6 mg., phosphorus 3.6 mg. The urine gave a 3 plus reaction for albumin and contained 20-30 red blood cells and 10-15 white blood cells per high power field, and many hyaline and granular casts; the benzidine reaction was 1 plus.

Impression: Terminal stage of chronic glomerulonephritis; uremia; hypertension; vascular retinopathy with papilledema, hemorrhages, and exudates.

Course: The patient was started on the rice diet immediately, but during the first few days was able to take only very small amounts of it. Four hundred and fifty to 1300 cc. of fruit juices were given daily, but partly lost by vomiting. Five hundred to 2000 cc. of 10 per cent glucose in water containing nicotinic acid, thiamine chloride, ascorbic acid, and vitamin K were given intravenously during the first two weeks. The only other medication was 1 cc. of dilute hydrochloric acid three times daily by mouth. After ten to fourteen days of mental confusion (excitation state alternating with stupor), with the nonprotein nitrogen rising to 153 mg. per 100 cc. of blood (fig. 38), and the hemoglobin falling to 52 per cent (red blood cells 2,500,000, benzidine reaction of the stool 4 plus), the patient was definitely better and able to take the greater part of the diet. On the fourteenth hospital day, the total nitrogen excretion in the urine was 2.55 Gm. in twenty-four hours. By that time, the blood pressure had gradually decreased to 156 systolic, 112 diastolic (fig. 38). The carbon dioxide combining power of the plasma was 57 volumes per cent. Chlorides (as sodium chloride) were 445 mg. per 100 cc. of plasma. Intravenous glucose was discontinued. The average daily fluid intake in the following two weeks was 1260 cc. of fruit juices. The patient was rational and could answer questions. She was able to distinguish light and dark, but was unable to see objects. On the fifteenth hospital day, she was strong enough to sit up a few minutes so that photographs of the eyegrounds could be taken (fig. 39). The nonprotein nitrogen fell gradually (fig. 38): on the twentieth hospital day, it was 136 mg. per 100 cc. of blood, on the twenty-seventh day 108 mg., on the thirty-fourth day 66 mg., on the forty-second day 42 mg. The blood pressure readings from the twentieth to the fiftieth day averaged 123 systolic, 97 diastolic. Eight days before discharge, the phenolsulfonphthalein excretion at the end of one-half hour was 0, at one hour 7.5 per cent, at one and a half hours 5 per cent, at two hours 5 per cent; the total excretion in two hours was 17.5 per cent. The urine contained 0.1-0.2 Gm. of albumin in 1000 cc.; the hemoglobin was 66 per cent, red blood cells 3,300,000; chlorides (as sodium chloride) were 508 mg. per 100 cc. of plasma. The patient was feeling completely well and was gradually regaining her eyesight. The eyegrounds were very much improved; the engorgement and tortuosity of the veins were decreasing, the papilledema was subsiding, and there were no new hemorrhages or exudates.

The patient was discharged on the fifty-second day on the strict rice regime. She followed this, except for six eggs taken in the last week, until her readmission on April 28. At this time, she was feeling "well and healthy," and said that she had had no headache and had been doing all her housework without getting tired. Her eyesight was fully restored. Her heart size was at the upper limits of normal. The rhythm was regular and there were no murmurs. Her blood pressure (average of seven days) was 130 systolic, 102 diastolic. The nonprotein nitrogen was 38 mg. per 100 cc. of blood, the hemoglobin 67 per cent. The urine contained only a trace of albumin and no red blood cells; the benzidine reaction was negative. The phenolsulfonphthalein excretion was about 20 per cent in two hours. The total nitrogen excretion in the urine was 1.17 Gm. in twenty-four hours. Examination of the eyegrounds (fig. 39) showed the discs sharply outlined; the papilledema had com-

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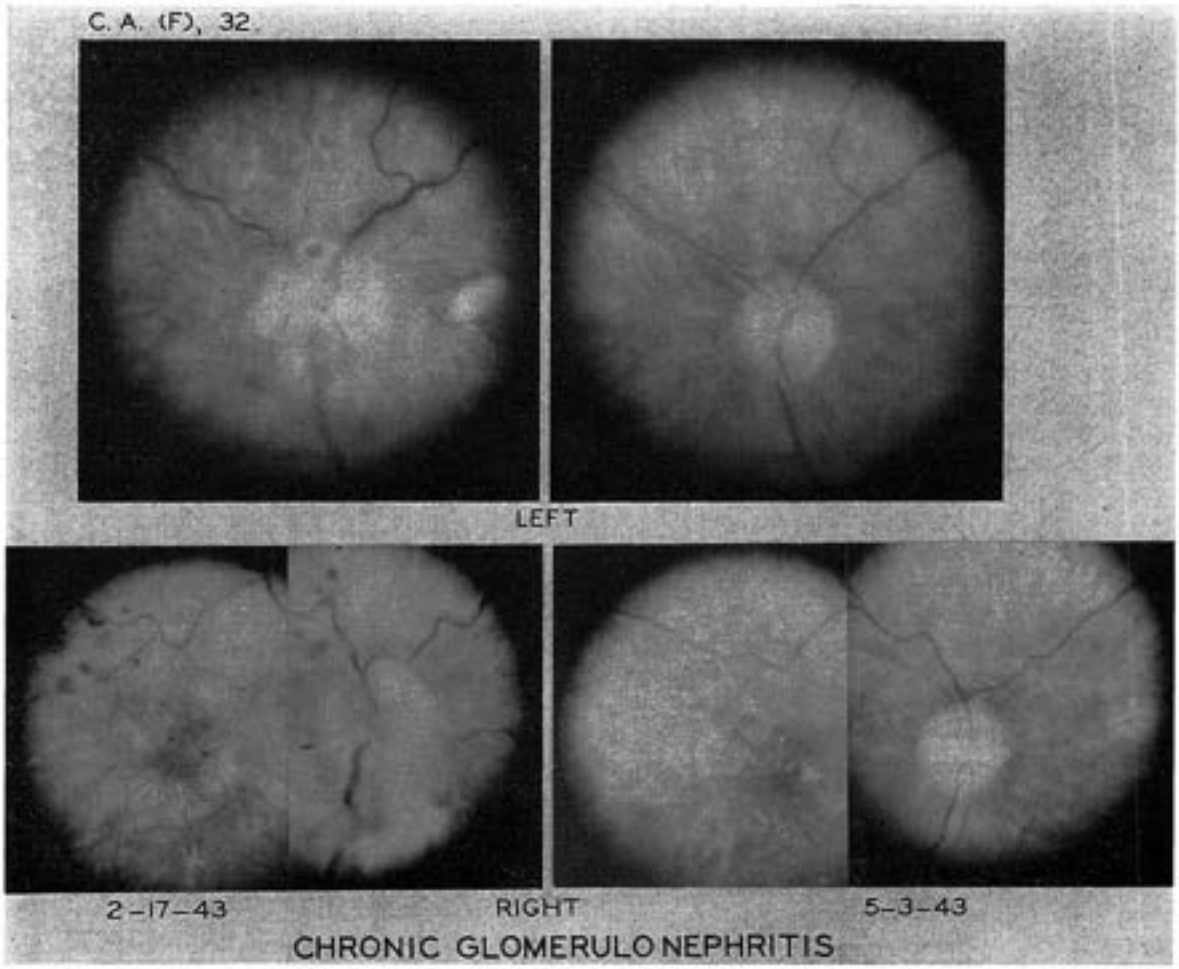

Fig. 39. C.A. (f., 32). Chronic glomerulonephritis. Rice diet started February 2, 1943. **Disappearance of papilledema, hemorrhages, exudates; marked decrease of venous tortuosity and engorgement, both eyes.**

pletely disappeared; hemorrhages and exudates had been absorbed, leaving some pigmentation and scarring; previously tortuous and engorged veins had become delicate and straight.

PATIENT 4. *Chronic pyelonephritis (total phenolsulfonphthalein excretion in two hours 9-25 per cent); hypertension (234 systolic, 144 diastolic); vascular retinopathy. No improvement on salt-poor, meat-free diet. Example of decrease of high blood pressure to normal and disappearance of retinal hemorrhages and heart enlargement on strict rice diet. Elevation of blood pressure following too liberal modification of diet.*

A.E.H. (B3008), a 36 year old white farmer's wife, was admitted to the hospital on April 5, 1943, with the chief complaints of headache, weakness, failing vision, substernal oppression, and exertional dyspnea.

History: The patient had had mumps and pneumonia in childhood, malaria at the age of 17, and influenza at 20 and 36. She had been pregnant six times, had had three abortions, and had three living children. Her last pregnancy had terminated in an abortion in the sixth month—July, 1942. In June and July, 1942, she had severe headache, failing vision, moderate edema, and high blood pressure. After the abortion, her blood pressure was said to have decreased. The headache was milder for one month, but there was no increase in visual acuity, and generalized weakness persisted. In August, 1942, a curettage was performed at the local hospital because of excessive vaginal bleeding. Her blood pressure at that time was said to be normal. She continued to have moderate headache and progressive visual disturbances until the end of September, when the headache increased in severity. The physician whom the patient consulted

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about her eyesight found her blood pressure high and suggested a salt-poor, meat-free diet, which she followed with no relief. Starting in December, 1942, she had continuous severe headache, blurred vision, nocturia (five to six times nightly), tachycardia, substernal oppression, and exertional dyspnea, but she had no edema. Her blood pressure was said to have remained high in spite of diet, sedatives, laxatives, and rest. The patient was unable to do her housework because of weakness and headache.

Examination: Her height was 157 cm., her weight 57 Kg., temperature 36.8 C., pulse 96, respiration 20, blood pressure 246 systolic, 159 diastolic. There was no edema. Acne was present over the anterior chest. Examination of the eyes showed mydriasis and moderate photophobia; the pupils reacted equally to light and accommodation. The disc margins in both eyes were not quite distinct. The arterioles were markedly constricted ("silver-wire" arterioles), the veins moderately engorged. Arteriovenous compression and several hemorrhages and patches of yellowish exudate were present in both eyes. The inferior nasal turbinates were swollen. The teeth were in good repair. The lungs showed no pathological findings on percussion and auscultation. The heart was moderately enlarged to the right and left. The sounds were loud and snapping; the aortic second sound was louder than the pulmonic second sound; no murmurs were heard. There were no masses or tenderness in the abdomen; the liver was not enlarged, and the spleen not palpable. The uterus was found to be small and in the mid-pelvis; there was a mild cervicitis. Neurological examination gave no pathological findings.

A chest film (fig. 40) showed the diameter of the great vessels to be 6.2 cm., the transverse diameter of the heart 11.9 cm., the internal chest diameter 26.8 cm. The electrocardiogram (fig. 41) showed diphasic T-waves in lead 1 and upright T-waves in leads 2 and 3; the angle of the electrical axis was + 22 degrees. A flat plate of the abdomen did not show any stones.

Accessory clinical findings: The hemoglobin was 97 per cent, red blood cells 4,960,000, white blood cells 6,040, with 7 per cent non-segmented polymorphonuclears, 58 per cent segmented polymorphonuclears, 2 per cent eosinophils, 5 per cent monocytes, 11 per cent large lymphocytes, 17 per cent small lymphocytes. The corrected sedimentation rate was 36 mm. in one hour. Serological tests for syphilis were negative. The non-protein nitrogen was 46 mg. per 100 cc. of blood, the carbon dioxide combining power of the plasma 49 volumes per cent. The total proteins were 7.7 Gm. per 100 cc. of plasma:

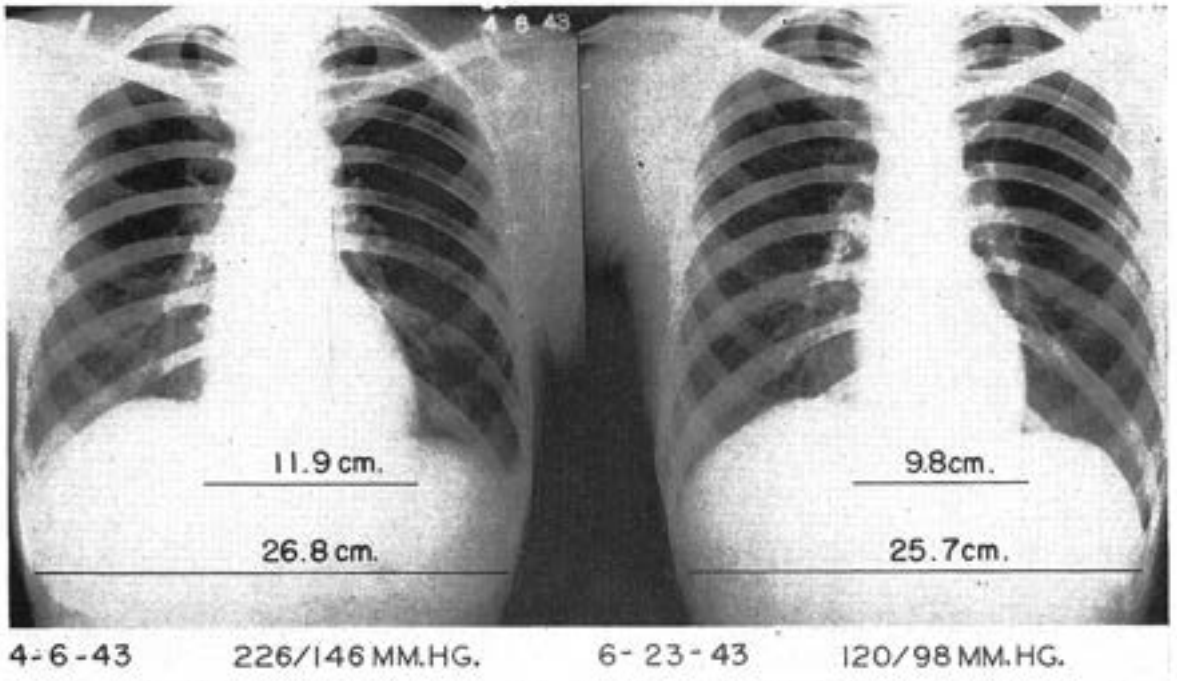

Fig. 40. A.E.H. Chronic pyelonephritis. Rice diet started April 13, 1943. No digitalis. Reduction in heart size with change in transverse diameter of 21 per cent.

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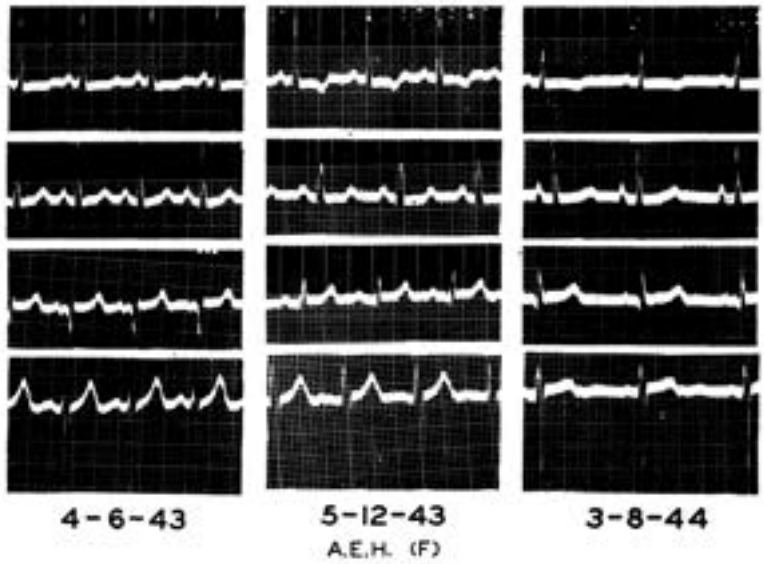

Fig. 41. A.E.H. Chronic pyelonephritis. Rice diet started April 13, 1943. No digitalis. **Increase in angle of electrical axis from +22° to +57°.**

Fig. 42. A.E.H. Chronic pyelonephritis. **Decrease of blood pressure to normal in 2½ months on rice diet. Increase of blood pressure following too liberal modification of diet.**

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albumin 3.5 Gm., globulin 4.2 Gm., albumin-globulin ratio 0.83. Chlorides (as sodium chloride) were 574 mg. per 100 cc. of plasma; calcium was 8.7 mg. per 100 cc. of serum, phosphorus 4.2 mg., cholesterol 270 mg. The urine had a specific gravity of 1.002-1.018, and contained 1-5 red blood cells and 3-35 white blood cells per high power field, and many granular casts. The benzidine reaction was 0-1 plus. The first ten albumin determinations showed an average excretion of 1.7 Gm. per 1000 cc. The results of a phenolsulfonphthalein test were as follows: 5 per cent excretion at first half hour, 2.5 per cent at one hour, 2.5 per cent at one and a half hours, less than 2.5 per cent at two hours; total excretion in two hours less than 12.5 per cent. The test was repeated a week later and showed 10 per cent excretion at the first twenty-three minutes, 5 per cent at forty-three minutes, 5 per cent at one and a half hours, less than 2.5 per cent at two hours; total excretion in two hours 20-22.5 per cent.

Impression: Chronic pyelonephritis with hypertension, vascular retinopathy, heart enlargement.

Course: After five days of strict bed rest on a diet containing 65 Gm. of protein, the blood pressure (average from the fifth to the ninth day) was 234 systolic, 144 diastolic (fig. 42). The lowest blood pressure readings during sodium amytal sleep were 190 systolic, 130 diastolic and 184 systolic, 138 diastolic. The patient complained of very intense headache every day. On the ninth hospital day the rice diet was begun (2000 calories, fluids limited to 1500 cc., after two weeks to 1000 cc.). The blood pressure level remained almost unchanged for about three weeks. In the fourth week, first the systolic, then the diastolic pressure began to decrease gradually. After five weeks of rice diet the blood pressure average of five days was 150 systolic, 119 diastolic. The plasma chlorides (as sodium chloride) at this time were 507 mg. per 100 cc. The nonprotein nitrogen was 42 mg. per 100 cc. of blood. The albumin in the urine had decreased to an average of 0.8 Gm. per 1000 cc. The urine sediment contained a great number of white blood cells, but no red blood cells or casts. There were still numerous hemorrhages in both eyes (fig. 43). The patient was discharged on the rice diet on May 21, 1943, feeling very much better. The headaches from which she had been suffering for seven months had become much milder after two weeks of the diet and had completely disappeared after four weeks.

The patient continued to follow the rice diet, to which some non-leguminous vegetables were added early in July, and was occasionally seen in the hospital. She had no headaches and no substernal oppression. Her eyesight improved markedly. The retinal hemorrhages were absorbed. The blood pressure decreased almost to normal: the average level from June 22 to July 3, 1943, was 128 systolic, 92 diastolic; from August 21 to 25, 1943, 118 systolic, 90 diastolic. The heart became smaller in size, with a change in the transverse diameter of 21 per cent (fig. 40). The total phenolsulfonphthalein excretion in two hours was 25 per cent.

On October 7, 1943, the patient was readmitted because of diarrhea, anorexia, and weakness. Her blood pressure at that time was 114 systolic, 82 diastolic. The transverse diameter of the heart was 10.05 cm. (as against 11.9 cm. six months before). The electrocardiogram showed the angle of the electrical axis to be +57 degrees (as against +22 degrees six months before). The hemoglobin was 78 per cent, the nonprotein nitrogen 35 mg. per 100 cc. of blood; the chlorides (as sodium chloride) were 466 mg. per 100 cc. of serum, the total proteins 5.9 Gm. per 100 cc. of plasma (albumin 2.3 Gm., globulin 3.6 Gm.). The total nitrogen excretion in the urine was 0.94 Gm. in twenty-four hours.

Sodium chloride (0.6 Gm. to 3 Gm. daily) was added to the diet during the first fourteen days. On the eighth hospital day, the temperature rose to 38.6 C. A catheterized specimen of urine was loaded with white blood cells. One and a half grams of sulfadiazine and 1.8 Gm. of sodium bicarbonate were given daily for seven days. After five days, the temperature returned to normal. The hemoglobin decreased from 78 per cent to 54 per cent, however, and sulfadiazine was discontinued. Because of persisting diarrhea (with stool cultures negative for the typhoid-dysentery group of bacilli, staphylococci, and hemolytic organisms) 2 Gm. of sulfaguanidine were given daily for eight days; the number of stools decreased to about three a day.

Since the patient insisted that she could not eat the strict rice diet any longer, toast, butter, potatoes, eggs, chicken, and liver were added in amounts of 100-800 calories

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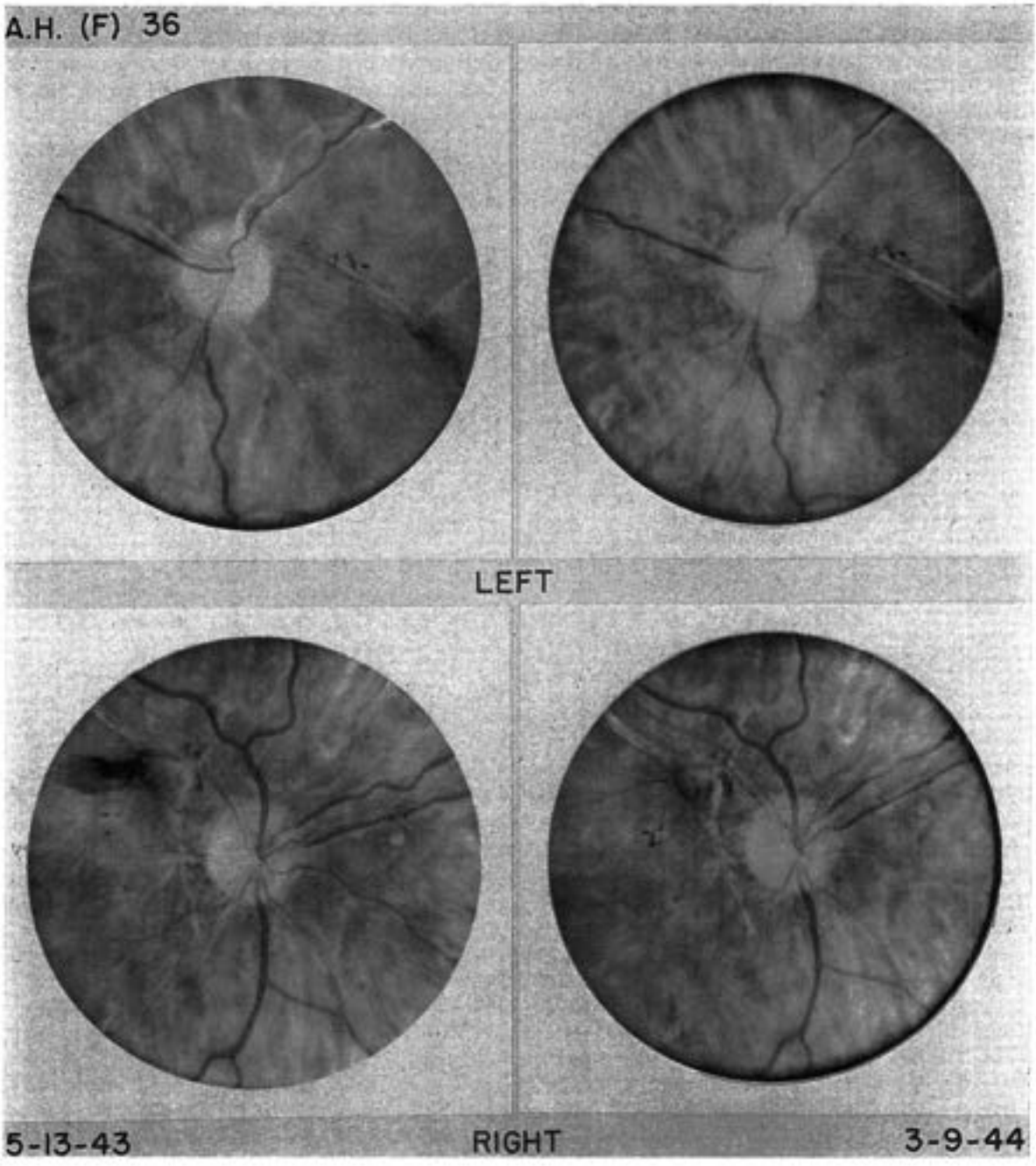

Fig. 43. A.E.H. (f., 36). Chronic pyelonephritis. Rice diet started April 13, 1943. "Silver-wire" arterioles. Disappearance of hemorrhage, right eye.

daily, yielding an extra amount of protein of 10-26 Gm. Her blood pressure, which for the past four months had consistently been at a level of 110-130 systolic, 70-95 diastolic, rose as high as 160 systolic, 112 diastolic in the fifth hospital week and averaged 143 systolic, 104 diastolic from the sixth to the eighth hospital week. The patient went home on the rice diet, supplemented by one egg three times weekly, and 2 ounces of beef, chicken, liver, or fish twice weekly. She did not follow this regime strictly but ate one egg about five times a week, and 2 ounces of beef or chicken four times a week. On January 18, 1944, the nonprotein nitrogen was 41 mg. per 100 cc. of blood and the total proteins were 7.1 Gm. per 100 cc. of plasma. She was "feeling strong and well" and had

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been working around the house. She had had no headache or any other complaint. Her blood pressure, however, was 138 systolic, 104 diastolic. The patient was warned of the possibility of a recurrence of her disease. Additions to the basic rice diet were restricted to carrots, one egg twice a week, and 2 ounces of beef, chicken, liver, or fish not more than twice a week.

When last seen on March 8-10, 1944, she had been following this diet. She was feeling "healthier than ever before" and doing all her work as a housewife and mother of three children.

The findings on the latest examination compared with those on the first hospitalization here were as follows:

	April, 1943	*March, 1944*
Blood pressure (mm. Hg.)	223/149 (average of 3 weeks)	116/92
Lowest blood pressure (mm. Hg.) in sodium amytal (0.6 Gm.) sleep	187/134	Caffeine given when systolic blood pressure fell below 72.
Hemoglobin (% of 15.5 Gm.)	97	93
RBC (per cubic mm.)	4,960,000	4,400,000
WBC (per cubic mm.)	6,040	7,240
NPN (mg. per 100 cc. of blood)	46	41
Albumin (Gm. per 100 cc. of plasma)	3.5	3.3
Globulin (Gm. per 100 cc. of plasma)	4.2	3.0
Chlorides (as mg. NaCl per 100 cc. of plasma)	574	552
Calcium (mg. per 100 cc. of serum)	8.7	9.8
Phosphorus (mg. per 100 cc. of serum)	4.2	2.6
Cholesterol (mg. per 100 cc. of serum)	270	148
Albumin in urine (Gm. per 1000 cc.)	1.65 (average of 3 weeks)	0.28
PSP (% excreted in two hours)	12.5, 20-22.5	22
Weight (Kg.)	55.82	42.25
Transverse diameter of heart (cm.)	11.9	10.1
Diameter of great vessels (cm.)	6.2	5.2
Angle of electrical axis	+22°	+57°
Retinal hemorrhages	++	0

PATIENT 5. *Nephrolithiasis; chronic pyelitis; terminal uremic stage of chronic nephritis (total phenolsulfonphthalein excretion in two hours 5-10 per cent); "hypertensive vascular disease" (blood pressure 230-270 systolic, 130-160 diastolic); vascular retinopathy with papilledema, hemorrhages, and exudates. Example of decrease of high blood pressure and nonprotein nitrogen and of recovery of eyesight with disappearance of papilledema, hemorrhages, and exudates.*

O.P. (A87953), a 41 year old white widow and office worker, was admitted to the hospital on July 16, 1942, because of intense headaches and progressive failure of vision.

History: The patient had her first attack of kidney colic at the age of 18; an appendectomy was performed at that time. Since then she had had repeated attacks, with fever, chills, nausea, hematuria, pyuria, and occasional passage of stones (about twenty in all). At 22 she developed hypertension and eclamptic convulsions during her first pregnancy. Her second and last pregnancy three years later was normal. Both her children are living. When she was 37 an operation was performed for the removal of a calculus obstructing the lower portion of the right ureter. Two years later three stones were removed from the left kidney pelvis. No stones had been passed since then, and she had had only two more attacks of kidney colic. Except for these attacks of acute pain, she had had very few symptoms referable to the urinary tract; there was occasional nocturia, but no burning on urination. The systolic blood pressure had ranged between 150 and 180 from the age of 22 until "a few years ago"; since then the blood pressure had been "excessively high." She had had occasional moderately severe headaches until 1941-42, when her headaches became very severe and she began having substernal oppression, nocturnal dyspnea, gradual loss of vision, and occasional slight ankle edema; she lost 20 pounds in weight. Since January, 1942, her systolic blood pressure had averaged 285; after two weeks of bed rest it was 250. Her headache became still worse and was only temporarily relieved by bromides and phenobarbital; morphine was given very rarely.

Examination: The patient's height was 157 cm., her weight 54 Kg., temperature 37 C., pulse 80. She looked very ill and pale. There was no edema. She was unable to dis-

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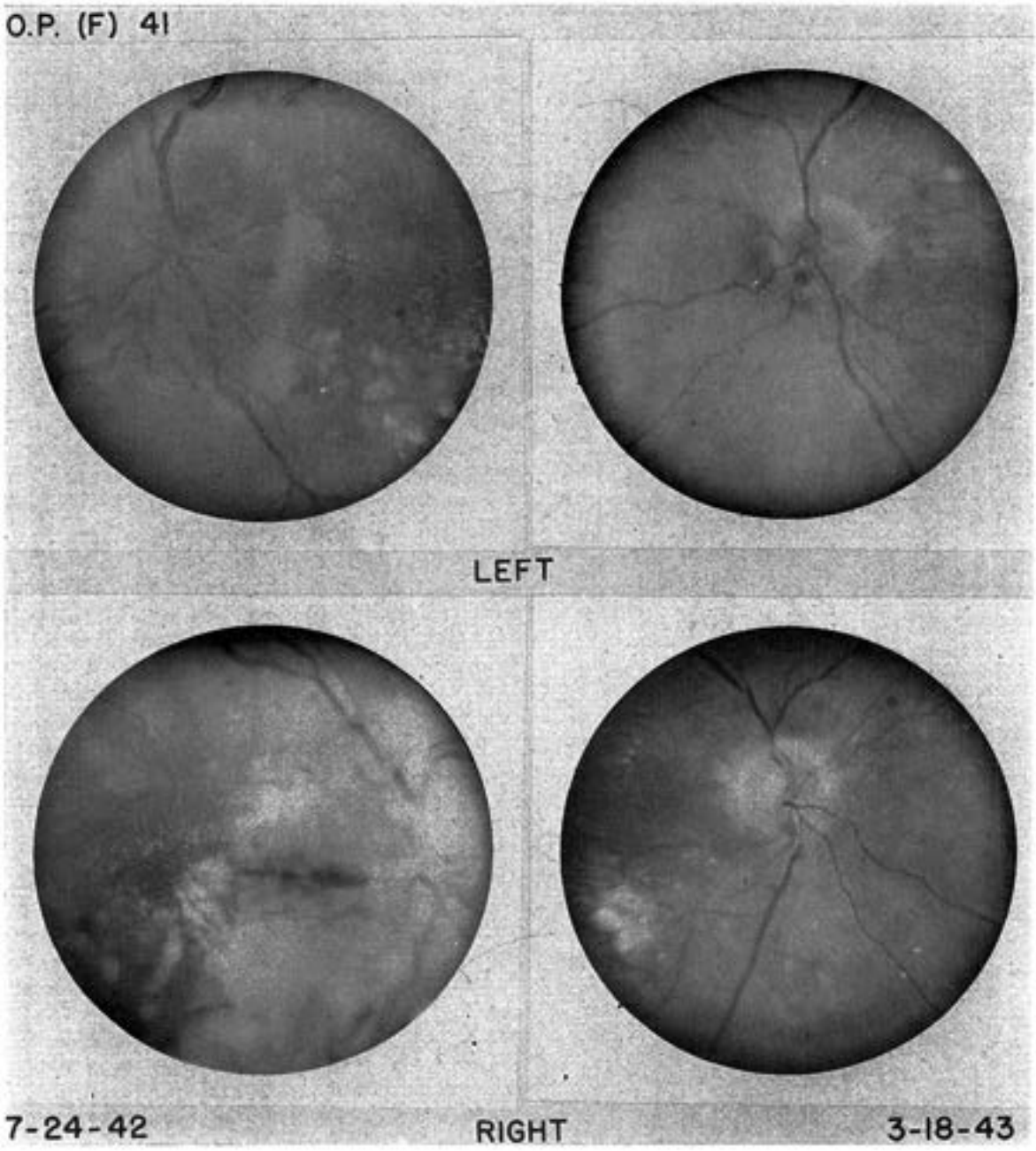

Fig. 44. O.P. (f., 41). Terminal uremic stage of chronic pyelonephritis. Rice diet started July 23, 1942. Disappearance of papilledema, hemorrhages; marked decrease of exudates, arteriovenous compression, venous engorgement and tortuosity, both eyes.

tinguish objects, but could distinguish light and dark. Marked bilateral papilledema was present, and there were numerous patches of exudate and numerous hemorrhages throughout both fundi; the arterioles, where visible, were narrow and tortuous; the veins were tortuous and engorged; there was marked arteriovenous compression (fig. 44). The teeth were in good condition; the pharynx was clear. The veins of the neck were not engorged. The lungs were clear on auscultation and percussion. The heart was slightly enlarged to the left; the rhythm was regular and no murmurs were heard; the aortic second sound was loud. The blood pressure range was 230-270 systolic, 130-160 diastolic. The liver was not enlarged and the spleen not palpable. There was tenderness over both kidneys. A chest film showed generalized bronchial thickening. Films of

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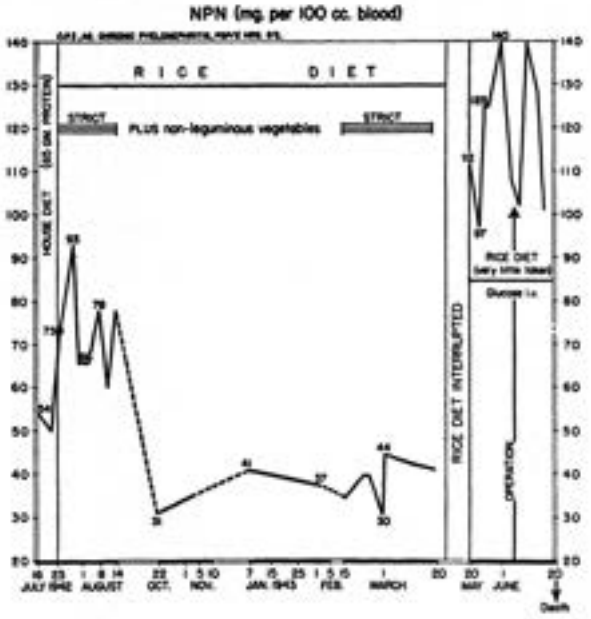

Fig. 45. O.P. Terminal uremic stage of chronic pyelonephritis. Decrease of nonprotein nitrogen on rice diet. Increase of nonprotein nitrogen after rice diet was interrupted.

the abdomen showed a collection of small stones in the region of the lower calyx of the right kidney and one large stone, more than 1 cm. in diameter, and numerous small stones below the lower calyx of the left kidney. Hydronephrosis was present on the right. The electrocardiogram showed inverted T-waves in lead 1 and a splintered QRS complex in lead 3; the angle of the electrical axis was +55 degrees.

Accessory clinical findings: The hemoglobin was 60-70 per cent and there were 10,500 white blood cells. The nonprotein nitrogen (fig. 45) ranged from 50-73 mg. per 100 cc. of blood; the carbon dioxide combining power of the plasma was 48 volumes per cent. Total proteins were 5.8 Gm. per 100 cc. of plasma: albumin 3.5 Gm., globulin 2.3 Gm., albumin-globulin ratio 1.5. Chlorides (as sodium chloride) were 556 mg. per 100 cc. of serum, calcium was 10.3 mg., phosphorus 4.0 mg., phosphatase 4.3 Bodansky units. The serum cholesterol was 230 mg. per 100 cc. The urine contained a moderate amount of albumin, 10-15 white blood cells per high power field, many red blood cells, and many small cocci from both kidney pelves. The total phenolsulfonphthalein excretion in two hours was 5-10 per cent.

Impression: Bilateral nephrolithiasis; chronic pyelonephritis with marked decrease of the renal excretory function; hypertension; vascular retinopathy with papilledema, hemorrhages, and exudates.

Course: The patient was able to eat only part of the regular hospital diet and vomited frequently. She complained of intense headache. Her blood pressure during the first eight days averaged 257 systolic, 153 diastolic. The rice diet (1800 calories, 1500 cc. of fruit juices) was started on the ninth day, July 23, 1942. Oxygen inhalation was given for two hours three times a day. After a few days, the nausea subsided, and the headache became less intense. After sixteen days both nausea and headache had completely disappeared, the blood pressure had decreased to a level of 190 systolic, 120 diastolic, and there were no new retinal hemorrhages or exudates. The nonprotein nitrogen remained high (average: 72 mg. per 100 cc. of blood).

After discharge from the hospital on August 14, 1942, the patient continued bedrest and followed the rice regime, with the addition of non-leguminous vegetables. She was readmitted on October 22, 1942. She had had no complaints in the interval. Her headache had never recurred, and she could read fine print with either eye. There was no papilledema; most of the hemorrhages and exudates were clearing up and no new exudates or hemorrhages were present; the previously engorged and tortuous veins were straighter and smaller in caliber; more arterioles were visible, and there was less arteriovenous compression. The blood pressure was 200 systolic, 120 diastolic. The hemoglobin was 68 per cent, and there were 3,480,000 red blood cells and 6,000 white blood cells. The nonprotein nitrogen was 31-35 mg. per 100 cc. of blood, the urea nitrogen 14.9 mg. Chlorides (as sodium chloride) were 596 mg. per 100 cc. of serum, calcium was 10.0 mg., phosphorus 3.4 mg., cholesterol 224 mg. Total proteins were 5.1 Gm. per 100 cc. of plasma: albumin 3.0 Gm., globulin 2.1 Gm., albumin-globulin ratio 1.4. The urine was loaded with white blood cells; there were a few red blood cells, and a 2 plus to 4 plus benzidine reaction; albumin excretion was 0.8-1.2 Gm. per 1000 cc. The total phenolsulfonphthalein excretion in two hours was 7 per cent. Total nitrogen excretion was 1.59 Gm. in twenty-four hours, urea excretion 2.12 Gm. in twenty-four hours (945 cc. of urine).

The patient continued the rice diet with non-leguminous vegetables for another four

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months; she felt very well and was up and around a great part of the day. She was seen in the hospital frequently. Her blood pressure averaged about 230 systolic, 130 diastolic, her nonprotein nitrogen 37-41 mg. per 100 cc. of blood; her hemoglobin ranged between 60 and 83 per cent. Total phenolsulfonphthalein excretion in two hours was 10 per cent.

On February 14, 1943, she was readmitted with severe kidney colic on the left side, the pain radiating anteriorly. She had three attacks of precordial pain in the next few days. Her temperature was 37 C., the white blood cell count 8,450. The electrocardiogram showed the T-waves in lead 1 more deeply inverted than on January 8. Her nonprotein nitrogen was 30-44 mg. per 100 cc. of blood. She had no recurrence of renal colic and, after February 20, no pain. Her weight remained unchanged, and she had no visual disturbances. Examination of the eyegrounds on March 18, 1943 (after eight months on a rice diet with non-leguminous vegetables) showed the discs sharply outlined. The hemorrhages and most of the exudates had disappeared, leaving a moderate amount of scarring; the tortuosity of the arterioles had diminished, and there was less arteriovenous compression and no engorgement or tortuosity of the veins (fig. 44).

The patient continued the rice diet at home and felt well until the beginning of April, 1943. Then she began having repeated attacks of severe kidney colic, and substernal oppression, nausea, and vomiting. In the early part of May visual disturbances recurred. She was readmitted to the hospital on May 20 in a critical condition, with edema of the ankles and face. She reported that *the rice regime had been discontinued* in April, and milk, eggs, broth, and toast had been given instead. Her temperature was 37 C., her pulse 100, the nonprotein nitrogen 112 mg. per 100 cc. of blood, the carbon dioxide combining power of the plasma 47 volumes per cent. The hemoglobin was 76 per cent and there were 3,760,000 red blood cells and 9,200 white blood cells.

For the first few days she was unable to take anything by mouth. She was given 800-1000 calories daily by intravenous glucose, and was digitalized. On May 25 anuria developed and she had a chill, her temperature rising to 39.8 C. Both ureters were catheterized; no obstruction was found on the right but the left ureter was obstructed by a large stone. The catheter was finally passed into the kidney pelvis and was left for continuous drainage. The patient's temperature returned to normal and she began to take fruit juices and small amounts of fruit. She felt relatively better and insisted on operation. The last nonprotein nitrogen determination before operation was 108 mg. per 100 cc. of blood.

On June 7, 1943, pyelolithotomy and nephrostomy were performed on the left kidney. The highest nonprotein nitrogen after operation (on June 11) was 140 mg. per 100 cc. of blood; the last nonprotein nitrogen determination (on June 17) was 101 mg. per 100 cc. of blood. An infection of the nephrostomy wound set in, and the patient died on June 20, 1943.

The anatomical diagnosis was: "Nephrolithiasis. Marked pyelonephritis, hydronephrotic atrophy, right; marked destruction of tubules and glomeruli; secondary endarteritis obliterans. Marked chronic pyelonephritis, moderate hydronephrotic atrophy, left. Marked endarteritis obliterans of large vessels of pancreas. Infection of nephrostomy wound with massive perirenal abscess and acute pyelitis and ureteritis. Hemorrhagic infarct of lower pole of left kidney. Infected infarct of spleen."

PATIENT 6. *Terminal stage of chronic nephritis (total phenolsulfonphthalein excretion in three hours less than 1 per cent); uremia (nonprotein nitrogen 156-174 mg. per 100 cc. of blood); hypertension (blood pressure 223 systolic, 141 diastolic); vascular retinopathy. Example of decrease of high blood pressure, nonprotein nitrogen, and cardiac enlargement.*

J.K. (B40490), a 33 year old white man was admitted to the hospital on November 1, 1944, with the chief complaints of intense headache, dizziness, and tinnitus.

History: The patient had had measles, mumps, chickenpox, and whooping cough in childhood. He was "always healthy and well" except for occasional sore throats. His blood pressure had been normal in 1941. In 1942, at the age of 31, he began having spells of slight burning on urination, "dull low back pain" on the right side and nocturia three to four times nightly. In the spring of 1943, there was a gradual onset of generalized malaise, sleeplessness, and easy fatigability. In the fall he developed ankle edema which persisted until the spring of 1944, when he

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had to give up his work as a painter. During all of 1944, he was conscious of a smothering sensation when he was walking or lying flat in bed. He noticed occasional puffiness around the eyes, increasing weakness, and blurring of vision. He was told that he had high blood pressure (220 systolic), kidney disease, and anemia. After "several blood transfusions and liver injections" he felt temporarily "stronger," but there was no improvement in the anemia, and his blood pressure remained high. In May, 1944, his physician placed him on a slightly modified rice diet. However, after an attack of dysuria, frequency, and back pain, the diet was discontinued. Further blood transfusions were given (making a total of nine) as well as vitamins, iron, and sedatives. For two weeks preceding admission, he had considerable distress from "throbbing headaches," dizziness, and tinnitus.

Examination: The patient's height was 180 cm., his weight 71.2 Kg., temperature 37 C., pulse 88, respiration 22, blood pressure 250 systolic, 130 diastolic. He was a well developed, pale man who appeared chronically ill and had a strongly uremic odor. There was no edema. The pupils reacted well to accommodation and light; the discs were blurred, and the arterioles tortuous; silvery and cottony exudates were scattered throughout both fundi. The nasal septum was deflected and breathing space was inadequate bilaterally. Several teeth were carious; the tongue was coated, the tonsils moderately enlarged. The lungs were clear. The heart was enlarged to the left. A blowing apical systolic murmur was heard, and the aortic second sound was accentuated. The liver was felt at the costal margin and descended two fingers' breadth on deep inspiration. The spleen was not palpable. There was no tenderness in either kidney region.

Accessory clinical findings: The hemoglobin was 53 per cent, red blood cells 2,490,000, white blood cells 7,280 with 71 per cent segmented polymorphonuclears, 1 per cent eosinophils, 28 per cent small lymphocytes. The corrected sedimentation rate was 10 mm. in one hour, the reticulocyte count 0.6 per cent, the hematocrit reading 17.4 volumes per cent. Serological tests for syphilis were negative. The nonprotein nitrogen was 156-174 mg. per 100 cc. of blood, the urea nitrogen 105 mg.; the blood sugar was 112 mg. per 100 cc. Chlorides (as sodium chloride) were 544 mg. per 100 cc. of plasma; calcium was 8.0 mg. per 100 cc. of serum, phosphorus 7.3 mg., cholesterol 295 mg. The total proteins were 6.8 Gm. per 100 cc. of plasma: albumin 4.0 Gm., globulin 2.8 Gm., albumin-globulin ratio 1.4. The urine contained 60-75 red blood cells and 1-2 white blood cells per high power field, occasional

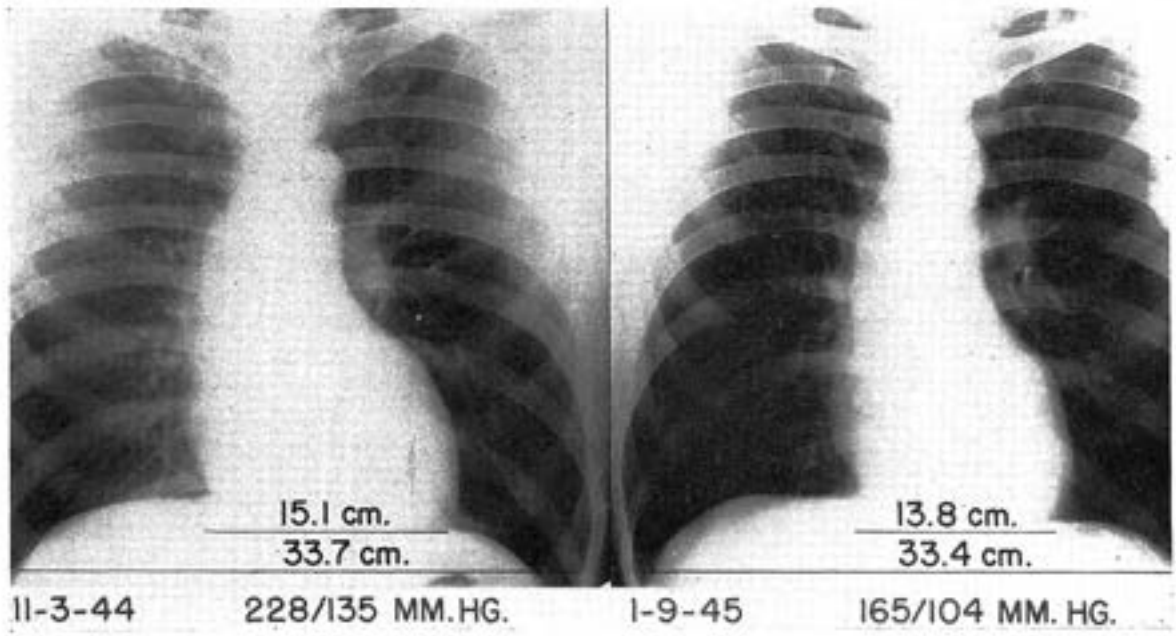

Fig. 46. J.K. Terminal uremic stage of chronic nephritis. Rice diet started November 1, 1944. No digitalis. Reduction in heart size with change in transverse diameter of 9 per cent. Right side of ascending aorta less bulging.

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epithelial cells, and occasional granular and hyaline casts. The average albumin excretion in the first five days was 5 Gm. per 1000 cc. Tests for sugar gave a trace to a 2 plus reaction. The concentration-dilution test showed a range of 1.011-1.014. In the phenolsulfonphthalein test no dye appeared, although collections were made every thirty minutes for three hours; when the test was repeated, only a faint trace of the dye appeared in the ninety minute specimen, although collections were again made every thirty minutes for three hours. The total nitrogen excretion was 5.9 Gm., the urea excretion 7.2 Gm., and the chloride excretion 1.27 Gm. in twenty-four hours (1140 cc. of urine).

A chest plate showed the lungs clear, the heart enlarged; the transverse diameter was 15.1 cm. (fig. 46), and the internal diameter of the chest 33.7 cm. The report on a flat plate of the abdomen was as follows: "Liver somewhat enlarged. Left kidney elongated." The electrocardiogram showed the T-waves in lead 1 inverted, in leads 2 and 3 upright, in lead 4 diphasic; the angle of the electrical axis was −11 degrees.

Impression: Terminal uremic stage of chronic nephritis; hypertension; cardiac enlargement; vascular retinopathy.

Course: The patient was immediately started on a 2400 calorie rice diet with fluids limited to 1000 cc. of fruit juices. He was kept on strict bed rest; no digitalis or other medication was given. During the four weeks he stayed in the hospital, his blood pressure (fig. 47) decreased from 223 systolic, 141 diastolic (average of the first week) to 197 systolic, 121 diastolic (average of the fourth week). By the twenty-seventh hospital day the nonprotein nitrogen had decreased from 156-174 mg. per 100 cc. of blood to 84 mg., the urea nitrogen from 105 mg. per 100 cc. of blood to 48.4 mg., the urea ratio from 67.3 to 57.6 per cent, the plasma chlorides (as sodium chloride) from 544 to 466 mg. per 100 cc. There were only 2-4 red blood cells per high power field in the urine; the amount of albumin excreted remained about the same. The weight had decreased from 71.25 to 67.2 Kg.

The patient continued the rice diet at home for six more weeks and was in bed for about twenty-two hours every day. He felt much better and "like a different person." He had had no dysuria, frequency, or back pain, and

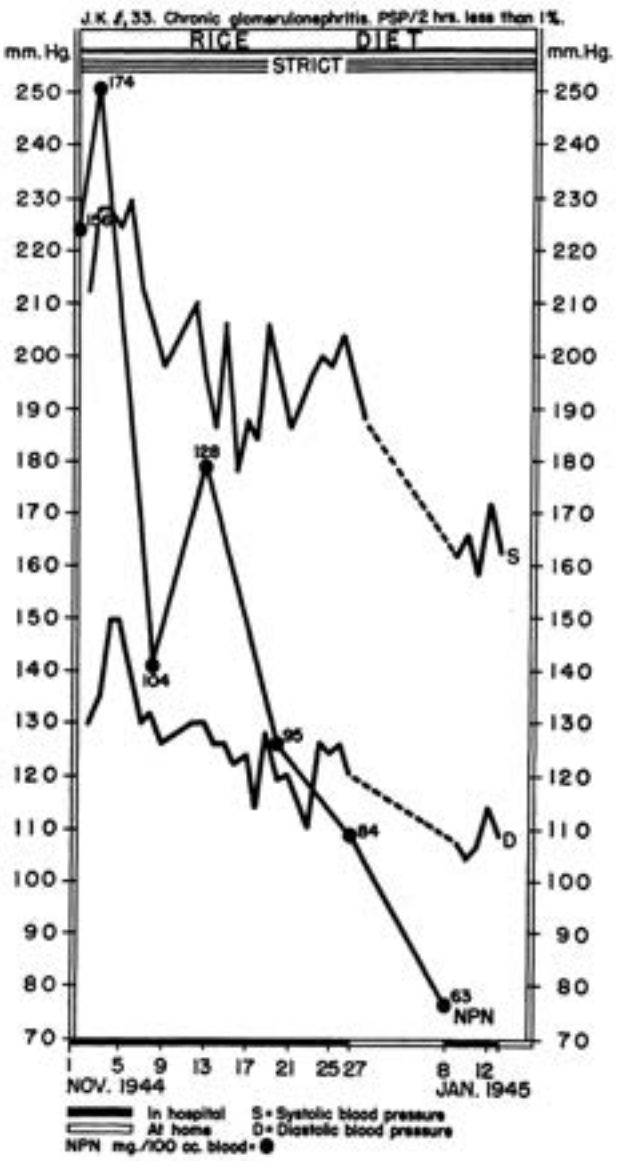

Fig. 47. J.K. Terminal uremic stage of chronic nephritis. Decrease of blood pressure and nonprotein nitrogen in 2 months on rice diet.

no dyspnea or orthopnea. The headaches, dizziness, and tinnitus had disappeared; his vision had improved.

When he was re-examined on January 8-13, 1945, his weight was 65 Kg., temperature 37 C., pulse 80, respiration 22, blood pressure 164 systolic, 106 diastolic (average of five days). The optic discs were sharply outlined, but numerous small silvery exudates were still present. The heart was smaller in size (fig. 46); there had been a 9 per cent change in the transverse diameter since November 3, and the right side of the ascending aorta was less bulging. The electrocardio-

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gram showed the T-waves in leads 1 and 2 inverted, in lead 4 diphasic; the angle of the electrical axis was +15 degrees. The liver was not enlarged. The hemoglobin was 50 per cent, red blood cells 2,500,000, white blood cells 7,000, reticulocytes 0.7 per cent. The corrected sedimentation rate was 0 mm. in one hour. The nonprotein nitrogen was 60-66 mg. per 100 cc. of blood, the urea nitrogen 34.1 mg., the urea ratio 51.7 per cent. Total proteins were 6.8 Gm. per 100 cc. of plasma: albumin 3.7 Gm., globulin 3.1 Gm., albumin-globulin ratio 1.2. Chlorides (as sodium chloride) were 452 mg. per 100 cc. of plasma; calcium was 9.4 mg. per 100 cc. of serum, phosphorus 5.2 mg., cholesterol 212 mg. Blood sugar was 123 mg. per 100 cc. The urine contained 3.6 Gm. of albumin per 1000 cc., 4-12 white blood cells per high power field, occasional red blood cells, no casts, and no sugar. Total nitrogen excretion in twenty-four hours (1710 cc. of urine) was 3.1 Gm., urea excretion 0.3 Gm., chloride excretion (as sodium chloride) 0.27 Gm. In the phenolsulfonphthalein test, no dye appeared in the first one and a half hours, and only a trace of the dye appeared in the three-hour specimen.

The patient was advised to continue the strict rice regime and to rest at least twenty hours a day for another eight weeks.

Findings on re-examination, compared with findings at the beginning of the rice diet, are as follows:

	November 1-7, 1944	*January 8-13, 1945*
Blood pressure (mm. Hg.)	223/141	164/106
Hemoglobin (% of 15.5 Gm.)	53	50
RBC (per cubic mm.)	2,490,000	2,500,000
WBC (per cubic mm.)	7,280	7,000
NPN (mg. per 100 cc. of blood)	156-174	60-66
Urea N (mg. per 100 cc. of blood)	105	34.1
Albumin (Gm. per 100 cc. of plasma)	4.0	3.7
Globulin (Gm. per 100 cc. of plasma)	2.8	3.1
Chlorides (as mg. NaCl per 100 cc. of plasma)	544	452
Calcium (mg. per 100 cc. of serum)	8.0	9.4
Phosphorus (mg. per 100 cc. of serum)	7.3	5.2
Cholesterol (mg. per 100 cc. of serum)	295	212
Urine albumin (Gm. per 1000 cc.)	5.0	3.6
PSP (% excreted in three hours)	Trace	Trace
Weight (Kg.)	71.2	65
Papilledema	+	0
Retinal exudates	++	+
Angle of electrical axis	−11°	+15°
T wave in lead 1	Inverted	Inverted
Transverse diameter of heart (cm.)	15.1	13.8

PATIENT 7. *Nephrolithiasis; chronic nephritis (total phenolsulfonphthalein excretion in two hours 18-35 per cent); "hypertensive vascular disease" (blood pressure 188 systolic, 111 diastolic); vascular retinopathy; anemia. Example of decrease of high blood pressure and nonprotein nitrogen to normal, disappearance of T_1 inversion, heart enlargement, and retinal hemorrhages and exudates.*

J.A.G. (A98258), a 52 year old white cotton mill worker was admitted to the hospital on January 11, 1943. His chief complaints were weakness, dizziness, headache, and failing vision.

History: The patient had had measles, chickenpox, mumps, whooping cough, and typhoid fever in childhood. Varicose veins and ulcers had been present on both legs since adolescence. In 1929 he had an appendectomy and a left inguinal herniorrhaphy. Since about 1938 he has had an indirect right inguinal hernia. In 1932 he had an attack of renal colic on the left side, with "pus in the urine." In 1940 erysipelas of the left leg developed and he was told again that he had "pus on the kidneys." Since that time he has had nocturia (six times nightly). There had been no edema and no hypertension until 1941, when he had a "bad cold" and his blood pressure was found to be "over 200." Shortly afterwards he began having generalized throbbing headaches, accompanied by dizziness, some nausea and vomiting, and blurring of vision with occasional "blind spells." The systolic blood pressure then ranged from 180 to 210. He had no dyspnea or precordial pain. Edema of the ankles and hands, and puffiness of the face and eyelids developed. He had to stop working about three weeks before admission to the hospital.

Examination: The patient was a pale man appearing chronically ill. His height was 179 cm., his weight 65 Kg., temperature 37.2 C.,

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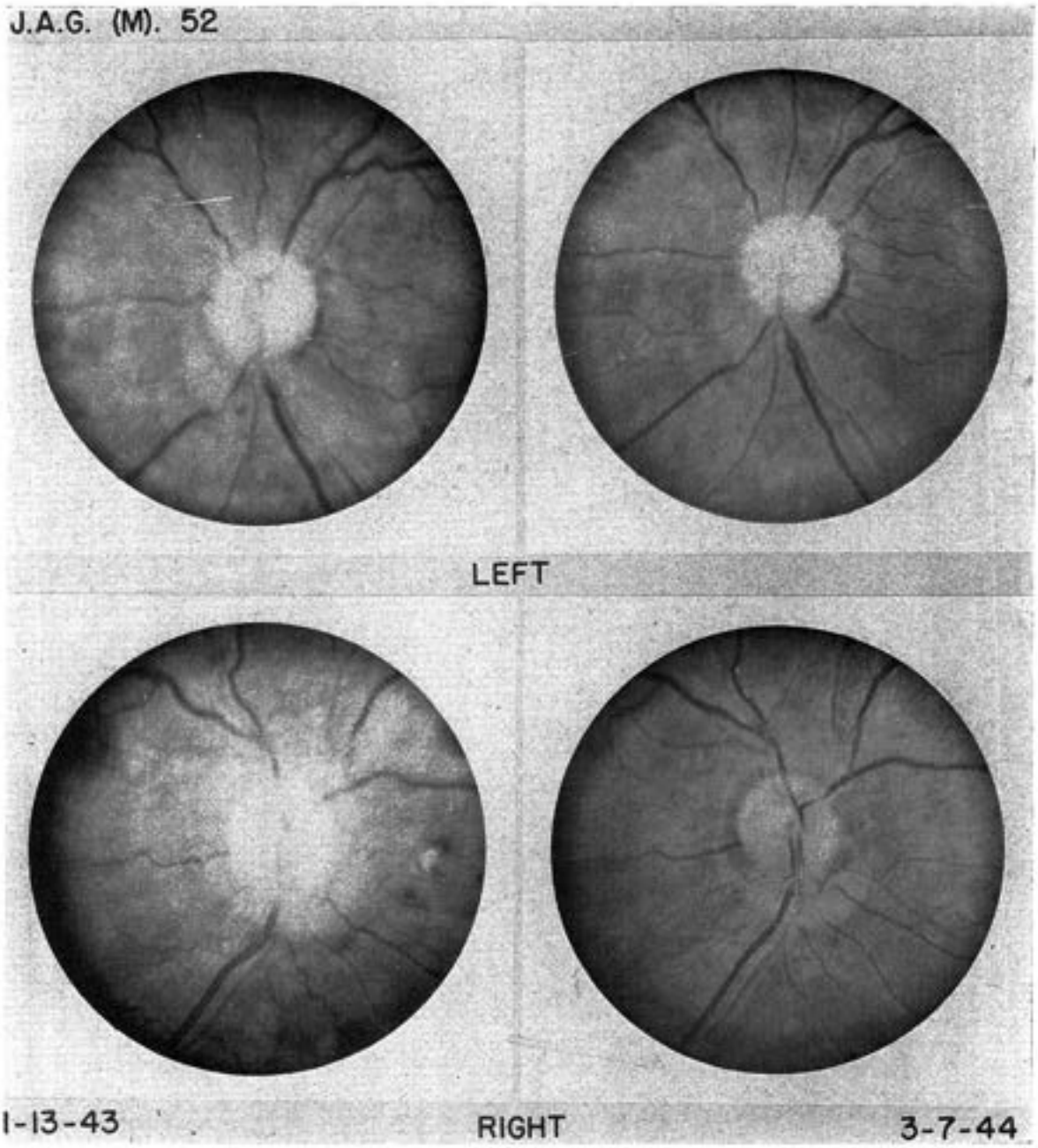

Fig. 48. J.A.G. (m., 52). Nephrolithiasis, chronic nephritis, "hypertensive vascular disease." Rice diet started January 21, 1943. Disappearance of hemorrhages, exudates, right eye; of edema and venous tortuosity, both eyes.

pulse 68, respiration 18, blood pressure 220 systolic, 120 diastolic. Moderate pitting edema of the feet and ankles and some puffiness of the eyelids were noted. He had a slight nephritic stare. The pupils were equal and reacted well to light and accommodation. The eyegrounds (fig. 48) showed moderate diffuse edema around both discs, blurred disc margins, and narrowed, "silverish," and tortuous arterioles. Arteriovenous compression and scattered fresh hemorrhages were seen in both eyes. There were a few exudates in the left eye, and several in the right eye. The patient had marked dental caries and pyorrhea. The tonsils were small. The veins of the neck were very slightly distended; the thyroid was not enlarged. A few moist rales were heard at the base of the left lung. The heart was enlarged to the left and right; the rhythm was regular; the sounds were

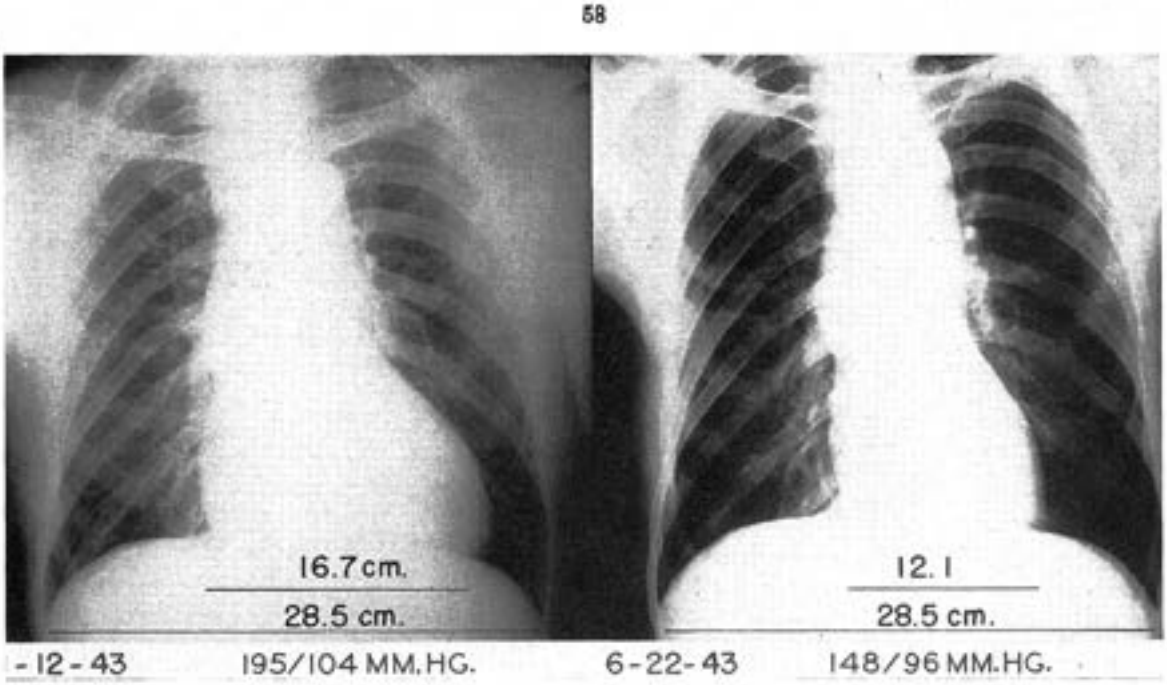

Fig. 49. J.A.G. Nephrolithiasis, chronic nephritis, "hypertensive vascular disease." Rice diet started January 21, 1943. No digitalis. Reduction in heart size with change in transverse diameter of 38 per cent.

loud, and there was a soft apical murmur. The liver was palpable 4 cm. below the costal margin and was moderately tender. The spleen was not palpable, and there was no tenderness in either kidney region. A right inguinal hernia was easily reducible. The prostate was slightly enlarged. The skin of both legs showed pigmentation from ulcers and dermatitis. The neurological examination gave no pathological findings.

X-ray examination showed marked alveolar absorption in both jaws and root infection in two incisors. Many teeth were carious. Some thickening of the membrane was seen in the left antrum, and a shadow (polyp ?) in the floor. The transverse diameter of the heart was 16.7 cm. (fig. 49); the aorta was tortuous. The lung fields were clear. A flat plate of the abdomen and a retrograde pyelogram were reported as follows: "Urinary tract indistinct. Opaque shadow overlying left kidney (appears to be stone)." "Calyces, pelves, ureters normal except for stone in superior calyx, left. Bladder small, outline irregular." The electrocardiogram showed a normal sinus rhythm and inverted T-waves in lead 1; the angle of the electrical axis was +3 (fig. 50).

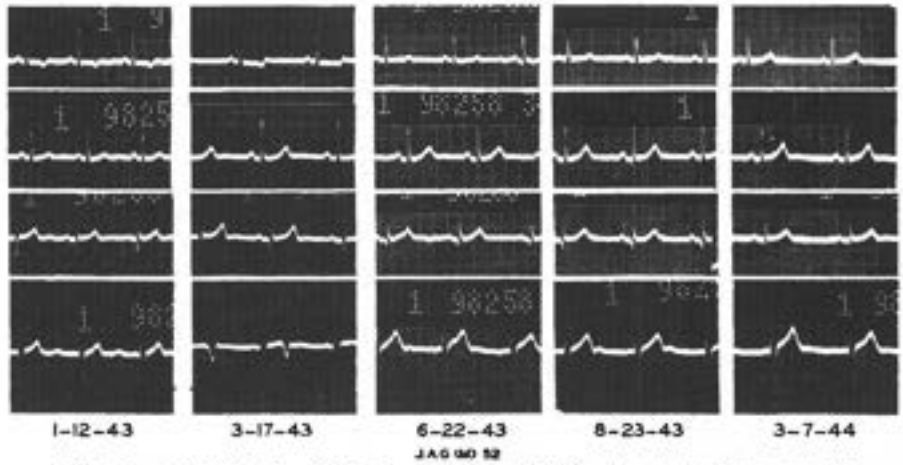

Fig. 50. J.A.G. Nephrolithiasis, chronic nephritis, "hypertensive vascular disease." Rice diet started January 21, 1943. No digitalis. Increase in angle of electrical axis from +3° to +46°. Inverted T_1 has become upright.

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Accessory clinical findings: The hemoglobin was 57 per cent, and there were 2,820,000 red blood cells and 7,600 white blood cells with 1 per cent juvenile polymorphonuclears, 2 per cent non-segmented polymorphonuclears, 63 per cent segmented polymorphonuclears, 1 per cent eosinophils, 7 per cent monocytes, 8 per cent large lymphocytes, 18 per cent small lymphocytes. The corrected sedimentation rate was 3 mm. in one hour. Serological tests for syphilis were negative. The nonprotein nitrogen was 46 mg. per 100 cc. of blood. Chlorides (as sodium chloride) were 582 mg. per 100 cc. of plasma, calcium was 8.6 mg. per 100 cc. of serum, phosphorus 2.2 mg., cholesterol 225 mg. Total proteins were 6.1 Gm. per 100 cc. of plasma (albumin 3.4 Gm., globulin 2.7 Gm., albumin-globulin ratio 1.2). The urine was loaded with red blood cells and contained occasional white blood cells and granular and hyaline casts; the benzidine reaction was 4 plus, the reaction for albumin 3 plus, the reaction for sugar negative. A culture from the urine of the right ureter was positive for Bacillus pyocyaneus. The results of the phenolsulfonphthalein test were as follows: Appearance time five minutes; excretion at the end of the first half hour 10 per cent, at one hour 5 per cent, at one and a half hours, 2.5 per cent, at two hours 2.5 per cent; the total execretion in two hours 20 per cent. The concentration-dilution test showed a range of specific gravity from 1.011 to 1.013.

Impression: Nephrolithiasis, left; chronic nephritis; "hypertensive vascular disease"; cardiac enlargement; T_1 inversion; vascular retinopathy; hypochromic anemia.

Course: For the first ten hospital days the patient was on a 65 Gm. protein house diet with 1500 cc. of fluids. No digitalis or other medication was given. His blood pressure during this time averaged 188 systolic, 111 diastolic (fig. 51). His nonprotein nitrogen on the ninth day was 58 mg. per 100 cc. of blood, the chlorides (as sodium chloride) were 602 mg. per 100 cc. of plasma. His weight was 60.25 Kg. From the eleventh hospital day until discharge (on the twenty-third hospital day) the patient was on the rice diet (2000 calories, 1500 cc. of fruit juices). His blood pressure level at discharge was 169 systolic, 112 diastolic, his nonprotein nitrogen 39 mg. per 100 cc. of blood, his hemoglobin 71 per cent. The urine contained few red blood cells per high power field; the benzidine reaction was negative. One and a half grams of albumin were excreted in twenty-four hours.

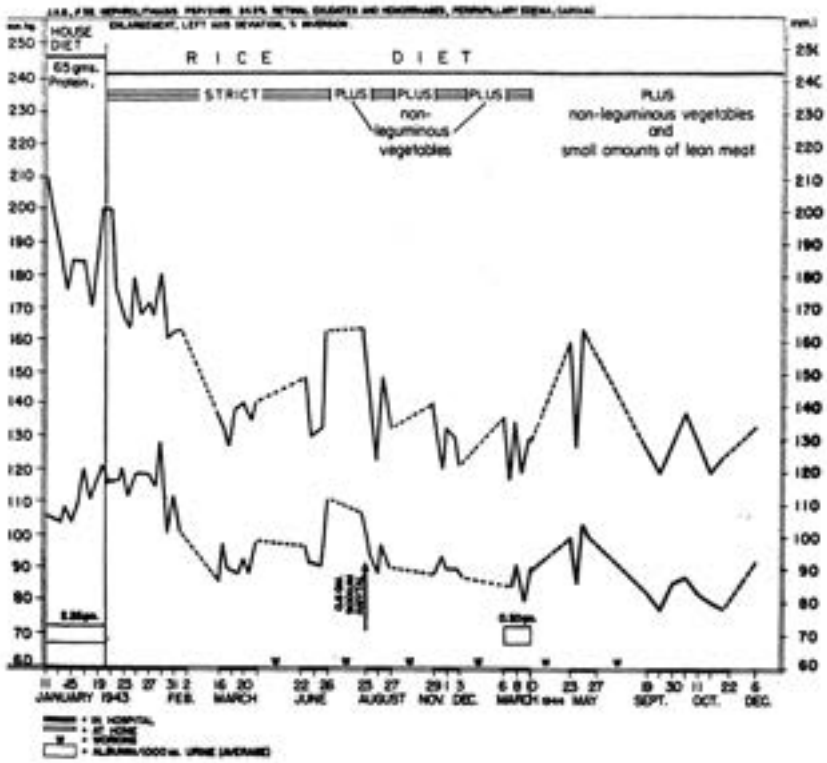

Fig. 51. J.A.G. Nephrolithiasis, chronic nephritis, "hypertensive vascular disease." Decrease of blood pressure to normal in eight weeks on rice diet. Moderate increase of blood pressure following too liberal modification of diet.

The patient followed the rice diet strictly at home for six weeks. He felt very well, except for occasional mild frontal headaches, a few episodes of epistaxis, and a short period of nervousness and insomnia. His vision was still impaired. At readmission (March 16-23, 1943) his average blood pressure was 136 systolic, 91 diastolic (fig. 51). His hemoglobin was 80-86 per cent, red blood cells 3,460,000-4,290,000, the corrected sedimentation rate 17 mm. in one hour. The nonprotein nitrogen was 37-40

mg. per 100 cc. of blood, chlorides (as sodium chloride) were 490 mg. per 100 cc. of plasma, calcium was 8.9 mg. per 100 cc. of serum, phosphorus 4.3 mg., cholesterol 160 mg. Total proteins were 7.1 Gm. (albumin 3.1 Gm., globulin 4.0 Gm.). The urine contained rare white blood cells, no red blood cells, no casts, and only a slight trace of albumin; the benzidine reaction was negative. The total nitrogen excretion was 3.44 Gm. in twenty-four hours, the urea excretion 4.92 Gm. in twenty-four hours (1645 cc. of urine). The results of the phenolsulfonphthalein test were as follows: Appearance time ten minutes; excretion at the end of the first half hour 15 per cent, at one hour 10 per cent, at one and a half hours 5 per cent, at two hours 5 per cent; total excretion in two hours 35 per cent. The eyegrounds showed marked decrease of peripapillary edema and less arteriovenous compression. Most of the hemorrhages and exudates present in January had been absorbed, but there were still a few scattered through both retinae. The electrocardiogram showed the T-waves in lead 1 to be diphasic, those in lead 4 inverted; the angle of the electrical axis was +27 degrees (fig. 50). A chest film showed the lungs clear, the aorta tortuous, the heart size "within normal limits" (transverse diameter 13.1 cm.).

The patient was advised to continue the rice diet at home for another five months; he returned twice to the hospital for re-examination during this period. He was completely asymptomatic (except for an episode of abdominal pain followed by weakness of about five days' duration) and went back to work as a janitor and night watchman in a cotton mill. His blood pressure remained at a level of 145 systolic, 97 diastolic (average of eight readings during the two admissions). His weight was 57.4-57.25 Kg., the hemoglobin 87-89 per cent, the nonprotein nitrogen 49-50 mg. per 100 cc. of blood; chlorides (as sodium chloride) were 500 mg. per 100 cc. of serum (in June) and 475 mg. per 100 cc. of plasma (in August). Calcium was 10.0-10.1 mg. per 100 cc. of serum, phosphorus 3.3-2.7 mg., cholesterol 124 mg. Total proteins were 6.8-6.3 Gm. per 100 cc. of plasma; the albumin-globulin ratio was 0.70-0.96. The urine contained 0-3 red blood cells and 0-8 white blood cells per high power field, and rare granular and hyaline casts; the benzidine reaction was negative. The average albumin excretion during three days in August was 0.27 Gm. per 1000 cc. of urine; the total nitrogen excretion was 4.8 Gm. in twenty-four hours in June, 1.7 Gm. in August; the urea excretion was 7.1 Gm. in twenty-four hours in June, 1.73 Gm. in August. The total phenolsulfonphthalein excretion in two hours was 21 per cent. Examination of the eyegrounds showed the discs sharply outlined; the edema had completely disappeared and the tortuosity and engorgement had decreased; all the hemorrhages and exudates were absorbed. A chest film showed the transverse diameter of the heart to be 12.1 cm. (fig. 49). The electrocardiogram showed the T-waves in leads 1 and 4 to be normally upright; the angle of the electrical axis was +44 degrees (fig. 50).

After the fourth admission, August 23-28, 1943 (seven months after the rice regime was started), non-leguminous vegetables were added to the diet. The patient was re-examined November 29 - December 3, 1943. He had been feeling very well and working six days a week. There had been no weakness, no urinary tract symptoms, and no visual disturbances. On this examination his blood pressure averaged 128 systolic, 91 diastolic; his weight was 58.2 Kg.; the hemoglobin was 79 per cent, red blood cells 3,900,000; the nonprotein nitrogen was 46 mg per 100 cc. of blood; the total proteins were 6.5 Gm. per 100 cc. of plasma. The transverse diameter of the heart was 13.2 cm., the angle of the electrical axis +49 degrees. He remained on the rice diet plus non-leguminous vegetables for the next three months. When he returned for re-examination on March 10, 1944, he reported that in the interval he had had several teeth extracted, and had had a head cold and an accidental cut in the arm with profuse bleeding; but he was completely asymptomatic with regard to his hypertensive cardiovascular disease and was feeling "strong and well." He had been working eight hours daily. The diet was further modified by the addition of 1 ounce of beef, chicken, liver, or fish four times a week.

On May 22, 1944, he was re-admitted for the sixth time because of a recurrence of the dermatitis on the leg, which healed well with elevation of the leg and the application of saline compresses and gentian violet. The average blood pressure during the six days in the hospital was 153 systolic, 98 diastolic. The patient was advised not to eat more than 2 ounces of meat per week for the time

being. He still was feeling "strong and healthy," and was working full time.

On September 13, 1944, he noticed the onset of painless jaundice with general weakness. He was re-admitted on September 18 with marked jaundice. The bilirubin was 20.1 mg. per 100 cc. of serum and increased to 30.5 mg. on September 29, then gradually decreased to 4.4 mg. on October 23. The liver could be felt 2-4 fingers' breadth below the costal margin and was slightly tender to palpation. The blood pressure was 120 systolic, 80 diastolic. The hemoglobin was 85 per cent, red blood cells 3,600,000, white blood cells 7,000; the nonprotein nitrogen was 45 mg. per 100 cc. of blood, the urea nitrogen 22.6 mg. Total proteins were 7.5 Gm. per 100 cc. of plasma (albumin 3.2 Gm., globulin 4.3 Gm.). Chlorides (as sodium chloride) were 480 mg. per 100 cc. of plasma, phosphorus was 4.1 mg. per 100 cc. of serum, cholesterol 117 mg. The urine showed an occasional granular cast; the benzidine reaction was negative. Albumin excretion was 0.6 Gm. per 1000 cc. of urine. The test for urobilinogen was negative for about twelve days, then strongly positive. The results of the bromsulfalein test (5 mg. of dye per kilogram of weight) were as follows: after fifteen minutes, 20 per cent retention; after thirty minutes, 20 per cent retention; after forty-five minutes, 10 per cent retention. The galactose tolerance test (40 Gm. of galactose) showed no sugar in the urine. Urine diastase and serum lipase were not increased. A barium enema and a gastrointestinal series were reported negative. The preliminary impression was "catarrhal jaundice."

One hundred grams of chicken (about 20 Gm. of protein) per day was added to the strict rice diet. Fluids were increased to 1600 cc. daily (1200 cc. of fruit juices, plus 200 cc. of 20 per cent dextrose with additional vitamins B and C and Hykinone intravenously twice a day). He was given 0.6 Gm. of choline chloride three times daily and kept on strict bed rest. His average blood pressure was 127 systolic, 83 diastolic. The angle of the electrical axis was +53 degrees.

He was discharged on October 23 and told to stay in bed and continue the rice diet, including non-leguminous vegetables and 100 Gm. of chicken daily. Upon reexamination (December 6-7, 1944), he was "feeling perfectly well." The serum bilirubin was 1.1 mg. per 100 cc. The liver had decreased in size, the edge being palpable only on deep inspiration. A gallbladder series showed a "poorly functioning gallbladder without stones." The blood pressure averaged 134 systolic, 92 diastolic. The angle of the electrical axis had decreased to +12 degrees. The patient was advised to continue the same regime for another three months and to resume work.

Findings on the latest examination, compared with findings on the first admission, before the beginning of the rice diet, are shown below:

	January 11-21 1943	*December 6-7 1944*
Blood pressure (mm. Hg.)	188/111	134/92
Hemoglobin (% of 15.5 Gm.)	57	73
RBC (per cubic mm.)	2,820,000	3,700,000
WBC (per cubic mm.)	7,600	7,400
NPN (mg. per 100 cc. of blood)	46, 58	32
Albumin (Gm. per 100 cc. of plasma)	3.4	4.0
Globulin (Gm. per 100 cc. of plasma)	2.7	3.0
Chlorides (as mg. NaCl per 100 cc. of plasma)	582, 602	524
Calcium (mg. per 100 cc. of serum)	8.6	9.8
Phosphorus (mg. per 100 cc. of serum)	2.2	3.6
Cholesterol (mg. per 100 cc. of serum)	225	153
Urine albumin (Gm. per 1000 cc.)	2.25	0.2
Hematuria	++++	0
PSP (% excreted in 2 hours)	20, 22.5	29
Weight (Kg.)	65-60	66.2
Transverse diameter of heart (cm.)	16.7	12.6
Angle of electrical axis	+3°	+12°
T wave in lead 1	Inverted	Upright
Retinal hemorrhages and exudates	++	0

PATIENT 8. *"Hypertensive vascular disease" with renal involvement (blood pressure 225 systolic, 130 diastolic). No improvement on rest, aminophylline, and reduction diets leading to a weight loss of 55 pounds. Example of decrease of high blood pressure and heart enlargement on strict rice diet. Increase in blood pressure when food of pa-*

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tient's own choice was added, although weight was lower than when the blood pressure was at its minimal level.

W.C.F. (A73824), a 63 year old white farmer and businessman, was admitted to Duke Hospital for the fourth time on February 16, 1943. His chief complaints were severe frontal headache, shortness of breath, nocturnal dyspnea, and wheezing.

History: Between the ages of 16 and 21, he had had "repeated" gonorrheal infections with bilateral epididymitis. At 21 he passed a "kidney stone," and when he was 26 a urethrostomy was performed for an impacted calculus. He had influenza and pneumonia at 37, and malaria at 61. He began to become obese when he was about 40. He had led a "very active life" until the age of 54, when moderate exertional dyspnea appeared and he had a "feeling of getting old." *At 56 he weighed 102 Kg.* (his height was 166 cm.). Between 56 and 61, his systolic blood pressure rose to 185. He had occasional albuminuria, nocturia, and frontal headaches; he was treated by rest, restriction of diet, diuretics, and laxatives. In November, 1941, he was admitted to Duke Hospital because of increasing dyspnea and rather sudden attacks of epigastric discomfort. *His weight at that time was 93 Kg.* Pulmonary emphysema was present and the heart was enlarged in all diameters (transverse diameter 17.7 cm.). There was marked widening and tortuosity of the aorta. His blood pressure ranged from 170 to 210 systolic and from 114 to 129 diastolic. The electrocardiogram showed the T-waves in leads 1 and 4 inverted; the angle of the electrical axis was −55 degrees. The urine gave a 1 plus reaction for albumin; the phenolsulfonphthalein excretion in one half hour was 23 per cent, the total excretion in two hours 44 per cent. There were prostatic stones. A diagnosis of "hypertensive vascular disease" was made, and the patient was put on a 1200 calorie reduction diet and given aminophylline.

Several re-examinations were made in this hospital because of the same complaints. The blood pressure was slowly rising (fig. 52), in spite of continued weight loss on the reduction diet.

The *examination* on the patient's fourth admission showed the following findings: *His weight was 77 Kg.*, his blood pressure 225 systolic, 130 diastolic. The heart (fig. 53) was greatly enlarged; the transverse

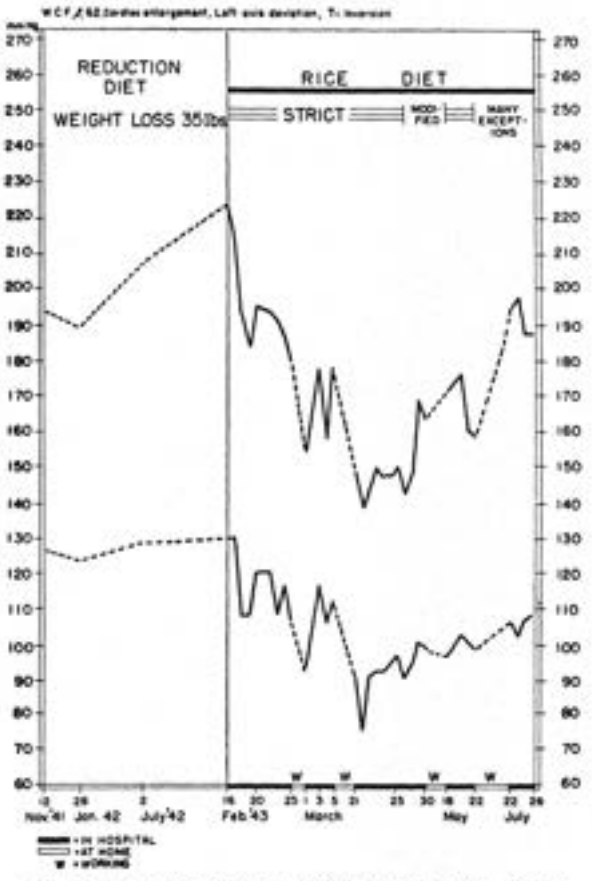

Fig. 52. W.C.F. "Hypertensive vascular disease." Increase of blood pressure in spite of weight loss of 35 pounds in 15 months before rice diet. Decrease of blood pressure in 5 weeks on rice diet. Increase of blood pressure in spite of further weight loss after eating other food in addition to the rice diet.

diameter was 18.0 cm. The electrocardiogram showed the T-waves in lead 1 inverted; the angle of the electrical axis was −66 degrees. The hemoglobin was 88 per cent, red blood cells 4,580,000, white blood cells 12,350. The serological tests for syphilis were negative. The nonprotein nitrogen was 42 mg. per 100 cc. of blood, chlorides (as sodium chloride) were 586 mg. per 100 cc. of plasma, calcium was 8.7 mg. per 100 cc. of serum, phosphorus 3.0 mg., cholesterol 172 mg. Total proteins were 7.2 Gm. per 100 cc. of plasma: albumin 3.6 Gm., globulin 3.6 Gm. The urine had a specific gravity of 1.011, and contained 1.8 Gm. of albumin per 1000 cc. and 40-60 white blood cells per high power field.

Course: The rice regime was started immediately (2000 calories, 1000-1200 cc. of fruit juices). No digitalis or other medication was given, and the only additional therapeutic measure was oxygen inhalation for

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two hours three times a day. The shortness of breath and nocturnal dyspnea disappeared completely within two weeks, and the patient felt very much improved. He followed the diet strictly for forty days. During part of this period he was at home and "quite active on his farm." When he was re-admitted on March 21, he was feeling "perfectly well." *His weight was 69 Kg.* His blood pressure during the first four days in the hospital averaged 149 systolic, 91 diastolic. The heart was smaller in size (fig. 53); there had been a change of 28 per cent in the transverse diameter since February 17, 1943. The albumin excretion had decreased from 1.8 Gm. to 0.5-1.0 Gm. per 1000 cc. of urine. Since the patient insisted that meat be included in his diet, he was given one trial meal of 100 Gm. of steak plus 10 Gm. of butter; following this his blood pressure rose to a slightly higher level (155 systolic, 96 diastolic). Urinary total nitrogen and urea nitrogen excretion in twenty-four hours were:

	Total nitrogen	*Urea nitrogen*
March 23	2.27 Gm.	1.15 Gm.
March 25 (100 Gm. steak plus 10 Gm. butter)		
March 26	3.89 Gm.	2.46 Gm.
March 29	3.08 Gm.	1.64 Gm.
March 30	2.23 Gm.	1.30 Gm.

The patient was advised to follow the diet strictly at home, but he did not do so. Although he took the rice, fruit, and fruit juices, he occasionally added small amounts of steak, oysters, fish, cheese, and cereal. He felt very well and had no dyspnea or headaches. On readmission, May 18-22, the heart was still much smaller than before the rice regime (transverse diameter 13.3 cm.), *the weight was 65.2 Kg.*, the albumin excretion in the urine was 0.3-0.4 Gm. per 1000 cc., and the phenolsulfonphthalein excretion in one half hour was 20 per cent (on the first admission, in November, 1941, it has been 23 per cent). The blood pressure, however, had risen to an average of 167 systolic, 99 diastolic. The patient was warned not to trust his subjective feeling of complete health, but to resume the rice diet without "modifications." He did so when he ate at home, but made a number of exceptions, including even barbecue, when eating with friends.

He returned to the hospital on July 21, stating on admission that he had been without complaints. *His weight was 66.4 Kg.*, his blood pressure during his stay at the hospital (six days) averaged 190 systolic, 104 diastolic. The electrocardiogram showed the T-waves in lead 1 inverted; the angle of the electrical axis was −70 degrees. The nonprotein nitrogen was 39 mg. per 100 cc. of blood, the urea nitrogen 18.9 mg., the urea ratio 48.5 per cent. Chlorides (as sodium chloride) were 614 mg. per 100 cc. of plasma; calcium was 9.8 mg. per 100 cc. of serum, phosphorus 4.3 mg., cholesterol 145 mg. Total proteins were 6.2 Gm. per 100

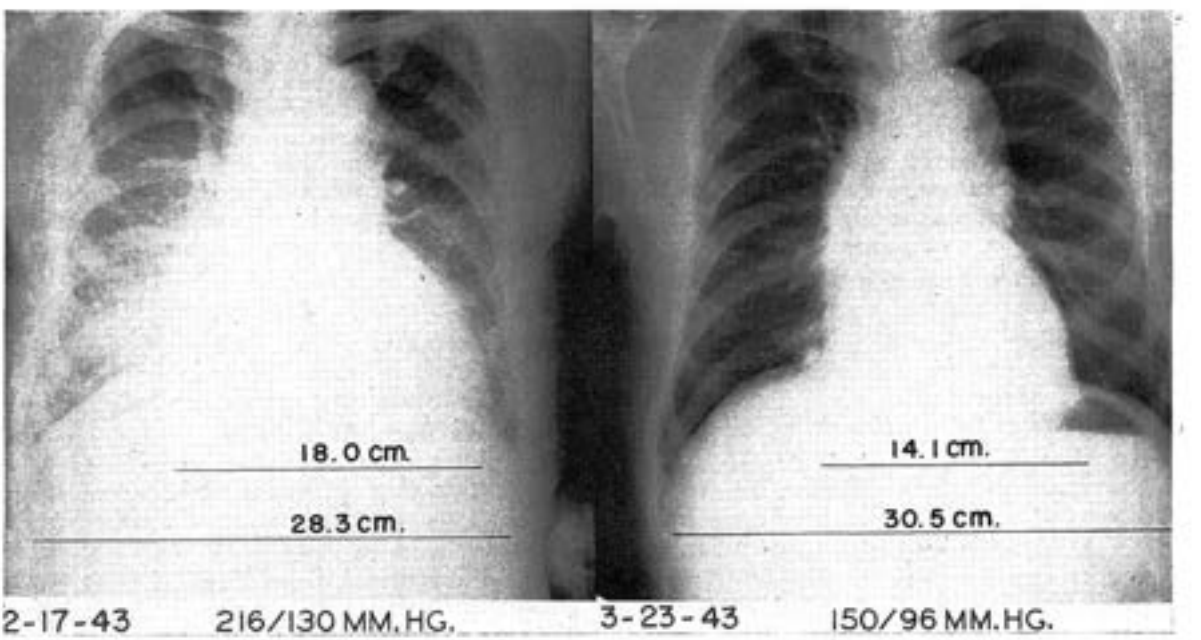

Fig. 53. W.C.F. "Hypertensive vascular disease." Rice diet started February 16, 1943. No digitalis. Reduction in heart size with change in transverse diameter of 28 per cent.

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cc. of plasma (albumin 2.6 Gm., globulin 3.6 Gm.). The urine had a specific gravity of 1.011, and contained 0.4 Gm. of albumin per 1000 cc. and 20-30 white blood cells per high power field. Urea excretion in the urine was 5.5 Gm. in twenty-four hours. At discharge the situation was again explained to the patient and he was warned of the danger of disregarding the diet. A short time later he was taken to a local hospital because of a cerebral vascular accident.

PATIENT 9. *"Hypertensive vascular disease" with renal involvement (blood pressure 230 systolic, 140 diastolic); cardiac failure; hypoproteinemia; vascular retinopathy. Example of decrease of blood pressure, loss of edema (63 pounds), increase in plasma proteins, decrease of T_1 inversion, disappearance of heart enlargement, and recovery of eyesight with disappearance of retinal hemorrhages, exudates, and papilledema.*

J.M. (A93523), a 44 year old white truck driver, was admitted to the hospital on October 19, 1942, complaining of swollen legs, failing vision, "sick headaches," shortness of breath, and substernal oppression.

History: The patient had had measles, mumps, chickenpox, and whooping cough as a child, influenza at 19, and malaria at 37 and 38. In 1932, when he was 34, he developed weight loss, weakness, polydipsia, and polyuria. He was told that he had diabetes and was treated with diet for one year. In 1935 blisters appeared on his big toe. He improved on a diabetic diet and insulin, but the weakness persisted. Shortness of breath and some swelling of the feet and legs developed in 1939, and he began to have paroxysmal nocturnal dyspnea in 1940. In February, 1942, his vision began to fail, objects becoming hazy and lights dim. Since May, 1942, he had noticed swelling about the face and eyes, particularly in the morning. The dyspnea grew progressively worse, and he began to have headache with nausea and vomiting. The swelling of the legs was increasing; the skin was reddened and peeling off in large scales.

Examination: The patient's height was 176 cm., his weight 88.15 Kg., temperature 36.1 C., pulse 80, respiration 20, blood pressure 230 systolic, 140 diastolic. He looked acutely ill and was in marked respiratory distress. There were moderate sacral and scrotal edema and severe pitting edema of the legs as high as the hips. Erythema with scaling was present on both lower legs. The eyelids were swollen. The nasal side of the left disc was blurred (fig. 54) and there was papilledema in the right eye. Numerous patches of exudates and hemorrhages were scattered throughout both fundi. The arterioles were very narrow, irregular and tortuous; some of them were invisible at a short distance from the disc. The veins were variable in caliber, and were tortuous and engorged; a loop (congenital?) was seen in the left inferior nasal vein. There was complete compensated edentia. Fine moist rales were heard over both lung bases. The heart was enlarged mainly to the left, the point of maximal impulse being 13 cm. from the midsternal line in the sixth interspace. There was a diastolic gallop rhythm, and a soft systolic murmur was heard over the entire precordium. The liver was felt 3 cm. below the costal margin; the spleen was not palpable; there was no tenderness in either kidney region. An indirect inguinal hernia was present on the left side. The neurological examination was negative. A portable film of the chest showed a transversely enlarged heart with moderate vascular congestion. The electrocardiogram showed inverted T-waves in leads 1 and 4, and diphasic T-waves in leads 2 and 3.

Accessory clinical findings: The hemoglobin was 87 per cent, and there were 3,960,000 red blood cells and 12,600 white blood cells with 5 per cent non-segmented polymorphonuclears, 67 per cent segmented polymorphonuclears, 6 per cent eosinophils, 1 per cent basophils, 3 per cent monocytes, 4 per cent large lymphocytes, 14 per cent small lymphocytes. The serological tests for syphilis were negative. The nonprotein nitrogen was 42 mg. per 100 cc. of blood, sugar 98 mg. per 100 cc. of blood. The carbon dioxide combining power of the plasma was 64 volumes per cent. Total proteins were 3.9 Gm. per 100 cc. of plasma (albumin 1.7 Gm., globulin 2.2 Gm., albumin-globulin ratio 0.77). Calcium was 8.5 mg. per 100 cc. of serum, phosphorus 5.0 mg., cholesterol 318 mg. The urine contained occasional red blood cells, clumped white blood cells and 4-5 cellular casts per high power field, and gave a 1 plus benzidine reaction; albumin excretion was 7.5-15 Gm. in twenty-four hours, sugar excretion 1.5-2.9 Gm. in twenty-four hours. The results of the phenolsulfonphthalein test were as follows: Excretion at the end of the first half hour 5 per cent, at one hour 10 per

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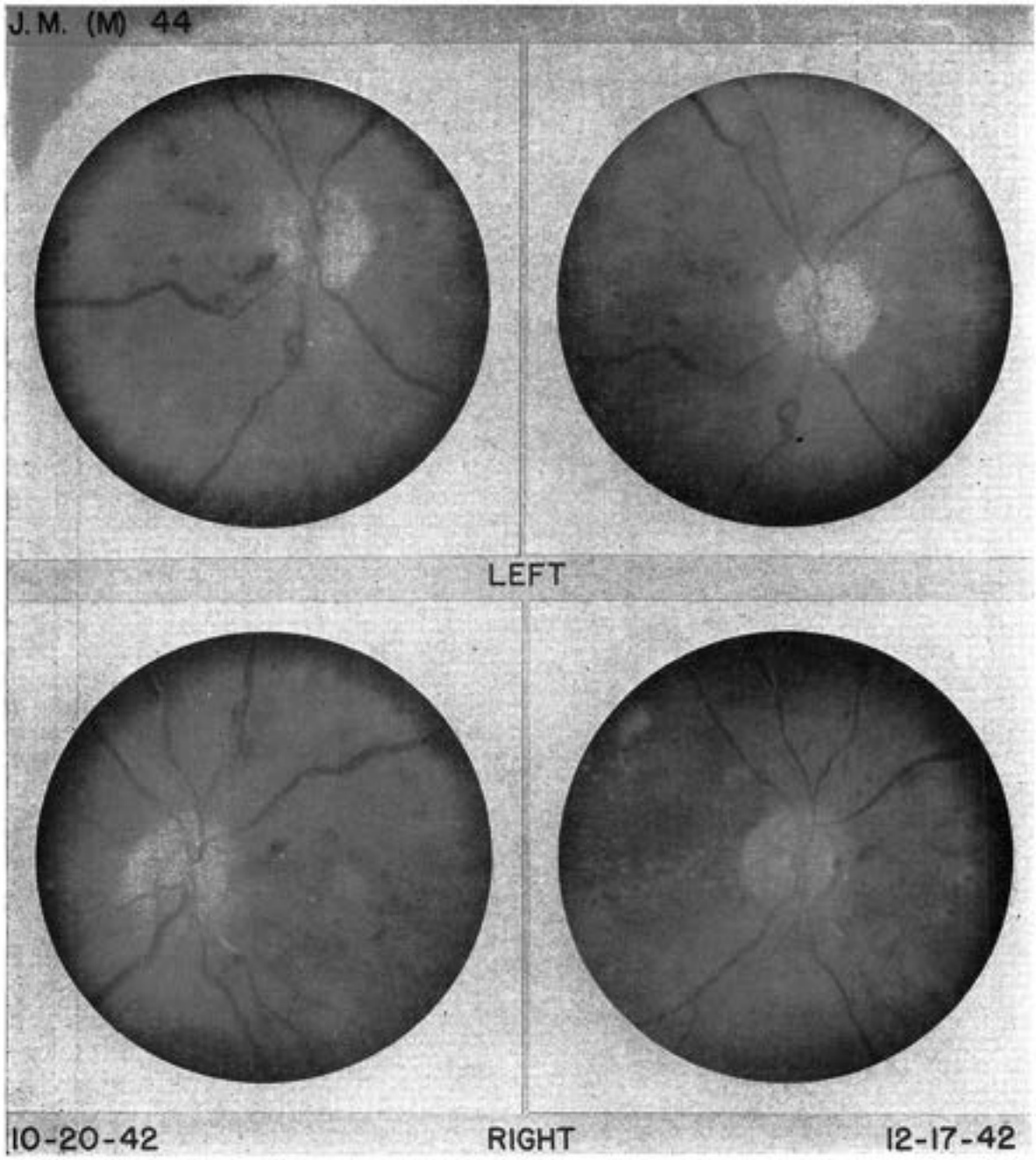

Fig. 54. J.M. (m., 44). "Hypertensive vascular disease." Rice diet started October 20, 1942. Disappearance of papilledema, right eye. Most of hemorrhages absorbed; marked decrease of venous engorgement, tortuosity, both eyes.

cent, at one and a half hours 5 per cent, at two hours 5 per cent; the total excretion in two hours was 25 per cent.

Impression: "Hypertensive vascular disease" with renal involvement; cardiac failure; vascular retinopathy with papilledema, hemorrhages, and exudates.

Course: The patient received a 1950 calorie diabetic diet (65 Gm. of protein, 140 Gm. of fat, 110 Gm. of carbohydrate) for one day and was then placed on the rice diet (2000 calories, 1000 cc. of fruit juices). He was given no digitalis, insulin, or other medication; the only therapeutic measure in addition to the diet was oxygen inhalation (one and a half hours three times a day). The edema and shortness of breath began gradually to subside. The urinary output increased and he excreted as much as 3600 cc. of urine in twenty-four hours. Within sixteen days he

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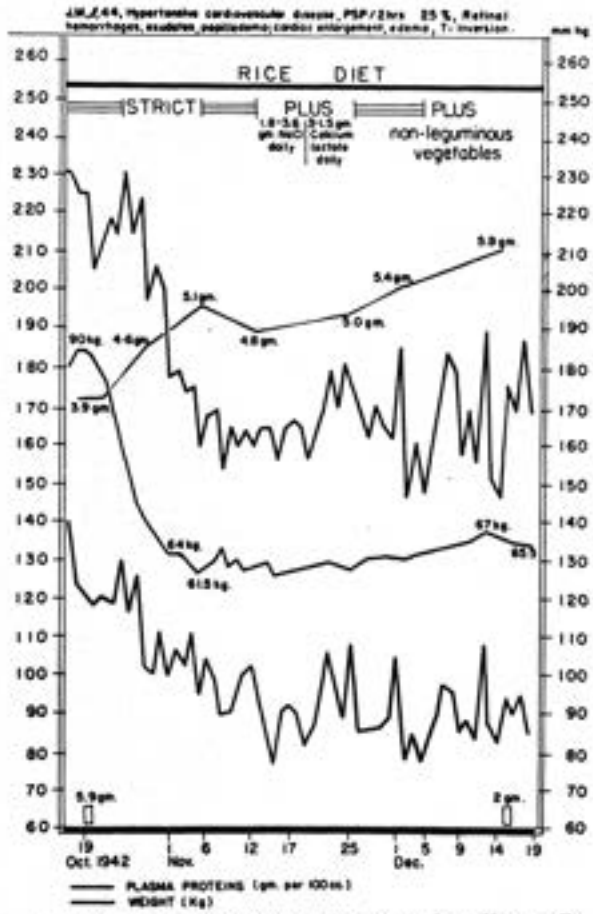

Fig. 55. J.M. "Hypertensive vascular disease." Decrease of blood pressure on strict rice diet. Loss of 63 pounds of edema in 16 days. Improvement in plasma proteins. Decrease of albuminuria (from 5.9 Gm. to 2 Gm. per 1000 cc.).

lost 63 pounds of weight. The total proteins increased from 3.9 Gm. to 5.1 Gm. per 100 cc. of plasma. The blood pressure ranged from 155 to 170 systolic, and from 90 to 105 diastolic (fig. 55). After twenty-three days of strict rice diet, the serum chlorides had decreased to 480 mg. per 100 cc., the serum calcium to 6.1 mg. per 100 cc. Sodium chloride (1.8-3.6 Gm.) was given for four days, and the chlorides increased to 510 mg. per 100 cc. of serum, the calcium to 8.8 mg. Calcium lactate (1.5-3 Gm. per day) was given by mouth for the next eight days. At the end of this time the serum calcium was 8.9 mg. per 100 cc., the plasma chlorides were 542 mg. per 100 cc. There was a definite rise in blood pressure (fig. 55). The total nitrogen excretion in the urine was 2.7 Gm. in twenty-four hours, the urea nitrogen excretion 1.85 Gm. in twenty-four hours.

After eight weeks of rice diet (twenty-three days strict diet, twelve days with additional sodium chloride and calcium, twenty-one days with the addition of some non-leguminous vegetables), the patient was up and feeling well. He had no edema, headache, dyspnea, or substernal oppression. The heart was smaller in size. The blood pressure varied between 148 and 190 systolic and 74 and 100 diastolic (fig. 55). The T-waves in leads 2, 3, and 4 were upright, the T-wave in lead 1 was flat diphasic. Total proteins were 5.9 Gm. per 100 cc. of plasma, the albumin-globulin ratio 1.2. There were only rare red blood cells and casts in the urine; the amount of albumin had decreased considerably and the reaction for sugar was negative.

Examination of the eyegrounds showed no papilledema. Most of the hemorrhages and exudates had been absorbed. The veins were still unequal in caliber, but engorgement and tortuosity had markedly decreased (fig. 54). The patient, who during the first hospital week was unable to recognize a hand at a distance of one or two feet, and after the first month of the rice regime still could not distinguish colors, was now able to read moderate size print and distinguish colors clearly.

Findings on discharge compared with those on admission were as follows:

	October 19-20, 1942	*December 17, 1942*
Blood pressure (mm. Hg.)	230/140	167/90 (average of last 10 days)
Hemoglobin (% of 15.5 Gm.)	87	77
RBC (per cubic mm.)	3,960,000	3,900,000
WBC (per cubic mm.)	12,600	7,500
NPN (mg. per 100 cc. of blood)	42	46
Albumin (Gm. per 100 cc. of plasma)	1.7	3.3
Globulin (Gm. per 100 cc. of plasma)	2.2	2.6
Calcium (mg. per 100 cc. of serum)	8.5	8.9
Phosphorus (mg. per 100 cc. of serum)	5.0	4.3
Urine albumin (Gm. in 24 hours)	10.0 (average of first week)	3.8
Weight (Kg.)	90.5	65.5
Retinal hemorrhages and exudates	+++	+
Papilledema	++	0
T-waves in lead 1	Inverted	Flat diphasic

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PATIENT 10. *"Hypertensive vascular disease" first noted in pregnancy (no conclusive evidence of renal involvement); vascular retinopathy with papilledema, hemorrhages, and exudates. Example of decrease of high blood pressure to normal and disappearance of retinopathy and heart enlargement.*

L.B. (B36420), a 24 year old white farmer's wife, was admitted to the medical ward of the hospital on October 30, 1944, complaining of intense headaches and progressive dimness of vision.

History: The family history was positive for hypertension, nephrolithiasis, and diabetes. The patient had had measles, whooping cough, and scarlet fever in early childhood; malaria and mumps at 15. Except for "some headache" since she was about 10, she had always been "strong and healthy" and "working hard." Her first pregnancy (at 19) was complicated by edema of the feet and severe headache; the systolic blood pressure went to 210. There were no symptoms of urinary tract disease and no albuminuria, so far as the patient knows. The systolic blood pressure after delivery was 170. After that the systolic blood pressure was "always over 200." She had frequent headaches (three or four times a week), most of which occurred on awakening in the morning. At 23 she became pregnant again and was not seen by a physician until the end of the fifth month (August 18, 1944). Her blood pressure was then found to be "extremely high" (above 260 systolic). On September 1, 1944, she was seen in Duke Hospital Obstetrical Clinic; her blood pressure was 260 systolic, 145 diastolic. Ophthalmoscopic examination at that time showed arteriovenous compression and narrowing of the arterioles, but no retinal exudates or hemorrhages. She had slight ankle edema and albuminuria. The urinary sediment showed only occasional white blood cells. Hysterotomy was advised but was refused by the patient. On September 5, 1944, her blood pressure was 248 systolic, 140 diastolic. On September 26, after bed rest, sedation with phenobarbital, and a "low salt, high protein, low calorie diet with limited fluids," it was 190 systolic, 135 diastolic; there was marked albuminuria, and occasional red blood cells and hyaline casts were seen in the urine. On October 2, 1944, she was admitted to the Duke Hospital Obstetrical Ward because of vaginal bleeding. Her blood pressure was higher than 260 systolic, 170 diastolic. On October 5, breech delivery of a stillborn infant was performed. Blood pressure readings (twice daily) from October 6 to October 11 averaged 224 systolic, 147 diastolic. After discharge on October 11, she continued to have progressive dimness of vision and headache. She was admitted to the Medical Ward of this hospital on October 30, 1944.

Examination: The patient was a moderately obese young woman in no acute distress. Her height was 158.5 cm., her weight 78.25 Kg., temperature 37.5 C., pulse 102, respiration 20, blood pressure 233 systolic, 157 diastolic. There was no edema. The pupils reacted well to accommodation and light. The discs (fig. 25 and 56) were obliterated by papilledema and peripapillary edema. The arterioles, as far as they were visible, were tortuous and narrowed; the veins were tortuous and distended, and their continuity was interrupted by retinal edema and massive hemorrhages and exudates of the cotton-wool and metallic type. The lungs were clear to percussion and auscultation. The heart was enlarged to the right and the left; the aortic second sound was very loud, but there were no murmurs. The liver was not enlarged and the spleen was not palpable; there was no tenderness in either kidney region.

A chest film (fig. 57) showed the transverse diameter of the heart to be 16.6 cm., the internal diameter of the chest 32.0 cm. No abnormalities were seen on a flat plate of the abdomen. The electrocardiogram showed the T-waves upright in all leads; the angle of the electrical axis was +18 degrees.

Accessory clinical findings: The hemoglobin was 95 per cent, red blood cells 4,800,000, white blood cells 9,900. The corrected sedimentation rate was 10 mm. in one hour. Serological tests for syphilis were negative. The nonprotein nitrogen was 26 mg. per 100 cc. of blood, the urea nitrogen 9.5 mg., the urea ratio 36.5 per cent. Chlorides (as sodium chloride) were 560 mg. per 100 cc. of plasma, calcium was 9.6 mg. per 100 cc. of serum, phosphorus 2.7 mg., cholesterol 240 mg. Total proteins were 7.2 Gm. per 100 cc. of plasma (albumin 3.9 Gm., globulin 3.3 Gm., albumin-globulin ratio 1.2). The blood sugar was 93 mg. per 100 cc. The urine showed an acid reaction and a specific gravity of 1.015; no sugar, no red blood cells and no casts were present, but there were many epithelial cells and 2-3 white blood cells per

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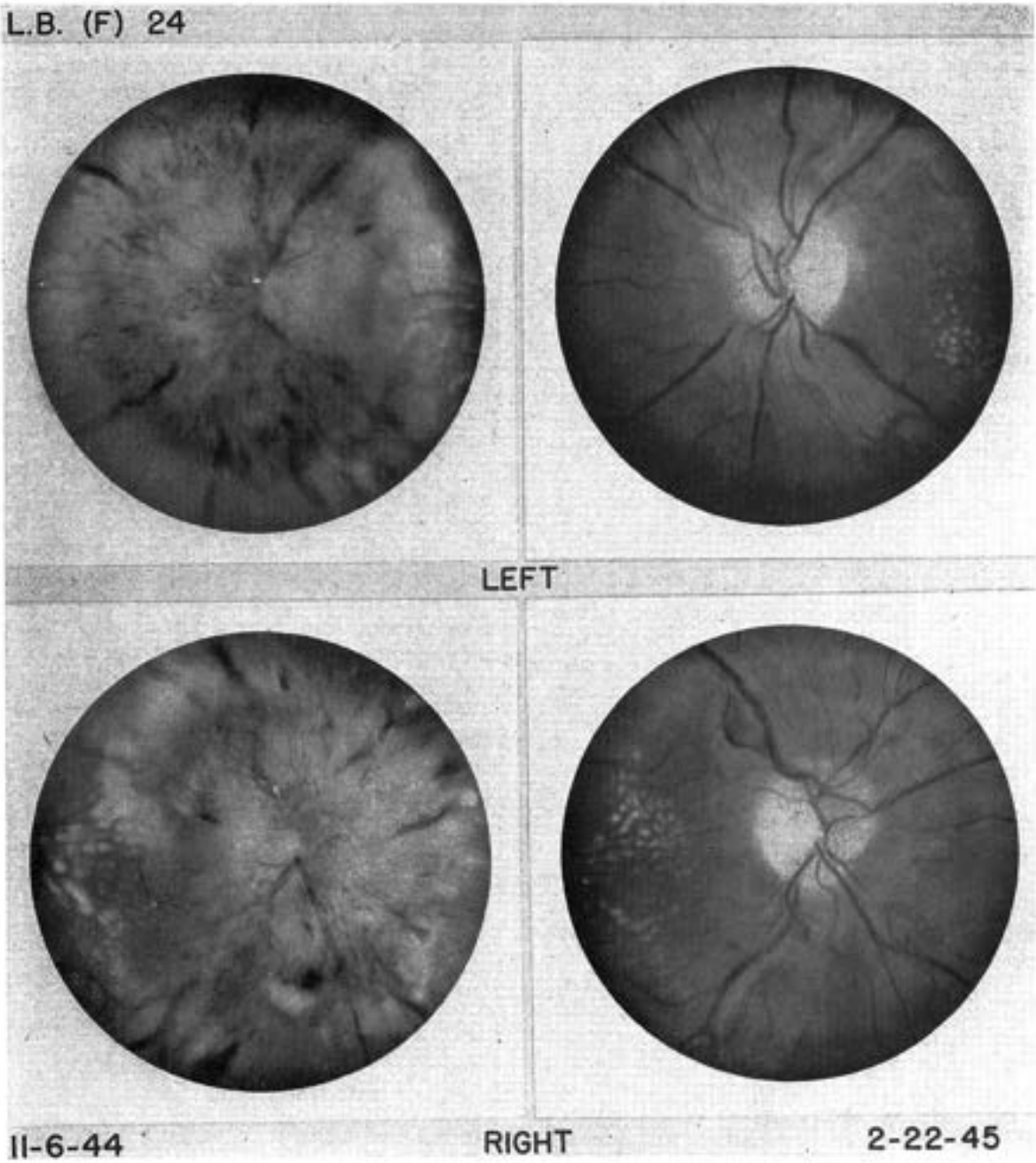

Fig. 56. L.B. (f., 24). "Hypertensive vascular disease." Rice diet started October 30, 1944. **Disappearance of papilledema, hemorrhages; marked decrease of exudates, both eyes.** See also fig. 25.

high power field; the benzidine reaction was negative; albumin excretion was 0.67 Gm. per 1000 cc. of urine. The results of the phenolsulfonphthalein test were as follows: Excretion at the end of the first half hour 35 per cent, at one hour 22 per cent, at one and a half hours 4 per cent, at two hours no specimen; total excretion in two hours was 61 per cent. The test was repeated and showed a total excretion in two hours of 58 per cent. The concentration-dilution test showed a range of specific gravity from 1.010 to 1.030. The urea clearance was 55.7 per cent of normal (after sixteen days on the rice diet).

Impression: "Hypertensive vascular disease" (first noted in pregnancy) without conclusive evidence of renal involvement; vascular retinopathy with papilledema, hemorrhages, and exudates.

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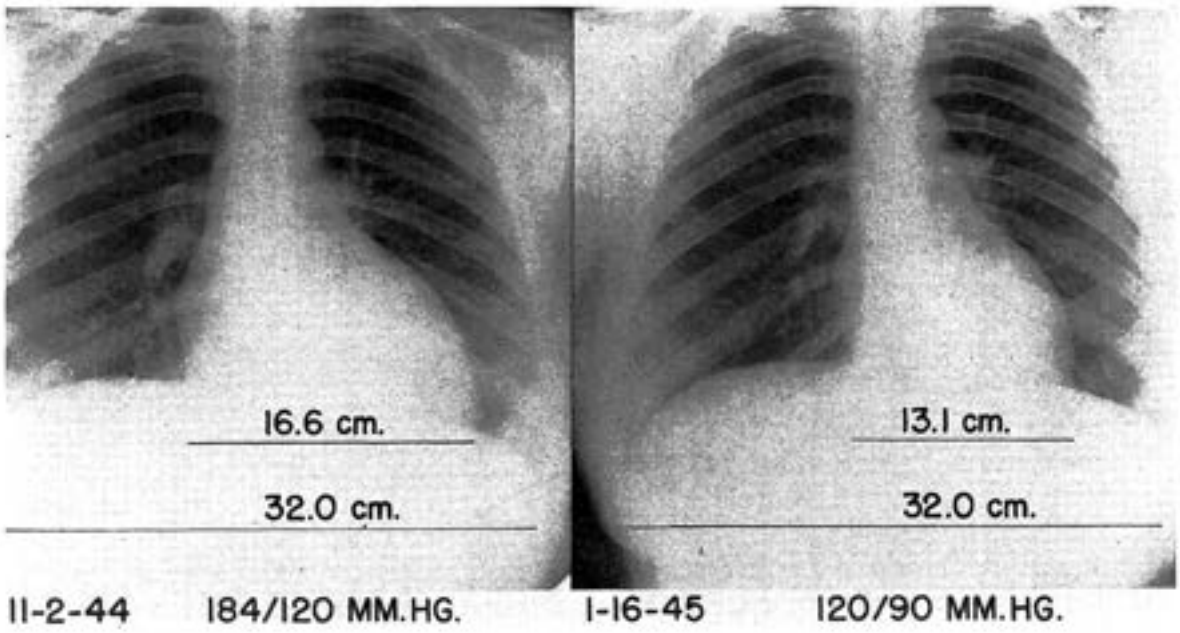

Fig. 57. L.B. "Hypertensive vascular disease." Rice diet started October 30, 1944. No digitalis. Reduction in heart size with change in transverse diameter of 26 per cent.

Course: The patient was immediately started on a 2000 calorie rice diet with fluids limited to 900 cc. of fruit juices daily. She was kept on strict bed rest, and oxygen inhalations were given for one hour three times daily (beginning November 5). She received no digitalis or any other medication except sodium amytal for the sodium amytal tests. The venous pressure on November 6 was 12.2 cm. of saline. The blood pressure decreased rapidly (fig. 58), averaging 180 systolic, 126 diastolic the first week, 155 systolic, 105 diastolic the second week, 138 systolic, 97 diastolic the third week, and 130 systolic, 91 diastolic the fourth week. The patient lost 5 Kg. of weight during the four weeks in the hospital. At the time of discharge on November 30, 1944, there was marked improvement in her eyesight, and the heart was smaller in size, with a change in the transverse diameter of 12.9 per cent. She had only occasional mild headaches. The average excretion of albumin in the urine during the fourth week was 0.24 Gm. per 1000 cc. The patient was advised to follow the strict rice diet at home and to be up for not more than one hour daily.

She returned to the hospital for re-examination on December 18, 1944. During the eighteen days at home she had had a slight

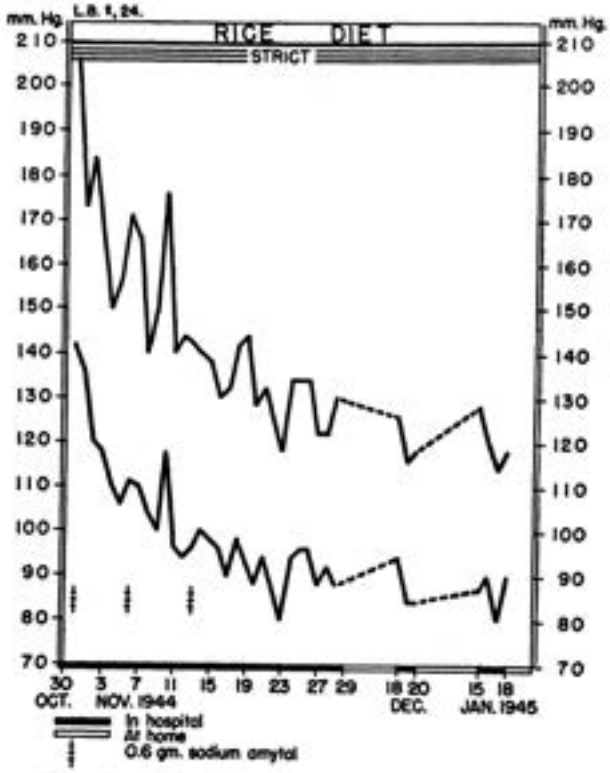

Fig. 58. L.B. "Hypertensive vascular disease." Decrease of blood pressure to normal in 3 weeks on rice diet.

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headache on only two occasions and her vision had continued to improve. She felt considerably better. Her blood pressure averaged 120 systolic, 87 diastolic. Her weight was 70 Kg. The retinae showed marked improvement; the papilledema had decreased, and there remained only a few hemorrhages and patches of exudates. The transverse diameter of the heart was 14.2 cm (a change of 16 per cent in seven weeks); the internal diameter of the chest was 32.2 cm. The electrocardiogram showed the angle of the electrical axis to be +51 degrees.

The hemoglobin was 103 per cent, red blood cells 5,000,000, white blood cells 5,900. The nonprotein nitrogen was 24 mg. per 100 cc. of blood, the urea nitrogen 1.2 mg., the urea ratio 5.0 per cent. Chlorides (as sodium chloride) were 572 mg. per 100 cc. of plasma; calcium was 9.4 mg. per 100 cc. of serum, phosphorus 4.0 mg., cholesterol 153 mg. Total proteins were 6.7 Gm. per 100 cc. of plasma: albumin 3.8 Gm., globulin 2.9 Gm., albumin-globulin ratio 1.3. The urine showed an acid reaction and a specific gravity of 1.010; there was no sugar; the albumin excretion was 0.2 Gm. per 1000 cc. Total nitrogen excretion was 2.9 Gm. per 1000 cc. of urine; urea excretion 4.3 Gm.; chloride excretion (as sodium chloride) 0.22 Gm. The results of the phenolsulfonphthalein test were as follows: Excretion at the end of the first half hour 15 per cent, at one hour 20 per cent, at one and a half hours 10 per cent, at two hours no specimen; total excretion in two hours 45 per cent.

The patient was discharged for another four weeks on strict rice diet and was advised to stay in bed except for about an hour and a half a day. Her vision continued to clear up and she had no headaches. Upon examination on January 15, 1945, the eyegrounds showed further improvement (fig. 25). The disc margins were more sharply outlined; some metallic exudates were still present, but the greater part of the retinal edema, hemorrhages and cotton-wool exudates had disappeared. The heart was smaller, with a change in the transverse diameter of 26 per cent compared with the chest film of November 2 (fig. 57). The aortic second sound was not louder than the pulmonic second sound. The patient was advised to continue on the strict rice regime and to rest at least twenty hours a day for another six weeks.

She followed the rice regime but was up and around for about eight hours every day doing the cooking and light housework for her family. She was completely asymptomatic and was feeling healthy and strong. Examination of the eyegrounds on Febuary 20 showed the optic discs sharply outlined; most of the exudates had disappeared (fig. 56). She was advised to continue the rice diet, to which non-leguminous vegetables were added, and to return to the hospital for re-examination after two months.

A comparison of the findings on the patient's four admissions is given below:

	Oct. 30-Nov. 9, 1944	*Dec. 18-Dec. 30, 1944*	*Jan. 15-Jan. 18, 1945*	*Feb. 20-Feb. 22, 1945*
Blood pressure (mm. Hg.)	233/157	120/87	120/87	121/87
Hemoglobin (% of 15.5 Gm.)	95	103	90	82
RBC (per cubic mm.)	4,800,000	5,000,000	4,610,000	4,600,000
WBC (per cubic mm.)	9,900	5,900	5,800	5,100
NPN (mg. per 100 cc. of blood)	26	24	26	25
Urea N (mg. per 100 cc. of blood)	9.5	1.2	1.8	3.0
Albumin (Gm. per 100 cc. of plasma)	3.9	3.8	3.8	3.8
Globulin (Gm. per 100 cc. of plasma)	3.3	2.9	3.1	3.3
Chlorides (as mg. NaCl per 100 cc. of plasma)	560	572	520	532
Calcium (mg. per 100 cc. of serum)	9.6	9.4	10.1	9.1
Phosphorus (mg. per 100 cc. of serum)	2.7	4.0	2.2	3.5
Cholesterol (mg. per 100 cc. of serum)	240	153	132	110
Urine albumin (Gm. per 1000 cc.)	0.67	0.2	0.18	0.28
PSP (% excretion in 2 hours)	61, 58	45	57	47
Weight (Kg.)	78.25	70	68.5	64
Papilledema	++++	+	0	0
Retinal hemorrhages and exudates	++++	+++	++	+
Angle of electrical axis	+18°	+51°	+43°	+58°
T wave in lead 1	Upright	Upright	Upright	Upright
Transverse diameter of heart (cm.)	16.6	14.2	13.1	12.9

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Summary

Two hundred and thirteen patients with acute or chronic primary kidney disease or with "hypertensive vascular disease," with or without cardiac involvement, retinopathy or uremia, were treated with a diet limited to rice, sugar, fruit and fruit juices, supplemented by vitamins and iron. The fluid intake was usually limited to 700-1000 cc. of fruit juices daily. The patients followed the diet strictly or with modifications for periods varying from four days to thirty-two months.

Protein equilibrium

In spite of the low protein intake, the protein equilibrium of the patients on the rice diet is maintained. The nitrogen excretion in the urine decreases to amounts considerably smaller than those found in fasting individuals (the average total nitrogen excretion per twenty-four hours after two months of the diet was 2.26 Gm.). Plasma proteins and hemoglobin remain at a constant level: The average concentration of the total plasma proteins in 120 patients was 6.3 Gm. per 100 cc., both before the rice diet and after ninety days (average) on the diet; the average hemoglobin value of 165 patients was 79.9 per cent (of 15.5 Gm.) before, and 80.1 per cent after seventy-five days (average) on the diet.

Plasma and urine chlorides

With the low chloride intake of the diet, the chloride concentration in plasma and urine decreases. After a month of the rice diet, the chloride concentration in the urine is about 100 mg. per 1000 cc. The average plasma chloride concentration of 91 non-uremic patients after an average of forty-four days on the rice diet was 91.7 milli-equivalents (as sodium chloride, 536 mg. per 100 cc.), as compared to 97.0 milli-equivalents (as sodium chloride, 567 mg. per 100 cc.) before the diet.

Blood pressure

Of 192 patients with hypertension on the basis of acute or chronic primary kidney disease or of "hypertensive vascular disease," 25 died after six to eighty-one days on the strict diet (average twenty-five days). In 60 of the remaining 167 patients *(36 per cent) there was no improvement in the hypertension*: The decrease in their mean arterial pressure was less than 20 mm. of mercury, the average blood pressure decreasing from a level of 196 systolic, 120 diastolic to a level of 180 systolic, 114 diastolic, after an average time of thirty-nine days* on the strict or modified diet. In 10 of 47 patients with chronic primary kidney disease the average blood pressure decreased from a level of 208 systolic, 132 diastolic to a level of 192 systolic, 124 diastolic in an average time of sixty-seven days*. In 22 of 50 patients who had "hypertensive vascular disease" with "secondary" kidney involvement, the average blood pressure decreased from a level of 212 systolic, 129 diastolic to a level of 200 systolic, 126 diastolic after an average of thirty-nine days. In 28 of 65 patients with "hypertensive vascular disease" without conclusive evidence of renal excretory dysfunction, the average blood pressure decreased from a level of 179 systolic, 108 diastolic to a level of 160 systolic, 102 diastolic in an average time of thirty days.

In 107 of the 167 patients *(64 per cent) the hypertension improved*: The decrease in their mean arterial pressure was 20-96.5 mm. of mercury, the average blood pressure decreasing from a level of 200 systolic, 122 diastolic to a level of 149 systolic, 96 diastolic after an average time of sixty-two days on the strict or modified diet. The blood pressure of 5 patients with acute glomerulonephritis decreased from a level of 170 systolic, 109 diastolic (average) to 108 systolic, 66 diastolic (average), in an average period of fifteen days on the rice diet. In 37 of 47 patients with chronic primary kidney disease, the average blood pressure decreased from a level of 194 systolic, 124 diastolic to a level of 140 systolic, 96 diastolic after seventy-seven days (average) on the rice diet. In 28 of 50 patients with "hypertensive vascular disease" with "secondary" kidney involvement, the average blood pressure decreased from a level of 219 systolic, 128 diastolic to a level of 165 systolic, 102 diastolic in an average of seventy-three days. In 37 of 65 patients with "hypertensive vascular disease" without conclusive evidence of renal excretory dysfunction, the average blood pressure decreased from a level of 197 systolic, 115 diastolic to a level of 151 systolic, 97 diastolic after an average of forty-eight days on the rice diet.

Electrocardiographic changes

In 23 of 82 patients with chronic primary kidney disease or "hypertensive vascular

* The average figure may be misleading because it includes one patient who was on the diet for 548 days.

disease" who followed the strict or modified rice diet for one to thirty-two months (average, four months) there was a definite change in T_1 during the treatment. In 3 patients (13 per cent) the change in T_1 was in the direction from upright to inverted; in 20 patients (87 per cent), from inverted to upright.

In 76 patients, the electrical axis could be evaluated. In 43 patients there were no changes, or only minor changes in the angle of the electrical axis (less than $\pm$15 degrees); 33 patients had a definite change in the angle of the electrical axis.

Six of the 33 patients (18 per cent) had a decrease in the angle of the electrical axis (average of 20.2 degrees); 27 of the 33 patients (82 per cent) had an increase in the angle of the electrical axis (average of 26.4 degrees).

Heart size

In 72 patients with chronic primary kidney disease or "hypertensive vascular disease" who followed the strict or modified rice diet for an average period of four months, the heart size could be measured.

In 6 of the 72 patients (8.3 per cent) the heart became larger: The transverse diameter of the heart increased by 0.9 to 4.9 per cent (average, 3.2 per cent).

In 66 of the 72 patients (91.7 per cent) the heart became smaller, with a change in the transverse diameter of 1.8 to 51.8 per cent (average, 13.3 per cent).

Nonprotein nitrogen

Of 171 patients whose nonprotein nitrogen was determined before and after the rice diet, 22 patients died after an average time of twenty-five days, one patient after twenty months. The average nonprotein nitrogen at the start of the diet in these patients was 115 mg. per 100 cc. of blood; the average nonprotein nitrogen before death was 186 mg. per 100 cc. of blood.

Of the remaining 148 patients, 35 (24 per cent) had either an increase or no decrease of the nonprotein nitrogen (average nonprotein nitrogen before the diet 42.7 mg. per 100 cc. of blood; after an average of sixty-three days on the diet, 50.2 mg. per 100 cc. of blood). In 113 patients (76 per cent) the nonprotein nitrogen decreased (average nonprotein nitrogen before the diet 53.1 mg. per 100 cc. of blood; after an average of seventy-eight days on the diet, 36.0 mg. per 100 cc. of blood).

Urea nitrogen

Of 63 patients whose blood urea nitrogen was determined before and after strict or modified rice diet, 6 patients (9.5 per cent), including 2 patients who died, had an increase of the urea nitrogen (average urea nitrogen before the diet 57.6 mg. per 100 cc. of blood; after an average of twenty-five days on the diet, 85.6 mg. per 100 cc.). In 57 of the 63 patients (90.5 per cent) the urea nitrogen decreased (average urea nitrogen before the diet 23.4 mg. per 100 cc. of blood; after an average of one hundred and twelve days on the diet, 11.6 mg. per 100 cc.). The lowest blood urea nitrogen after the rice diet was 1.2 mg. per 100 cc. The average urinary urea nitrogen excretion of 30 patients who had followed the rice diet for two months or more was 1.1 Gm. per twenty-four hours.

Cholesterol

Of 82 patients whose serum cholesterol was determined before and after strict or modified rice diet, 9 patients (11 per cent) had an increase in the cholesterol concentration of 2-38 mg. per 100 cc. of serum (average concentration before the diet 173 mg. per 100 cc. of serum; after an average of ninety-one days on the diet, 190 mg. per 100 cc.). The remaining 73 patients (89 per cent) had a decrease in the serum cholesterol concentration of 5-430 mg. per 100 cc. (average concentration before the diet 266 mg. per 100 cc. of serum; after an average of ninety-one days of the diet, 183 mg. per 100 cc.).

Retinopathy

Of 33 patients with advanced vascular retinopathy (papilledema, hemorrhages, or exudates) who followed the diet for at least eight weeks, the retinopathy of 1 patient became worse. In 11 of the 33 patients the retinopathy came to a standstill and papilledema, hemorrhages, and exudates partially cleared up. In 21 of the 33 patients, the retinopathy improved greatly or even cleared up completely under the rice regime.

I am indebted to Dr. Frederic M. Hanes and to the members of the staff and house staff of the Department of Medicine who have given me constant support and helpful criticism.

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SOME EFFECTS OF THE RICE DIET TREATMENT OF KIDNEY DISEASE AND HYPERTENSION*

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KIDNEY cells can be kept "alive" for a few hours in the Warburg apparatus and their chemical reactions examined in a rather simplified set-up.[1] Tissue slices thin enough to permit optimal diffusion are suspended in salt solutions, serum or exudate. The concentration of oxygen, carbon dioxide, sodium bicarbonate, sugar, aminoacids, ketoacids, lactic acid, etc., in the suspension milieu can be quantitatively controlled. Factors such as the rate of arterial and venous blood flow, the lymph flow, and the excretion of urine do not complicate the experiment. From one five-minute period to another one can measure manometrically what these isolated kidney cells do under varying conditions.

Like all other animal tissue, kidney cells have two main sources of energy, oxidation and fermentation. Values of about 10 are given in the literature for QO_2 and QM_{N_2} of human kidney cortex,[2,3] i.e., the approximate amount of oxygen used for oxidative processes by 100 Gm. of fresh kidney substance would be about 5 liters in 24 hours; the approximate amount of lactic acid formed anaerobically in the same time would be about 2 Gm.

If in the course of a disease, renal tissue is destroyed and replaced by a scar, obviously the only metabolic reactions to be found will be those of the scar tissue and no longer those of the kidney cells. Between normal and completely destroyed cells, there are as far as disturbances of cellular metabolism are concerned, the following possibilities:

1. The cells are uninjured, but metabolize in a pathological environment.
2. The cells are injured, but the environment in which they metabolize is normal.

* From the Department of Medicine, Duke University School of Medicine, Durham, N. C. Read January 15, 1946 before the Section of Medicine of The New York Academy of Medicine.

TABLE I—CHANGES IN CHEMICAL COMPOSITION OF "INFLAMMATION FLUID"

	Serum	*Fluid from Sterile Blister of Skin (Normal person)*
Oxygen (mm. Hg.)	110	6
Sugar (mg./100 cc.)	90	6
Lactic Acid (mg./100 cc.)	10	125
Bicarbonate (10^{-3} molar)	25	9
PH	7.4	6.3

3. The cells are injured and metabolize in a pathological environment.

In order to learn something about the chemical composition of such a "pathological environment" we measured the metabolic reactions which take place during an inflammation. We produced sterile cantharidin blisters on the skin of normal people and of patients with various diseases and measured the metabolism of the leukocytes in the blister fluid and the chemical changes produced by them.[4] As Table I shows, the concentration of some biologically essential substances shows a decisive change during inflammation.

The next step was to determine what effects on the metabolism of kidney cells were produced by these environmental changes. We found the anaerobic splitting of sugar into lactic acid to be markedly dependent on changes of the sodium bicarbonate, sugar, and hydrogen ion concentration. The rate of oxidation was, to a large extent, independent of sodium bicarbonate, sugar, and PH, but was dependent on variations of oxygen concentration.

We could show further that the deamination of aminoacids and the formation of ammonia by slices of kidney tissue are inhibited by lowered oxygen concentrations. This applies both to the so-called "unnatural" d-aminoacids and to those naturally present in the plasma of man, rat, and rabbit, and in the tissue slices themselves.[5]

Besides the inhibition of the rate of deamination, which is reversible, there is another effect of low oxygen concentration on kidney cell metabolism which causes irreversible changes. If we kept slices of

kidney tissue for about one hour in an oxygen free atmosphere and then re-established conditions of optimal oxygen concentration the cells were still able to deaminize aminoacids and to form ammonia but they had lost the ability to oxidize ketoacids.[6] This means that by the removal of oxygen for a given time one can injure kidney cells selectively as to their oxidative reactions.

The obvious question is: What practical significance have these cellular physiological findings in the treatment of diseases in which renal metabolic dysfunction may play a role. Some simple examples may show the trend of our reasoning. Let us assume that the oxygen *supply* to any one kidney cell has been decreased by some pathological condition and that we are unable to increase it; still, it might be possible to increase the oxygen *concentration* by reducing the amount of work required from this cell, thus decreasing its oxygen demand. Or let us assume that the rate of oxidation of ketoacids in any one diseased kidney cell is decreased; still, it might be possible to reduce the amount of ketoacid offered to the cell if we were able to remove from the diet those substances from which ketoacids are derived. Deductions of a similar kind might be drawn from observation of the role played in renal metabolism by aminoacids, sugar, sodium bicarbonate, etc.

It would be most desirable, of course, to substitute for the natural ferments that have been destroyed, extracts of animal kidneys, or even better, synthetic substances with the same chemical properties as those in normal kidney cells. Unfortunately, such substances are not yet available.

I have been asked to speak to you this evening about a less perfect approach, but one which has led to rather satisfactory results: the compensation of renal metabolic dysfunction with the rice diet.

The consensus of opinion at the present time is that dietary treatment is useful in kidney disease, but of little or no value in hypertension without obvious renal involvement. Goldring and Chasis in 1944 summed up the prevalent view in their book on hypertension: "The diet in uncomplicated hypertension requires no essential change from the normal."[7]

Compared to diets previously used in hypertension, the rice-fruit-sugar diet is rigid. It contains in 2000 calories about 5 Gms. of fat and 20 Gms. of protein derived from rice and fruit, and not more than 0.2 Gm. of chloride and 0.15 Gm. of sodium.[8]

TABLE II—SERUM CHOLESTEROL OF PATIENTS WITH HYPERTENSIVE VASCULAR DISEASE ON RICE DIET

(Mg. per 100 cc. of serum)

Case	*Before*	*After*	*Days*	*Case*	*Before*	*After*	*Days*
1.	205	178	67	41.	283	205	203
2.	220	191	42	42.	238	210	84
3.	168	175	240	43.	333	270	28
4.	173	170	56	44.	266	154	112
5.	225	177	143	45.	345	258	74
6.	238	200	61	46.	293	200	20
7.	248	200	156	47.	268	170	133
8.	255	215	47	48.	302	217	100
9.	290	150	288	49.	222	70	99
10.	354	275	134	50.	210	190	109
11.	242	172	72	51.	300	225	166
12.	292	237	212	52.	242	152	126
13.	234	173	73	53.	145	188	21
14.	187	186	85	54.	220	166	105
15.	325	226	31	55.	290	160	102
16.	260	192	110	56.	195	168	21
17.	217	190	125	57.	318	235	9
18.	212	176	130	58.	220	187	53
19.	228	166	35	59.	246	220	136
20.	317	186	52	60.	210	205	24
21.	224	155	32	61.	225	200	16
22.	172	160	35	62.	273	230	9
23.	218	135	90	63.	210	143	43
24.	221	192	40	64.	215	155	221
25.	255	146	139	65.	230	158	17
26.	210	225	228	66.	210	175	212
27.	230	164	35	67.	292	168	78
28.	300	198	6	68.	215	110	76
29.	231	213	166	69.	239	149	60
30.	209	181	12	70.	192	215	24
31.	250	247	32	71.	308	246	155
32.	250	260	65	72.	258	175	41
33.	252	161	14	73.	193	153	16
34.	185	108	14	74.	260	170	178
35.	188	150	83	75.	168	160	240
36.	300	203	45	76.	317	170	146
37.	284	235	18	77.	200	175	6
38.	230	228	21	78.	304	169	66
39.	332	246	14	79.	186	102	205
40.	137	175	28				
				Average:	243.2	185.9	
				Average Difference 57.3 mg.			

It has been argued that this diet is nothing but starvation and that at least the "wear and tear quota" of 45 Gms. of protein is needed to maintain protein equilibrium. This figure, however, has no other basis than the 7 Gms. of nitrogen excreted per day by people who are fasting and represents only the body's effort to meet its caloric requirements by breaking down its own protein. The daily urinary nitrogen excretion of patients who have followed the rice diet for two months or more averages 2.26 Gms., which means that with a daily intake of little more than 15 Gms. of protein due to the protein sparing effect of carbohydrates, the nitrogen equilibrium is maintained.[9] In fasting, the daily urea nitrogen excretion in the urine is about 5.5 Gms. The average daily urea nitrogen excretion in the urine of patients who have followed the rice diet for two months or more is 1.1 Gms.[9]

In fasting, the blood urea nitrogen concentration is higher than it is normally. In patients on the rice diet, the urea nitrogen concentration is below the level of normal (average of 6.6 mg. per 100 cc. of blood). In starvation, hemoglobin and plasma protein concentrations decrease; in patients on the rice diet, the hemoglobin and plasma protein levels are maintained.[9]

It has been argued that the restriction of fat in the rice diet is too rigid and that patients with hypertension should eat "well-balanced meals." On the other hand the relation between hypercholesterolemia and hypertensive vascular disease has been stressed repeatedly, especially with regard to vascular retinopathy, coronary disease, and arteriosclerosis. In a series of 79 patients with hypertensive vascular disease 53 (i.e., 67 per cent) had a cholesterol concentration of at least 220 mg. per 100 cc. serum at the beginning of the treatment. As Table II shows, the hypercholesterolemia decreased with the rice diet in 52 of the 53 patients, the average decrease being 74 mg. per 100 cc. serum; in 37 of these 52 patients, the cholesterol concentration became normal. The hypercholesterolemia increased in 1 of the 53 patients (from 250 to 260 mg.). In 1 patient the cholesterol concentration increased from normal (210 mg.) to a hypercholesterolemic level (225 mg.).

It has been argued that the restriction of salt has no effect on hypertensive vascular disease. Therapeutic results such as those of Allen and Sherrill[10] and of Volhard[11] have been explained by Fishberg[12] on the assumption that salt-poor diets, because of their unpalatability lead to restriction of caloric intake and thus to reduction of the metabolic

TABLE III—CONCENTRATION (GM.) PER 1000 CC. OF URINE OF PATIENTS ON "NORMAL" DIET AND ON RICE DIET

	Normal Diet	*Rice Diet (after 2 months)*
Urea N	12	1.1
Chloride	6	0.1
Sodium	4	0.01
Potassium	2	3.0
Sodium/Potassium Ratio	2	0.003

rate. According to Page,[13] the effects obtained were due not to salt restriction, but to rest in bed, and the "psychotherapy of constant attention."

With the rigid restriction of sodium and chloride in the rice diet, the sodium and chloride excretion in the urine decreases to minimal amounts. In the urine of patients who have followed the rice diet for one month or longer, the average chloride concentration is about 100 mg., the sodium concentration about 10 mg., the potassium concentration about 3 Gms. per liter, i.e., the potassium concentration is slightly higher than that in the urine of patients on an ordinary diet, the chloride concentration is decreased to about 1/60, the sodium concentration to about 1/400. The sodium-potassium ratio, which in the urine of patients on an ordinary diet is about 2, decreases on the rice diet to 0.003 (Table III).

Grollman and Harrison repeated some experiments with the rice diet, using rats with experimental hypertension; they confirmed our finding, that the rice diet leads to marked blood pressure reduction.[14] Since the hypotensive effect was not obtained when the strict rice diet was changed by the addition of NaCl (not of KCl), this hypotensive effect was ascribed by the authors merely to sodium restriction. Unfortunately, no sodium, potassium, or chloride determinations in blood or urine were made.

No matter which single factor in the rice diet is of greatest importance in compensating the various manifestations of renal metabolic or excretory dysfunction, it remains true that in 203 of 322 patients,

TABLE IV

B 50182

White married man. Born 1902. "Always healthy until 1939." Blood pressure checked at two year intervals since 1927. B. P. known to be normal in 1936.

1939 Blood pressure elevated. Treated with Barbiturates.

March 1940 NEW YORK HOSPITAL B.P. 200-165/135-105.
Retrograde pyelograms: "Normal."
"Hypertensive vascular disease."

January 1941 PRESBYTERIAN HOSPITAL, NEUROLOGICAL INSTITUTE
"Hypertensive cardiovascular disease." B. P. 200/140.

February 1941 ROCKEFELLER HOSPITAL B. P. 200/140.
Variations: 196-174/140-120.
"Hypertensive vascular disease; arterial hypertension."
Daily injections of Tyrosinase intravenously for 23 days: Slight decrease in B. P.
Daily injections of Tyrosinase subcutaneously for 13 days: Decrease in B. P. to 150/100.
After one week, B. P. at previous level.
November 1941 B. P. 200/140.
During Tyrosinase treatment: B. P. 164/110.
Because of severe shock-like reaction, Tyrosinase therapy discontinued.

MASSACHUSETTS GENERAL HOSPITAL (Dr. Smithwick):
Lumbodorsal sympathectomy (Dec. 1941-Jan. 1942).

	BLOOD PRESSURE DATA			EKG
	Admission	*Lying*	*Standing*	
Dec. 1941 Before sympathectomy	172/135	180/134	186/145	12-18-41 T_1 upright
Mar. 1944, 26 mos. after sympathectomy	204/144	196/140	150/123	12-29-43 T_1 upright

Beginning 1945 Therapeutical trial with Testosterone: *"Blood pressure higher."*
March 31, 1945: DUKE HOSPITAL Admission 220/132.
(All B. P. readings taken while lying.)
March 31 - April 19, 1945: Average of 20 days in hospital on 1500 cal. reduction diet:
B. P. 197/129.
PSP (total excretion in 2 hours): 62%.
Urea clearance: 125%.
T_1 diphasic. Transverse diameter of heart 14.8 cm.

April 20, 1945: Rice diet started.
Averages:

May 15-21, 1945	129/94	June 1, 1945 full time job resumed.
July 1945	125/90	
August 1945	120/87	
September 1945	126/88	
October 1945	129/87	
November 1945	128/89	
January 8-14, 1946	128/91	T_1 upright. Transverse diameter of heart 13.9 cm.

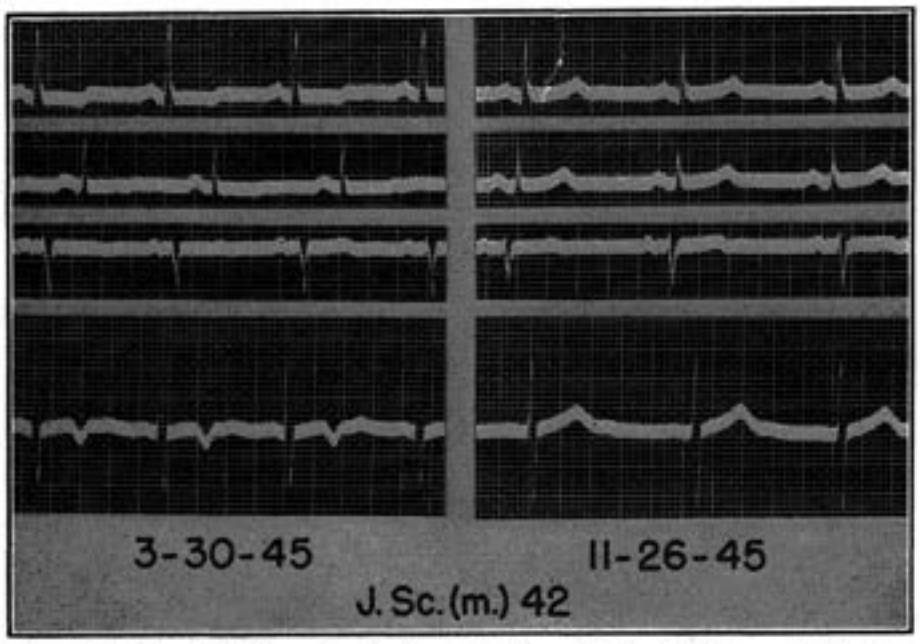

Fig. 1. J.S. (m. 42) "Hypertensive Vascular Disease." Rice diet since 4-20-45. No digitalis. Diphasic T 1 has become upright.

on most of whom other forms of therapy had previously been tried, the rice diet led to objective improvement.

Of 100 patients with primary kidney disease, 65 per cent showed improvement on the rice diet. Of 222 patients where a diagnosis of hypertensive vascular disease was made, 62 per cent improved.

Those who question the value of diet in the treatment of hypertensive vascular disease say that in those patients who responded to the diet our diagnosis was probably incorrect. I think that in most cases the differential diagnosis presents no difficulties. Table IV shows the summary of a typical history.

It would not be right to use such a case as an argument against sympathectomy. I have seen marked blood pressure reduction following sympathectomy, in patients with severe hypertension, and I have seen patients whose blood pressure was not improved. But I do think that the sequence of surgical treatment and dietary treatment should be reversed since the treatment with the rice diet, if it proves to be ineffective, can simply be discontinued.

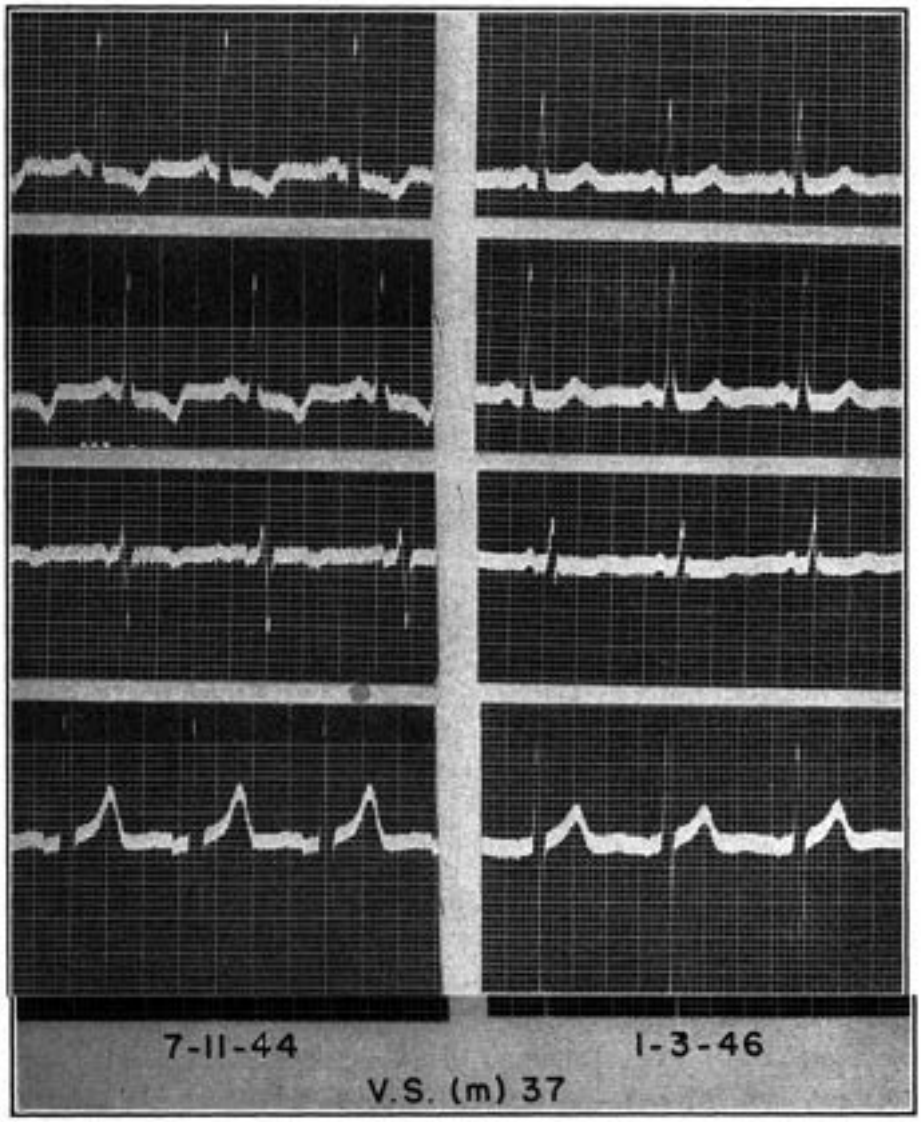

Fig. 2. V.S. (m. 37) "Hypertensive Vascular Disease." Advanced retinopathy. Rice diet since 8-16-44. No digitalis. Change in electrical axis. Inverted T 1 has become upright.

In the patient just mentioned, in spite of the sympathectomy, the electrocardiogram began to show myocardial involvement. T 1 which in December 1941 and December 1943 was upright, had become diphasic by April 1945. With the rice diet, however, the diphasic T 1 reverted to normal (Fig. 1).

We have studied the electrocardiographic changes in 100 patients

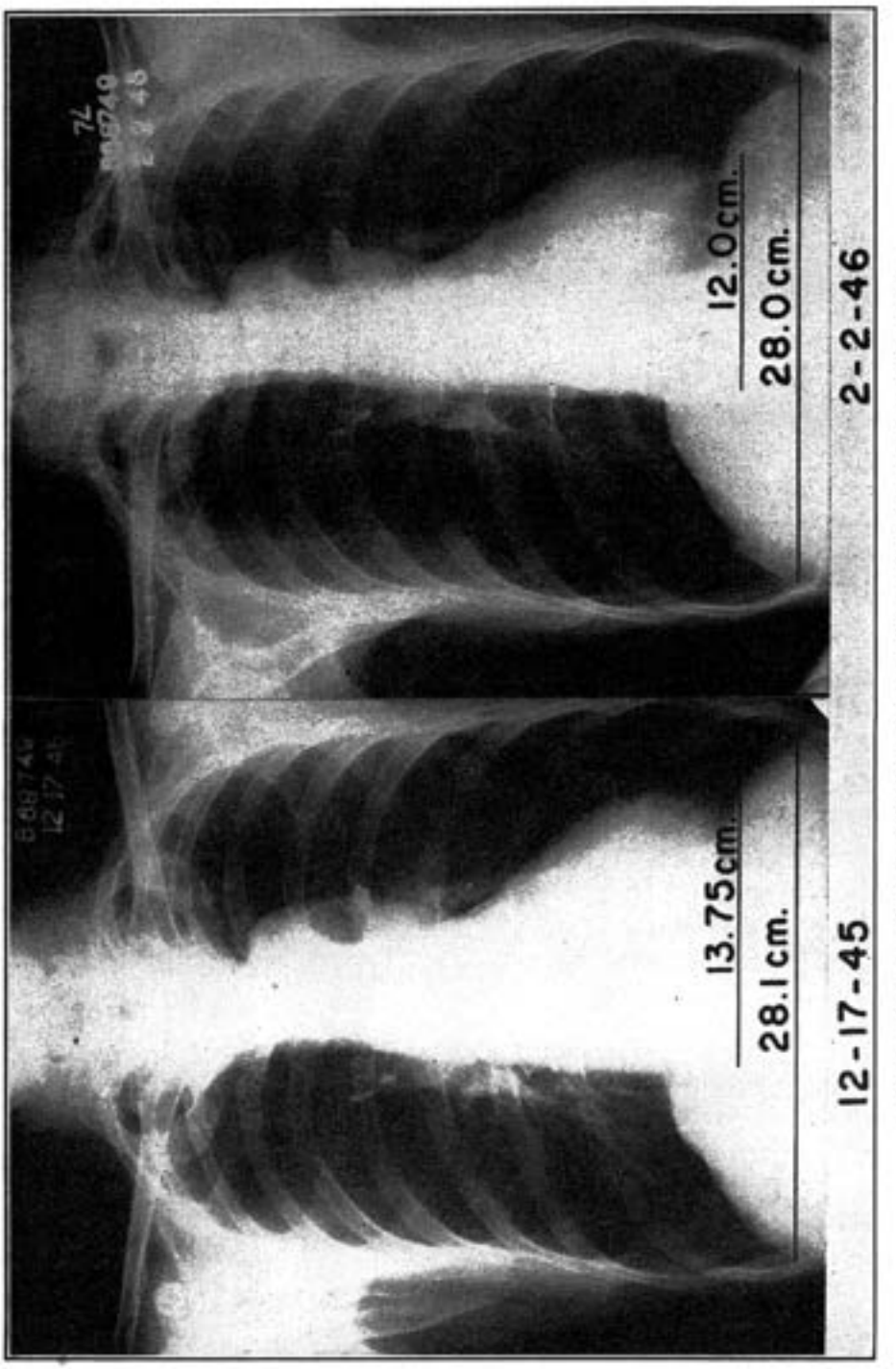

Fig. 3. McD. (m. 62) "Hypertensive Vascular Disease." Rice diet since 1-6-46. No digitalis. Reduction of heart size with change in transverse diameter of 14 per cent.

with hypertensive vascular disease, who have followed the rice diet for two months or longer. In 31 of these patients, the T 1 waves were completely inverted before treatment. In 11 of these 31 patients, T 1 became normally upright with the diet (Fig. 2). In no patient did the reverse occur. The shortest time in which a completely inverted T 1 became upright was two months, the average was six months.

In 77 of 87 patients with hypertensive vascular disease, the heart became smaller in size (Fig. 3). The average change in the transverse diameter was 10.1 per cent. The average chest diameter decreased by less than 0.7 per cent.

In 10 of the 87 patients the heart became larger. In these the transverse diameter of the heart showed an average increase of 2.5 per cent. The average chest diameter increased by 0.54 per cent.

I am sometimes told that enlarged hearts in hypertensive vascular disease become smaller "spontaneously," that electrocardiograms became normal "spontaneously," and that papilledema, hemorrhages, and exudates in the retina disappear "spontaneously."

I have not been fortunate enough to see many of these "spontaneous" recoveries, but I have often seen blindness as a result of advancing vascular retinopathy and death from heart failure, myocardial infarction, renal insufficiency, or cerebral vascular accident in patients who were not willing to submit to any drastic form of treatment because they believed that their disease would clear up spontaneously or that at least it would not become worse.

I have shown you some electrocardiograms and chest films of patients with hypertensive vascular disease who were treated with the rice diet. I will close this talk by showing you eyeground photographs of a number of patients (Fig. 4). Forty-four patients with hypertensive vascular disease who had papilledema, hemorrhages or exudates, followed the rice diet for two months or longer. In all of them the retinopathy was arrested. In 20 of the 44 patients papilledema, hemorrhages, or exudates cleared up partially, in 20 completely.

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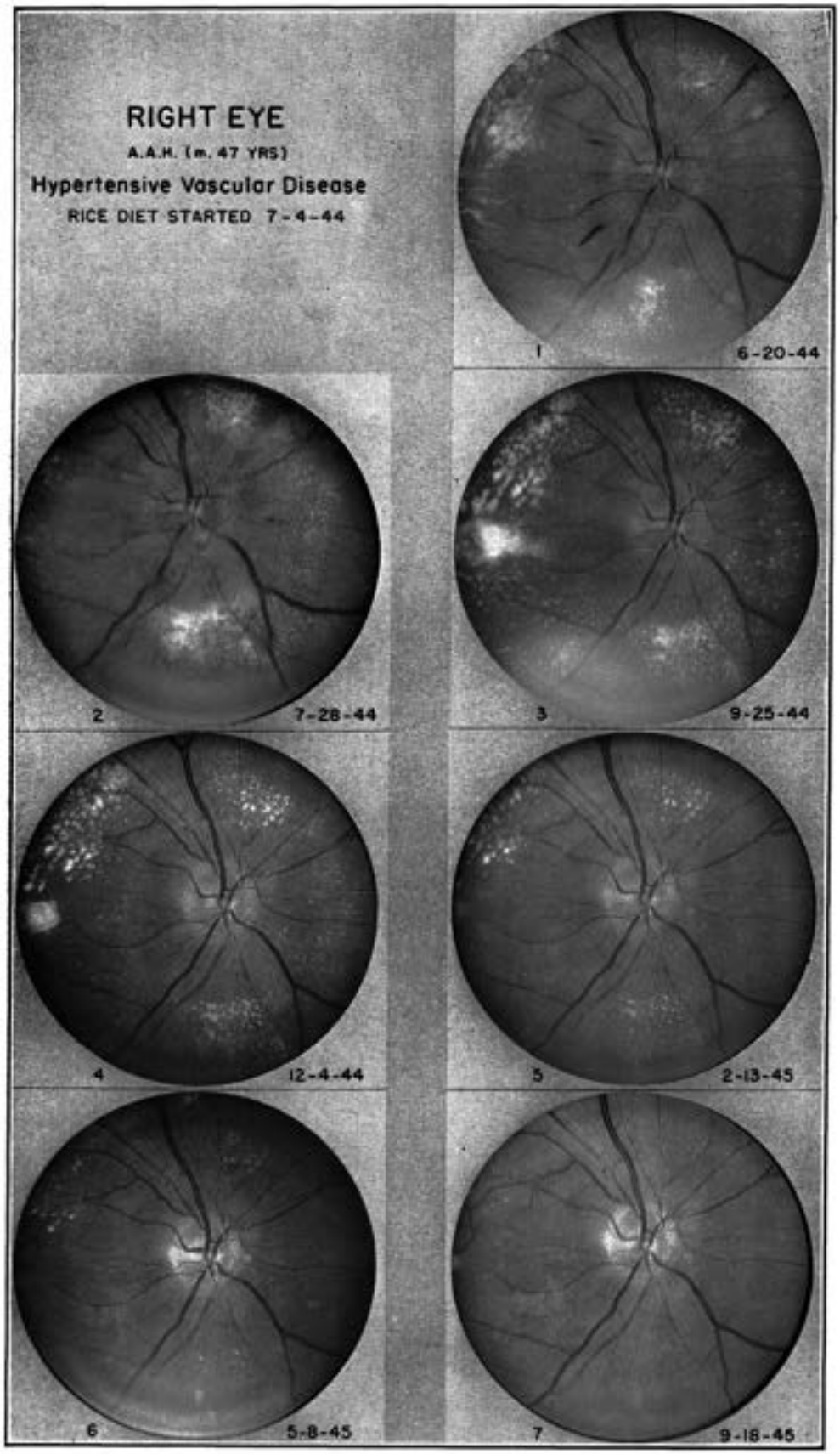

Fig. 4. A.A.H. (m. 47) "Hypertensive Vascular Disease." Rice diet since 7-4-44. *Right eye:* Disappearance of papilledema, hemorrhages, exudates.

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Treatment of Cardiac Failure with the Rice Diet

Treatment of Cardiac Failure With the Rice Diet

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TREATMENT OF CARDIAC FAILURE WITH THE RICE DIET

History of a Patient with Myocardial Aneurysm

In a large number of patients with kidney disease and hypertensive cardiovascular disease treated with the rice diet, the enlarged heart became smaller, the inverted T_1 became upright, and the signs and symptoms of cardiac failure disappeared[1]. The rice diet has also proved beneficial in patients with cardiac failure due to other causes (aortic and mitral valvular lesions, auricular fibrillation, left bundle branch block, and so forth).

The diet contains in 2000 calories not more than 200 mg. of chloride and 150 mg. of sodium. The daily fluid intake is, in most instances, not more than 800 cc. In patients who have no sodium chloride retention at the beginning of the rice diet and no "renal leakage" of sodium chloride, the urinary chloride concentration after two months on the diet is about 10 mg. per 100 cc., the sodium concentration about 1 mg. per 100 cc.; the sodium-potassium ratio in the urine is about .003 (compared with 2 on a "normal" diet).

The history of a patient with myocardial infarction followed by myocardial aneurysm is given as an example of the effect of the rice diet in cardiac failure.

Case Report

M. C. (B85425), a 45-year-old white county farm agent, was admitted to Duke Hospital August 5, 1946.

From the Department of Medicine, Duke University School of Medicine, Durham, N. C.

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History: The patient's father died at 54 of heart trouble; his mother died at 58 of a stroke. The patient's general health had always been very good except for increasing obesity. "Hypertension and overweight" (250 pounds) forced him "to take it easy since the spring of 1944."

In April, 1945, the patient suddenly developed fever and dizziness, and was sent to a hospital. He was unconscious for several hours and "out of his head for some time afterwards." The systolic blood pressure, which according to the patient had been around 200, fell to 140. There was no precordial pain at any time. The fever persisted for two weeks. At discharge, he was advised to rest and to take digitalis.

In June, 1945, the patient developed "fluid in his chest," dyspnea, and orthopnea. The systolic blood pressure was 150. In August, 1945, for two weeks, he was treated in another hospital with oxygen, a low-protein, salt-poor diet, and ammonium chloride. He felt better and was able to be up and about. In November, 1945, albumin (2 to 4 plus) and casts were found in the urine. Ascites and ankle edema began. From January, 1946 on, his condition grew steadily worse, the dyspnea causing the greatest discomfort. For five days in May, 1946, he felt mentally confused. About the same time, he developed a decubitus ulcer over the coccyx. Since June, he had had considerable soreness of the tongue.

He was under medical care during all this time, and between January and July, 1946, he spent one hundred and twenty-six days in three different hospitals. In addition to digi-

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talis for more than a year (1.7 grains of digitora daily since June 15, 1946) and a salt-poor diet, he was given salyrgan (seven injections since May 15, 1946), aminophyllin (twelve injections since May 15, 1946) and glucose intravenously, and ammonium chloride (3 to 6 Gm. daily from August 30, 1945, to May 15, 1946), theominal, coramine, barbital, and other sedatives.

In spite of this treatment, the cardiac failure increased. On July 29, a paracentesis was done and 2 gallons of fluid were removed, but a week later the abdomen was swollen as much as before and the edema had become worse.

Physical examination (August 5, 1946): The patient's weight was 187 pounds, height 5 feet, 10 inches, temperature 37 C. (98.6 F.), pulse 86, respiration 16. His blood pressure during the first week averaged 126 systolic, 88 diastolic. He was a well developed, poorly nourished, white man in considerable respiratory distress. There was generalized anasarca, and the skin was pale. Over the coccyx was a decubitus ulcer measuring approximately 1 inch in diameter. The eyes had a marked stare; the eyegrounds showed only slight tortuosity of the vessels. The tongue was very red, smooth, and sore, and along the lateral margins were several ulcers. There was engorgement of the neck veins, and rales were heard at both lung bases.

The heart was markedly enlarged, chiefly to the left. The maximum apical impulse was in the fifth interspace 14 cm. from the midsternal line. The sounds at the base were forceful, and the second pulmonic sound was

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louder than the second aortic. The first sound at the apex was weak and was followed by a loud, long, blowing systolic murmur. During the period of this murmur, a high-pitched murmur of shorter duration was heard.

The abdomen was large, round, distended, and filled with fluid. A non-tender liver edge was felt 6 cm. below the costal margin. There was marked sacral and scrotal edema and severe pitting edema of the ankles and legs.

Accessory findings: The chest film showed a slight increase in the markings at both lung bases. The heart appeared enlarged, especially to the left, and there was an area of increased density along the left border of the heart that was thought to be due to a myocardial aneurysm (Dr. J. G. Whildin). Further x-ray studies by fluoroscopy and films (Drs. G. Baylin and R. J. Reeves) confirmed the presence of a myocardial aneurysm of the postero-lateral wall of the left ventricle (fig. 1).

As is shown in table 1, the electrocardiogram showed right axis deviation; the venous pressure was increased, the renal reserve was diminished, and hypoproteinemia, hypocalcemia, and albuminuria were present.

Impression: Myocardial aneurysm following myocardial infarction. Advanced myocardial failure.

Course: On August 7, the patient was started on a 2600-calorie rice diet with 800 cc. of fruit juices, supplemented by vitamins A, B, C, and D, and ferrous sulfate (0.6 Gm. three times a day). All other medication was discontinued except digitalis (1 cat unit of digifolin daily), and oxygen inhalation.

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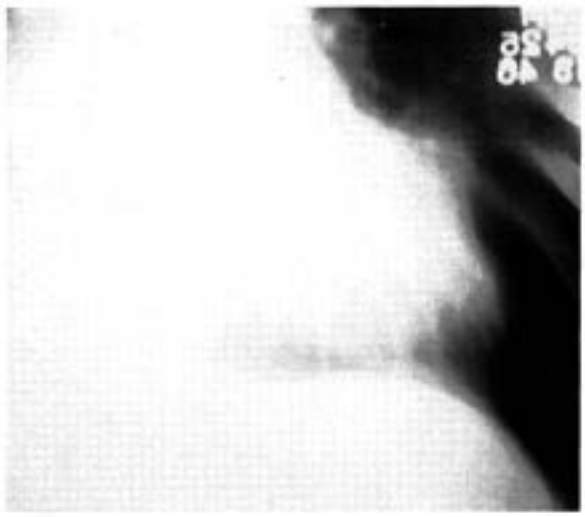

Fig. 1

A paracentesis was done on the ninth hospital day; 8000 cc. of fluid were removed. Four days later, the patient had a chill and fever. The temperature became normal twenty-four hours after treatment with penicillin was started.

The patient ate the diet well; it was increased to 2900 calories on August 30, and to 3100 calories on October 16.

By the end of the fifth week, his weight had decreased from 85 Kg. (187 pounds) to 67 Kg. (148 pounds). The urine volume was regularly greater than the fluid intake. Most of the edema had disappeared, and the liver was smaller in size. The decubitus ulcer had healed. The total plasma proteins had risen from 5.7 to 6.2 Gm., the plasma albumin from 2.9 to 3.4 Gm. per 100 cc.

Table 1

Accessory Findings

	Aug. 5-12, 1946	Oct. 29-Nov. 18, 1946
Blood pressure (mm. Hg.)	126/88	100/70
Hemoglobin (percent. of 15.5 Gm.)	86	85
Red blood cells	4,200,000	4,400,000
White blood cells	6,100	7,000
Nonprotein nitrogen (mg. per 100 cc. of blood)	32	23
Urea nitrogen (mg. per 100 cc. of blood)	12.9	7.9
Urea ratio (percent.)	40.3	34.3
Sugar (mg. per 100 cc. of blood)	87	
Total proteins (Gm. per 100 cc. of plasma)	5.7	7.1
Globulin (Gm. per 100 cc. of plasma)	2.9	3.4
Albumin (Gm. per 100 cc. of plasma)	2.8	3.7
Albumin-globulin ratio	1.04	0.91
Calcium (mg. per 100 cc. of serum)	7.2	8.5
Phosphorus (mg. per 100 cc. of serum)	3.9	4.2
Cholesterol (mg. per 100 cc. of serum)	160	140 (Sept. 5)
Chlorides (as mg. NaCl per 100 cc. of plasma)	616	584
Phenolsulfonphthalein (percent. excreted in 2 hours)	41	50
Urea clearance (percent. of normal)	9.9	
Mosenthal (concentration-dilution) test	1.019-1.024	
Urine albumin (Gm. per 1000 cc.)	0.85	0.06
Urine chlorides (as mg. NaCl per 100 cc.)	429	26
Total nitrogen excreted in urine in 24 hours (Gm.)		2.75

Basal metabolic rate (percent.)	+21	+5
Electrocardiogram		
T waves	T_1 isolectric, $T_{2,3}$ flat, T_4 inverted, $ST_{2,3}$ depressed.	$T_{1,2,3}$ more upright. ST_3 depressed. T_4 upright.
Angle of electrical axis (degrees)	+106	+95
Venous pressure (mm. of saline)	185	70 (Oct. 3)
Transverse diameter of heart (cm.)	19.75	17.15
Diameter of great vessels (cm.)	8.85	6.3
Weight (Kg.)	85	64.1
Liver enlargement (cm. below costal margin)	6	0
Circumference of abdomen, at umbilicus (cm.)	110	83
Circumference of each leg, 7 cm. above lateral malleolus (cm.)	25	20.5

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Although the venous pressure had not decreased (192 mm. of saline on September 7 compared with 185 mm. on admission), digifolin was discontinued on September 10. Some respiratory distress persisted for another two weeks, but gradually subsided.

Because the tongue had remained sore and some ulcers on the margin were still present, 25 mg. of folic acid by mouth were given daily from September 26 to November 7. After the middle of October, the tongue no longer caused any discomfort.

By the end of October, edema and liver enlargement had completely disappeared. The heart was smaller, and the venous pressure was normal. The urinary albumin had decreased from 0.85 to 0.07 Gm. per 1000 cc.; the total plasma proteins had risen to 7.1 Gm. per 100 cc. The patient felt well and was able to take short walks without dyspnea or fatigue.

The weight, which had dropped to 62 Kg. (137 pounds) on October 2, remained constant for one month and then gradually rose. By November 21, it was 64.5 Kg. (142 pounds).

The amounts of chloride and sodium excreted in the urine had decreased very slowly (tables 2 and 3). In the eighth week after the rice diet was begun, the chloride concentration was 66.5 mg., the sodium concentration 32 mg. per 100 cc. of urine. The sodium-potassium ratio in the urine was 0.18. In the fifteenth week, the chloride concentration was 15.2 mg., the sodium concentration 1.3 mg. per 100 cc. of urine. The sodium-potassium ratio in the urine was 0.006.

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Table 2

Urinary Chloride Concentration

Week of Rice Diet (Diet started Aug. 7, 1946)	*Mg. Chloride in 100 cc. of urine (averages)*
6th	81.7
7th	88.3
8th	66.5
9th	57.5
10th	35.2
11th	26.6
12th	18.7
13th	17.0
14th	18.8
15th	15.2
16th	15.7

Table 3

Concentrations of Sodium, Potassium, and Chloride in Blood, Serum, and Urine

	Eighth week of diet (Sept. 28, 1946)	*Fifteenth week of diet (Nov. 18, 1946)*
	milli-equivalents per liter	
Sodium:		
blood	84.3	81.7
serum	139.7	142.2
urine	13.9	0.57
Potassium:		
blood	46.2	50.0
serum	4.8	5.3
urine	45.0	57.2
Chloride:		
blood	84.0	79.3
serum	94.2	100.0
urine	14.0	4.1

The patient returned home on November 21. He was advised to continue the rice diet, to which one ounce of meat twice a week was added. Fluids were limited to 750 cc. per day.

Summary

The history of a patient with myocardial aneurysm following myocardial infarction is

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given. He was admitted to Duke Hospital in advanced cardiac failure with marked sodium chloride retention. For a period of seven months, four of which the patient spent in various hospitals, he had been treated with salt-"poor" diets, digitalis, ammonium chloride, theominal, aminophyllin, salyrgan, and a paracentesis. In spite of this treatment, the cardiac failure had become progressively worse and the patient had developed severe dyspnea, generalized anasarca, cardiac enlargement, liver enlargement, ascites, albuminuria, hypoproteinemia, hypocalcemia, and a decubitus ulcer. In five weeks of treatment with the rice diet, supplemented by vitamins and iron, the patient improved so much that digitalis, the only medication that had been continued, could be stopped. In nine more weeks, during which the patient was given no treatment except the rice diet, vitamins A, B, C, and D, folic acid, and iron, all signs and symptoms of cardiac failure disappeared.

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Treatment of Hypertensive Vascular Disease with Rice Diet

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Sulfate and Phosphate Excretion in Urine of Patients on Rice Diet

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SULFATE AND PHOSPHATE EXCRETION IN URINE OF PATIENTS ON RICE DIET*

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THE course of renal and hypertensive vascular diseases has been modified by the use of a diet consisting of rice, fruit, and sugar.[5,6,7,8] Ninety-five per cent of the caloric intake is furnished by carbohydrate; in 2000 calories there are about 20 gm. of protein and not more than 5 gm. of fat, 0.2 gm. of chloride, and 0.15 gm. of sodium. On this regime the nitrogen equilibrium is maintained, and the patient can be made to gain weight if the caloric intake is raised.

Quantitative data on all aspects of metabolism are needed to determine the factors responsible for the favorable effect of the rice diet on the course of hypertensive and renal diseases. This paper summarizes the changes in urinary phosphate and sulfate excretion which occur on the rice diet.

Procedure. The sulfate and phosphate were measured in each of 3 successive 24 hour urine collections. The sulfates were determined by the benzidine method of Rosenheimer and Drummond as modified by Hoffman and Osgood.[4] The inorganic phosphate P was determined with a photo-electric colorimeter according to the phosphomolybdate method of Fiske and SubbaRow.[2]

The studies were carried out on patients with hypertensive vascular disease without evidence of renal failure. The diet of many of the patients had been restricted before the rice diet was started. The daily urinary excretion of total sulfate and of inorganic sulfate was determined in 14 patients (10 men and 4 women) who had followed the rice diet for periods of 30 to 46 days (average 36 days). The urinary inorganic phosphate was measured in 17 patients (13 men and 4 women) who had followed the diet for 14 to 59 days (average 34 days).

The results are summarized in Table 1.

The inorganic sulfate excretion in all 14 patients showed a decrease ranging from 68 to 92% (average 82%). The ethereal sulfate excretion increased in 2 patients and fell in 12. For the 14 patients the average decrease was 56%. The total sulfate excretion in all 14 patients showed a decrease ranging from 58 to 91% (average 79%). The ratios of inorganic sulfate to total sulfate ranged from 0.56 to 0.90, average, 0.77, before the diet, and from 0.41 to 0.81, average 0.65, after the diet.

The inorganic phosphate excretion in all 17 patients fell from 40 to 75%, with an average fall of 62%.

In Table 2, the lowest amounts of

TABLE 1.—EFFECT OF RICE DIET ON SULFATE AND INORGANIC PHOSPHATE EXCRETION IN URINE OF PATIENTS WITH HYPERTENSIVE VASCULAR DISEASE

	Range		Average	
	Before	After Rice Diet	Before	After Rice Diet
Total Sulfate (mg S in 24 hrs.)	761–471	254–58	592	126
Inorganic Sulfate (mg S in 24 hrs.)	547–362	185–40	452	81
Ethereal Sulfate (mg S in 24 hrs.)	328– 52	115–15	140	45
Inorganic Phosphate (mg P in 24 hrs.)	1055–501	435–170	761	289

* This work was supported by a grant from the Life Insurance Medical Research Fund.

† Students in the Schools of Medicine of Duke University, Johns Hopkins University, and the University of North Carolina, respectively.

sulfate and phosphate in a single 24 hour urine collection in this group of patients are recorded and compared with the amounts excreted on an egg-milk diet, a starch-cream diet and in fasting.

Discussion. The data are of value for two reasons. First, they demonstrate that the kidney is called upon to excrete much less phosphate and sulfate when a patient is on the rice diet than when he is on a regular diet or while fasting. What this means in terms of renal work is not known. Observations are needed on patients with hypertensive disease on a rice diet with added phosphate and sulfate. Secondly, these data serve as a rough check on the data previously reported on nitrogen equilibrium.[6] The patients had a daily protein intake of 20-25 gm. But they could not have been breaking down appreciable amounts of body protein because of the low excretion of nitrogen, phosphates, and sulfates as compared to that of fasting individuals.

Summary. The average amount of inorganic sulfate excreted in the urine of 14 patients on the rice diet was about 90% lower than that of persons on a normal diet; the average amount of ethereal sulfate was about 45% lower, that of total sulfate was about 85% lower. The average amount of inorganic phosphate was about 70% lower than that of persons on a normal diet.

TABLE 2.—MAXIMAL-MINIMAL URINARY SULFATE AND PHOSPHATE EXCRETION ON EGG-MILK DIET, STARCH-CREAM DIET, FAST AND RICE DIET

	Egg-Milk Diet* (120 gm. of protein)	Starch-Cream Diet* (6 gm. of protein)	Fasting§ (10th day)	Rice Diet (20-25 gm. of protein)
	Highest Values	Lowest Values		Lowest Values
Total Sulfate (mg S in 24 hrs.)	1315†	194†	579†	50
Inorganic Sulfate (mg S in 24 hrs.)	1252	168		25
Ethereal Sulfate (mg S in 24 hrs.)	76	24		2
Inorganic Phosphate (mg P in 24 hrs.)	1613‡	276‡	709‡	117

* According to Folin[3]
§ According to Benedict[1]
† Calculated as 90% of Total Sulfur.
‡ Calculated as 90% of Total Phosphorus

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Rice Diet in Malignant Hypertension: A Case History

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Rice Diet in Malignant Hypertension

A Case History*

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THE HISTORY of a patient with hypertensive vascular disease is given. The hypertension was picked up during a routine examination and remained benign for five years thereafter. A malignant phase began without apparent cause. The picture was complicated by the fact that the patient also had bronchial asthma and intestinal disturbances.

During the benign phase the treatment consisted of sedatives, weight reduction and restriction of smoking. After the malignant phase had begun, the patient was advised to have a sympathectomy immediately. He decided to postpone the operation and to make a therapeutic trial of the rice diet first. This probably was the correct form of treatment in his case, but the following report will show some of the difficulties † involved in this diet, and also that serious dangers may result if these difficulties are not dealt with correctly.

The patient (Duke unit number C-20124), a 45-year-old business man from New York, entered the clinic October 27, 1947, with the chief complaints of shortness of breath and visual impairment.

The father died, age 64, of coronary occlusion. The mother died, age 52, of diabetes mellitus. One brother has had "rheumatism" since the age of 20.

The patient had been married for five years. The wife was in good health. There had been no pregnancies.

The past history was uneventful: the patient was always healthy except for measles in childhood. He had a tonsillectomy and adenoidectomy at 6 and again at 37 when the uvula was clipped. A nasal polyp was removed in January 1947. There were no other operations nor injuries.

The review of systems was negative, except for some acne in adolescence and rhinitis with sneezing and watery discharge "when exposed to draught." The weight averaged 167 lb.; the maximum was 174 lb.

Before March, 1947, the patient had smoked 50 cigarettes a day. He has not smoked since. Years ago he drank alcohol in moderate amounts. For the past five years, however, he has taken alcohol only infrequently. On three occasions when he drank some whiskey he had sneezing, watery nasal discharge and coughing.

The blood pressure had been checked occasionally; it was always satisfactory until 1941. In 1930, it was 130/80, in 1932 110/85, in 1937 115/85 and in 1941 145/80. The present illness began in 1942 (Fig. 1). The patient, then 40 years of age, learned during a routine checkup by his physician that his blood pressure was elevated. He was advised to lose weight and to cut down on smoking. A few weeks later he was told the blood pressure was normal. In 1943, he donated blood to the Red Cross. Six months later when he tried to donate blood again "he was turned down because his blood pressure was too high." He consulted another physician and was put on a weight reduction program and given a sedative. On December 15, 1946, he consulted a third physician because of an "upper respiratory infection." He had been having periods of orthopnea apparently related to coughing. The blood pressure was 170/108. A diagnosis of essential hypertension was made. Nasal polyps were found and, one month later, removed. Following the polypectomy the patient continued to have upper respiratory infections which never subsided completely. He also had "grippe" during this time. Since then, he has had marked paroxysms of coughing which have persisted. Otherwise he felt very well, worked regu-

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† Dr. Henry Schroeder, George Washington University, St. Louis, reported in the American Journal of Medicine (April 1948) that the rice diet had caused him to lose one of the six patients on whom he tried it. He repeats what we emphasized in previous papers[1-3] that the rice diet should only be given "under conditions in which the patient can be carefully watched and plasma chloride levels followed." But, unfortunately, in his case, Dr. Schroeder had not determined the plasma chloride level, nor the CO_2 combining power, nor the sodium concentration in the serum, nor the sodium and chloride concentrations in the urine until "the patient became drowsy, disoriented and developed nitrogen retention and diminished urine volume." (These determinations had not been made before the start of the rice diet either.) When shortly before the death of the patient they finally were made, the chloride was 69 mEq. and the sodium 118.4 mEq. per liter of serum.

larly and played golf. The asthmatic attacks were treated with cough medicines containing codeine and ammonium chloride. He saw his doctor every few weeks. His blood pressure readings were: May 23, 1947, 200/130; July 3, 1947, 175/125; September 22, 1947, 180/140.

Since the end of September, 1947, the patient has had severe coughing spells and dyspnea almost every morning and on walking short distances. In the early part of October he had an excruciating headache last-

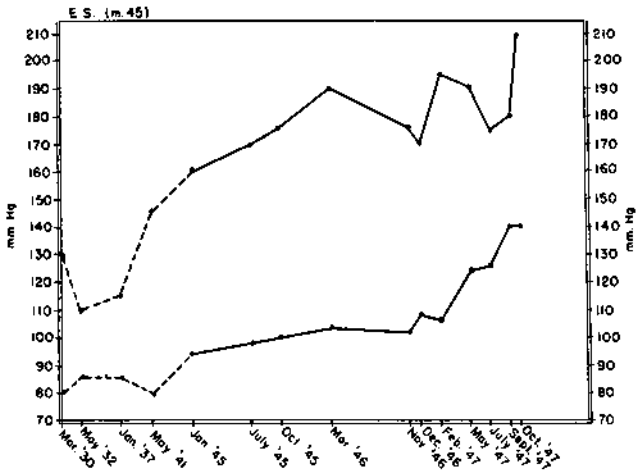

FIG. 1. Blood pressure (systolic and diastolic), 1930 to October, 1947.

sputum was investigated and found to be unremarkable and the lungs showed only slight apical scarring on x-ray." The day before the sympathectomy was to take place, the patient decided to postpone the operation and to make a therapeutic trial with the rice diet.

When he entered the clinic of Duke Hospital on October 27, he appeared ill, dyspneic and orthopneic. He was five feet eight inches tall; his weight was 150 lb. The blood pressure was 210/140. The skin was

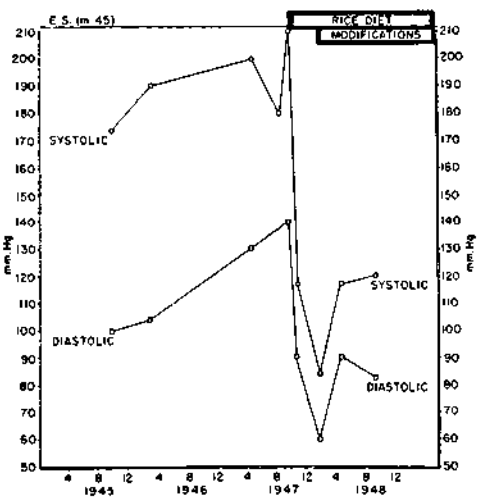

FIG. 2. Blood pressure before and after treatment.

ing more than 12 hours. On the same day he noticed blurring of vision. Because his vision gradually became worse in the next few days he consulted an ophthalmologist, who found a severe hypertensive retinopathy with papilledema, hemorrhages and exudates. The patient was sent to a consultant internist, who found the blood pressure to be 202/144 and who told him that immediate sympathectomy would be his only chance and referred him to a surgeon. From October 19 to 26 the patient was on the surgical service in the New York Hospital. Here his physicians reported that "the examination in the hospital revealed a blood pressure averaging 210–190/150–130. The heart was within normal limits in size and configuration. The electrocardiogram showed depression of the RT segments, diphasic QRS complexes, absence of left axis deviation, which in the presence of hypertension suggests a counterbalancing pulmonary lesion. The eyegrounds showed hemorrhages and papilledema. Intravenous pyelogram was normal; urine was free of albumin and casts. Blood counts were normal. Blood urea nitrogen was 14 mg. Urine dilution was 1,002 and concentration 1,016. Total PSP output was 63 per cent. Because of his chronic cough the clear, but there were a number of small (acne) scars over the back. There was no edema. Skeletal: there was an increase in lumbar lordosis and some kyphosis of the dorsal spine. There was no glandular enlargement. Eyes: pupils were round, regular and equal and reacted well to light and on accommodation. Extraocular movements were normal. There was bilateral arcus senilis. Both fundi (Fig. 6) showed marked papilledema and peripapillary edema. The veins were engorged and tortuous. Arteriovenous compression was marked. In both eyes there were fresh hemorrhages and cottony exudates and streaks of hard exudate between disc and macula pointing to the macula. Ears: drums and canals were normal. Nose: mucous membranes were pale. There was a small polyp posteriorly on the left with discharge around it. Nasopharynx was clean with normal appearing eustachian cushions. Sinuses were dark to transillumination. The teeth were in good repair. The tongue showed no atrophy or redness. The tonsils were out. Thorax: the chest showed limitation of lateral expansion. The circumference at the fourth costal cartilage was 90 cm. on expiration and 93 cm. on inspiration. The diaphragms were low and

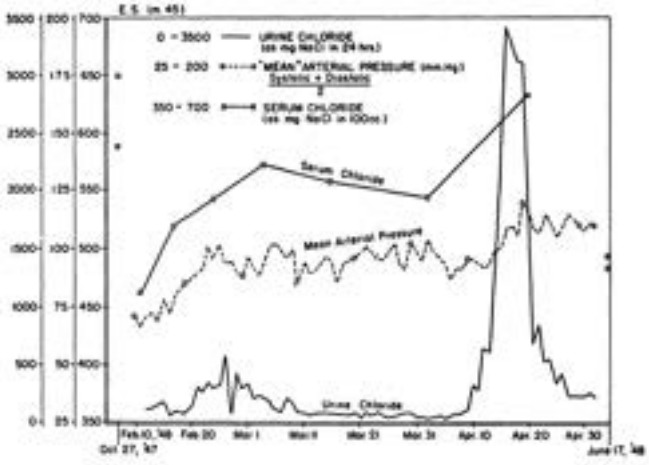

FIG. 3. Urine chloride, serum chloride and blood pressure.

descended 3.5 cm. Expiration was prolonged, and throughout both lung fields anteriorly and posteriorly there were numerous coarse wheezes and groans and musical râles after coughing. The heart apex was 1.5 cm. beyond the midclavicular line in the fifth interspace. The rate was about 90. The rhythm was regular. The sounds were very loud; there was no murmur. Abdomen: the liver was felt slightly below the costal margin. The spleen was not palpable. There was no tenderness in either kidney region. External hemorrhoids were present. The neurologic findings were normal.

X-ray: The heart size was within normal limits (Fig. 5); the lungs were clear; the sinuses showed generalized infection except for the left antrum; the kidneys appeared to be of normal size; the liver was rather low. The electrocardiogram showed normal sinus rhythm, no axis deviation. Rate was 100. P-R interval 0.16 second. QRS interval 0.10 second. Slurred QRS 1, 2, 3. Small Q 2, 3 present. T 1 low upright. T 2, 3 upright. Precordial lead normal.

The hemoglobin was 13.5 Gm. The white blood cell count was 12,900. The differential count showed: PMN segmented 54, eosinophils 18, basophils 1, monocytes 8, large lymphocytes 4, small lymphocytes 15. Serologic tests for syphilis were negative. The NPN was 30 mg. per 100 cc. of blood; the urea nitrogen 9.0 mg., the urea ratio was 30. The sugar was 101 mg. per 100 cc. of blood. The chloride was 100.5 mEq. per liter of serum. The cholesterol was 230 mg. per 100 cc. of serum. The total proteins were 8.3 Gm. per 100 cc. of plasma. The urine had an acid reaction. The specific gravity was 1.022. There was no sugar present. There was 0.2 Gm. of protein per liter. There were occasional white cells in the sediment. The PSP test showed a total excretion of 48 per cent in two hours.

The impression was that the patient had bronchial asthma and sinusitis and malignant hypertension with severe vascular retinopathy and diminished renal reserve.

In view of the severe retinopathy the rice diet was started immediately. The patient took the diet very well and did not complain about its unpleasant taste. There was no pain in head or eyes but the asthma caused a great deal of discomfort.

The patient was started on breathing exercises and received the following medication: October 27 through November 1, 0.2 Gm. of sodium amytal every night; November 3 through November 15, 100,000 units of penicillin daily; November 4 through November 27, 1–3 (average 2) "asthma capsules" daily, each containing 100 mg. of aminophyllin, 16 mg. of ephedrin and 16 mg. of phenobarbital. During December and January the asthma became very mild.

The blood pressure decreased rapidly (Fig. 2). After one week of the rice diet it was 160/118, after two weeks 130/99, after three weeks 118/90, after six weeks 118/88, and after nine weeks 100/74. In these nine weeks the patient had lost nine pounds. He was feeling all right. The retinopathy had improved.

The patient tolerated the rice well, but developed a diarrhea probably from the fruit.

On January 7 the blood pressure was 102/78. The hemoglobin was 14.9 Gm. The white blood cell count was 8,000. The NPN was 56 mg. per 100 cc. of blood; the urea nitrogen 40.2 mg.; the urea ratio was 72. The sugar was 100 mg. per 100 cc. of blood. The chloride was 103.9 mEq. per liter of serum. The cholesterol was 205 mg. per 100 cc. of serum. The total proteins were 7.9 Gm. per 100 cc. of plasma.

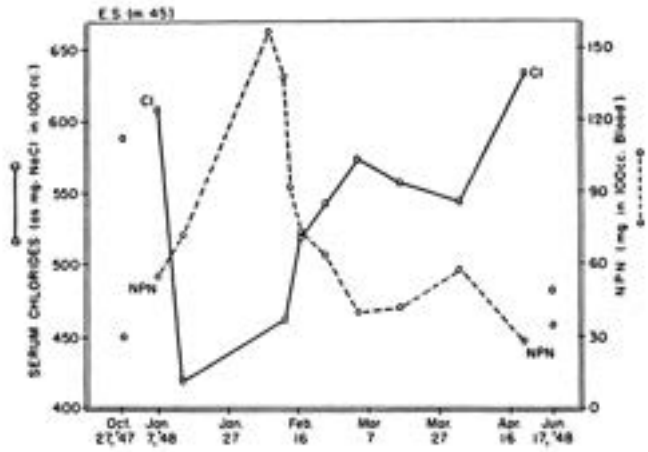

FIG. 4. Serum chlorides and blood NPN, October 1947 to June 1948.

The urine had an alkaline reaction. The specific gravity was 1.011. There was no sugar present. There was 0.14 Gm. of protein per liter. The microscopic examination was negative except for occasional white cells.

The diarrhea became more severe and the patient felt weak. On January 14 the blood pressure was 102/80; the NPN was 72 mg. per 100 cc. of blood; the chloride was 71.1 mEq. per liter of serum. (Because of the considerable change in the blood chemistry, the determinations were checked.) The patient was urged to remain in town, but because of an important business appointment he had to return home.

From January 14 the patient received each day in addition to the basic rice diet a small piece of tomato; from January 17 two small tomatoes and one stalk of celery; on January 28 a small potato was added.

A few days later, because the diarrhea persisted, the fruit juices were replaced by tea, and bismuth subnitrate was given. This apparently stopped the diarrhea, but the patient felt so weak that he had to stay in bed most of the day. The weakness became extreme when the patient stood up and he was finally unable to stand even long enough to dress himself. A generalized pruritus developed. The blood pressure during this time was about 85/65 (lying).

On February 10, the patient returned to Durham. The blood pressure was 84/62 while lying and 60/30 while standing. The temperature was 37° C. The pulse on admission was 120 (one day later it was 88). The weight was 133 lb. (an 8 lb. weight loss in the past six weeks). The hemoglobin was 12 Gm. The white blood cell count was 9,500. The NPN was 156 mg. per 100 cc. of blood, the urea nitrogen 130.3 mg.; the urea ratio was 83.5 The chloride was 79.3 mEq. per 1,000 cc. of serum. The cholesterol was 240 mg. per 100 cc. of serum. The calcium was 9.8 mg. and the phosphorus 5.6 mg. per 100 cc. of serum. The total proteins were 7.1 Gm. per 100 cc. of plasma. The A/G ratio was 1.4. The CO_2 combining power was 55 volumes per 100 cc. of plasma.

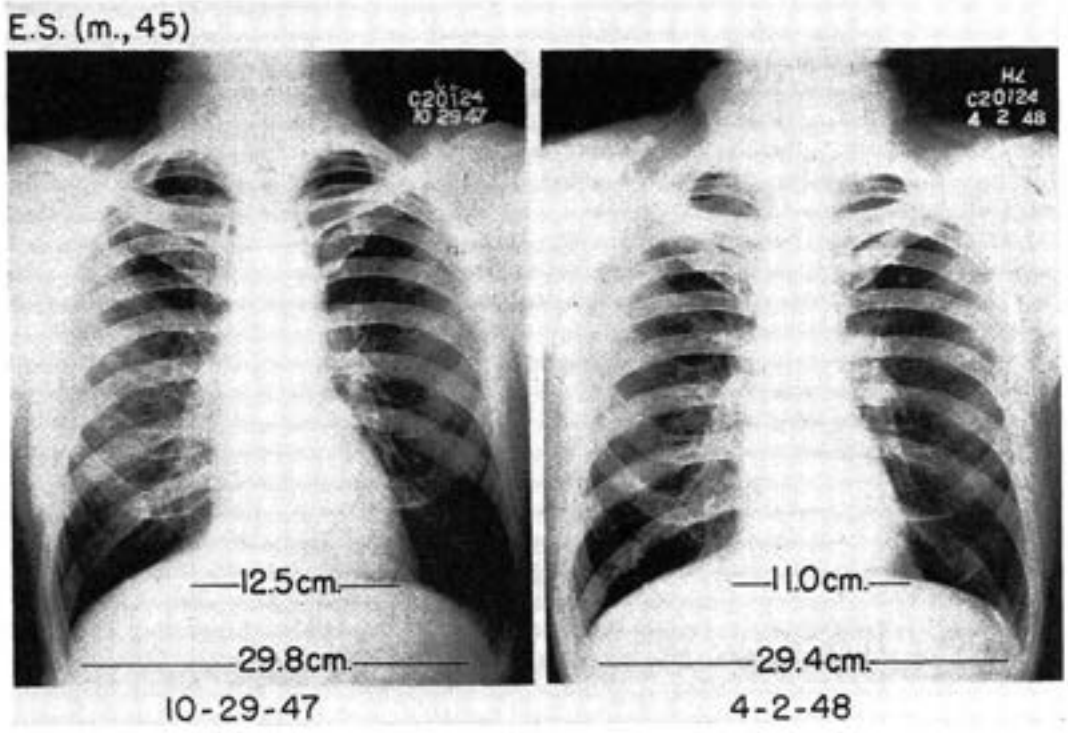

FIG. 5. Chest films.

The patient was given a diet consisting of rice, sugar and tea, supplemented during the first week by nine slices of toast (ordinary bread) daily; during the second week the diet was supplemented by six slices of toast, four ounces of chicken, two tomatoes and two potatoes daily. During the third week the same diet was continued with the exception that the toast was no longer given.

On February 11, the patient received 1 mg. of desoxycorticosterone, and on February 12, 2 mg. of desoxycorticosterone without appreciable change in blood

pressure. A zinc oxide and calamine liniment was used for the pruritus and a total of 500 mg. of Benadryl was given from February 10 to 12.

The patient rapidly began to feel better and after about 8 to 10 days he was able to be up and around without difficulty. It took him about three weeks to recover from this episode completely. The blood pressure (lying) which had averaged 84/60 during the week of February 10 to 16 averaged in the following weeks 104/74, 110/77, 111/80. The serum chlorides rose, and the NPN decreased.

In the beginning of March the patient again suffered from severe bronchial asthma. The amount of sputum which he brought up each day was about 250 cc. The attacks were relieved by breathing exercises and by two to four of the "asthma capsules" daily. The amount of sputum, however, remained between 130 and 290 cc. each day until the end of April. In

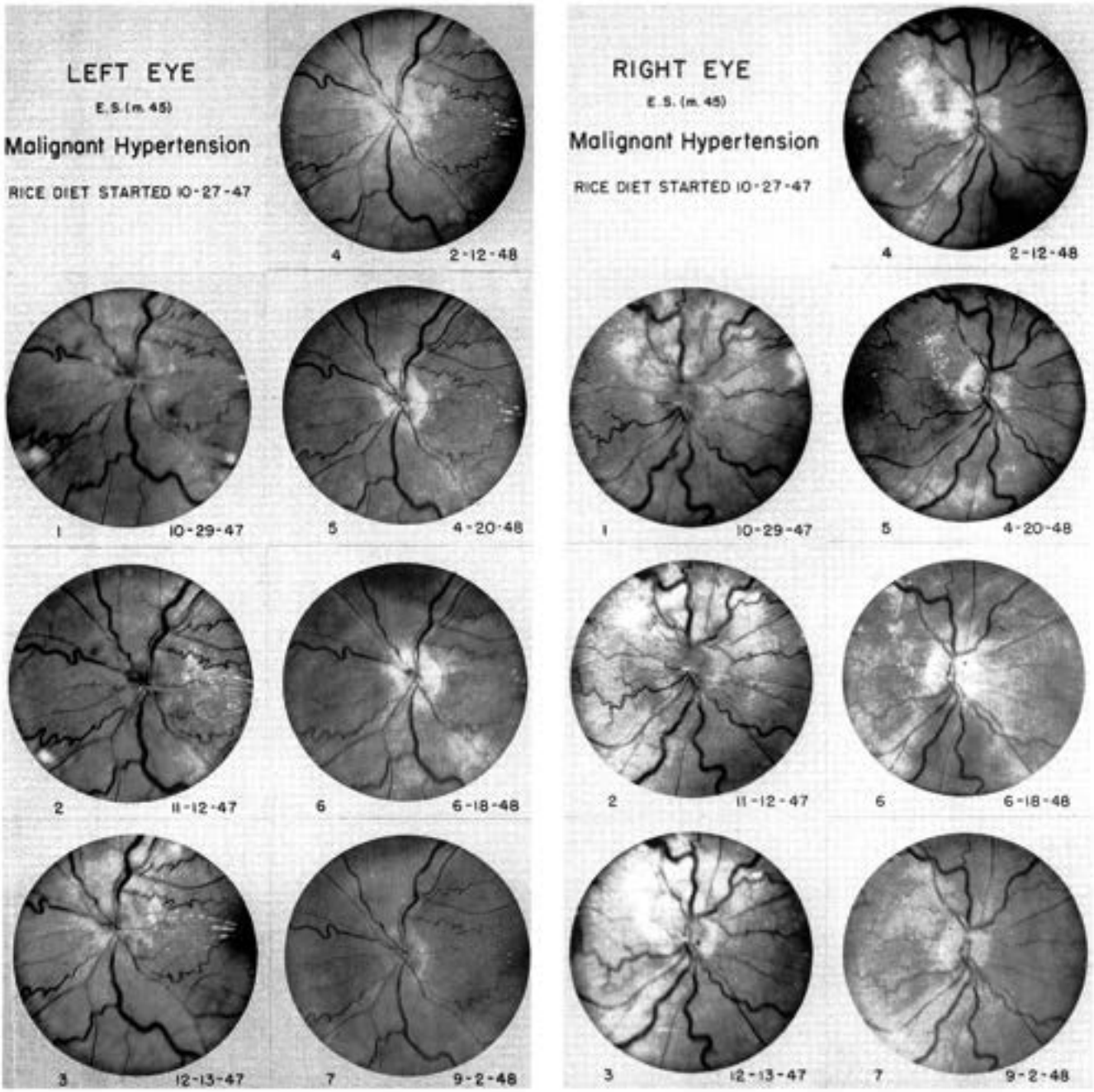

FIG. 6. Eyeground photographs, October, 1947, to September, 1948.

the differential white count there was 8 and 6 per cent of eosinophils on March 4 and 16. (There had been 18 per cent when the patient was first seen, October 29, and 13 per cent on December 19. On April 20 there was 25 per cent.) Skin tests did not show any positive allergy reaction.

The excretion of sputum with its high concentration of chloride probably affected the chloride concentration of the serum and the urinary chloride excretion considerably. The concentration of the sputum chloride determined on 18 consecutive days was 63.2–102.6 mEq., average 79.7 mEq. per 1,000 cc.

The urine chloride corresponds to the chloride intake, unless there is an extraordinary chloride loss "to the outside or the inside." The chloride concentration in the sputum does not vary with the urine chloride and does not correspond to the chloride intake (Table 1).

A patient who for six weeks or more has been following the strict rice diet without any additions usually excretes 1.7–3.4 mEq. of chloride per 1,000 cc. of urine; about 2.6 mEq. per day.

TABLE 1.—*Independence of Sputum Chloride Excretion of Chloride Intake and of Urinary Chloride Excretion*

DATE (1948)	ADDITIONS TO BASIC RICE DIET (per day)				URINE CHLORIDES (mEq. per 1,000 cc.)	URINE CHLORIDES (mEq. per 24 hrs.)	SPUTUM CHLORIDES (mEq. per 1,000 cc.)	SPUTUM CHLORIDES (mEq. per 24 hrs.)
	potatoes (oz.)	vegetables (oz.)	toast (slices)	NaCl (Gm.)				
April 7	8	10	5	3	0.6	1.0		
8	8	10	5	3	0.7	1.2		
9	8	10	5	3	1.4	1.8		
10	8	10	5	3	3.1	5.3	97.1	15.5
11	8	10	5	3	4.1	5.1	75.1	13.5
12	8	10	5	3	7.9	11.1	82.0	
13	8	10	5	3	7.2	10.6	80.3	23.7
14	8	10	5	3	12.6	23.1	79.0	19.3
15	8	10	5	3	28.3	35.3	74.2	17.1
16	8	10	5	3	44.8	58.4	63.2	10.4
17	8	10	5	2	85.4+	53.0+	78.3	10.2
18	8	10	5	2	58.7	53.5	73.5	14.0
19	8	10	2	1	38.1	53.0	79.0	18.6
20	8	10			16.6	29.4	71.8	10.8
21	8	10			7.7	11.7	76.9	14.6
22	8	10			9.1	14.5	75.1	13.5
23	8	10			8.9	8.9	73.5	13.2
24	8	10			6.2	9.2	91.9	21.1
25	8	10			4.1	5.7	73.5	9.9
26	8	10			3.1	7.1	86.5	14.7
27	8	10			2.1	3.6	102.5	16.4

The urine chloride concentration of this patient fell below this level and remained so even when his diet was supplemented to contain more than three times as much chloride as the basic diet. The average figures for the chloride excretion in the urine during successive weeks on the diet are given in Table 2.

Table 3 and Figure 3 show serum and urine chloride concentrations together with the blood pressure values. It is evident that there is not a simple relationship between blood pressure and serum chloride level.

TABLE 2.—*Effect of Diet on Chloride Excretion in Urine*

WEEK OF DIET	ADDITIONS TO BASIC RICE DIET (per day)						URINE CHLORIDES (mEq. per 1,000 cc.)	URINE CHLORIDES (mEq. per 24 hrs.)
	potatoes (oz.)	vegetables (oz.)	legumes (oz.)	meat (oz.)	toast (slices)	NaCl (Gm.)		
1							28.5	
2							6.3	3.9
3							4.4	1.6
4							2.4	.9
5							1.7	.7
6							2.1	.9
7							4.6	3.0
8							1.4	.8
9							1.4	.7
10							1.4	.6
11							1.7	.8
12		1					1.2	.9
14		7					1.9	
16					9		1.2	1.9
17	8	6		4	6		3.2	3.4
18	8	6		4			5.1	5.8
19	8	6		4			2.1	3.1
20	8	6		4			1.4	1.6
21	8	6		4	2		1.0	1.1
22	8	6		4	5		.9	1.0
23	8	6		4	5		.7	.8
24 first half	8	10		4	5		.9	1.2
second half	8	10		4	5	3	5.9	8.0
25	8	10		4	5	2–3	55.4	43.7
26	8	10		4			5.8	8.7
27	8	10		4			1.4	3.2
28	8	10		4			1.2	2.2
29	8	10		4			1.2	2.8
30	8	10		4			1.5	3.1
31	8	10		4			1.7	3.7
32	8	10		4			1.4	2.7
33	8	10		4			1.9	4.3
34	8	10		4			2.4	2.6
35	8	10	2	4			1.2	2.4
36	8	10	2	4			1.2	2.7
37	8	10	2	4			1.4	1.5

TABLE 3.—*Relationship of Serum Chloride and Urine Chloride to Blood Pressure*

DATE	SERUM CHLORIDE (mEq. per 1,000 cc.)	BLOOD PRESSURE	URINE CHLORIDE (mEq. per 1,000 cc.)
Oct. 27, 1947	100.5	210/140	
Jan. 14, 1948	71.1	102/80	1.0
Feb. 10, 1948	79.3	84/62	1.7
Feb. 17, 1948	88.9	90/68	1.0
Feb. 24, 1948	93.0	108/82	4.8
Mar. 4, 1948	97.8	108/78	2.0
Mar. 16, 1948	95.0	108/80	1.0
April 2, 1948	93.0	122/84	0.5
April 20, 1948	108.0	136/92	16.6
June 17, 1948	82.7	114/80	4.1
Sept. 28, 1948	100.0	120/82	5.1

At the time when treatment with the rice diet was started, the blood pressure was 210/140, the serum chloride was 100.5 mEq. per liter. After five months of treatment the blood pressure was 108/78, the serum chloride 97.8 mEq. When after six months of treatment the sodium chloride intake was increased so much that the serum chloride went up to 108.0 mEq., the blood pressure rose to 136/92.

During the periods in which the serum chloride concentration was below 85 mEq., there still were considerable variations in the blood pressure levels. In the fourth month of treatment when the serum chloride was 79.3–78.6 mEq., the blood pressure fell to 84/62 (lying) with a hypotension of 60/30 on standing. However, one month previously when the serum chloride had been 71.1–72.5 mEq., the blood pressure was 102/80, and four months later, with a serum chloride concentration of 82.7 it was 114/80.

The relationship between serum chloride and NPN is obvious (Table 4 and Fig. 4). It is, however, not a

TABLE 4.—*Relationship of Serum Chloride and NPN*

DATE	NPN (mg. per 100 cc. blood)	UREA N (mg. per 100 cc. blood)	CHLORIDE (mEq. per 1,000 cc. of serum)
Oct. 27, 1947	30	9.0	100.5
Jan. 15, 1948	87	50.0	72.5
Feb. 10, 1948	156	130.3	79.3
April 20, 1948	28	10.7	108.0
June 17, 1948	35	14.7	82.7
Sept. 28, 1948	38	16.2	100.0

simple relationship either. In the fourth month of treatment when the serum chloride was 78.6–79.3 mEq., the NPN was 156. One month previously when the serum chloride had been 71.1–72.5, the NPN was 72–87, and four months later when the serum chloride was 82.7, the NPN was 35.

Table 5 shows the concentration of the total nonprotein nitrogen, the urea nitrogen and nonurea nitrogen in the blood. It is obvious that the increase in the total nonprotein nitrogen was for the greatest part due to the increase of the urea nitrogen fraction.

The patient returned home at the end of April. His diet consisted of rice, sugar, ten ounces of leafy vegetables, and 1½ potatoes daily, and small amounts of nuts, dates and avocados. He was allowed tea and water ad libitum. He felt well except for mild attacks of bronchial asthma for which he continued to take one or two aminophyllin suppositories and two to four "asthma capsules." Urine chlorides and blood pressure were determined daily. The urine chlorides ranged from 0.9 to 3.1 mEq. per 1,000 cc., the average was 1.5 mEq. per 1,000 cc. with a total excretion of 1.4 to 7.6 (average 3.1) mEq. per 24 hours. The blood pressure ranged from 130–100/96–76, the average was 116/87.

TABLE 5.—*Urea and Nonurea Fraction in Blood NPN*

DATE	NPN	UREA N	NONUREA NPN
	(mg. N per 100 cc. blood)		
Oct. 27, 1947	30	9	21
Jan. 7, 1948	56	40.2	15.8
Jan. 15, 1948	87	50.0	37.0
Feb. 10, 1948	156	130.3	25.7
Feb. 12, 1948	138	108.2	29.8
Feb. 24, 1948	64	33.2	30.8
Mar. 16, 1948	45	25.6	19.4
April 20, 1948	28	10.7	17.3
June 17, 1948	35	14.7	20.3
Sept. 2, 1948	38	16.9	21.1

When the patient returned to the clinic on June 17, he looked and felt well. The blood pressure was 114/80. The vision was good. The papilledema had cleared up completely. The hemorrhages and cottony exudates had disappeared. The previously tortuous and engorged veins had straightened out and were smaller in caliber. There were still a few small spots of hard exudate to be seen between disc and macula. The heart was normal in size as in April (Fig. 5). The rhythm was regular. The sounds were normal; there were no murmurs. The lungs were clear except for some musical râles, especially in the left base. The BMR was — 15 per cent. The hemoglobin was 14.6 Gm. The white blood cell count was 9,800. The NPN was 35 mg. per 100 cc. of blood. The urea N was 14.7 mg. per 100 cc. of blood; the urea ratio was 42 per cent. The sugar was 108 mg. per 100 cc. of blood. The chloride was 82.7 mEq. per 1,000 cc. of serum. The cholesterol was 190 mg. per 100 cc. of serum. The calcium was 10.3 and the phosphorus 4.4

mg. per 100 cc. of serum. The total protein was 7.7 Gm. per 100 cc. of plasma.

The diet was further increased to include 2 oz. of meat, 2 oz. of peas, beans or corn and ½ oz. of vegetable oil daily. During the next two months the amounts of meat, vegetables, and vegetable oil were increased slightly and three to nine slices of toast, ½ oz. of butter and 2 oz. of oatmeal daily were added.

Starting in July the patient again had frequent and severe asthmatic attacks. In spite of the asthmatic attacks and the increase in the diet with consequent rise of serum chloride to 106.8 mEq. per liter, the blood pressure has remained normal (average, September 28–October 12, 1948: 119/81 mm. Hg). The NPN is 38 mg. per 100 cc. of blood, the urea N 16.2 mg., the urea ratio 42.6. The retinopathy has disappeared (Fig. 6), and there is no longer any evidence of vascular disease.

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Treatment of Heart and Kidney Disease and of Hypertensive and Arteriosclerotic Vascular Disease with the Rice Diet

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TREATMENT OF HEART AND KIDNEY DISEASE AND OF HYPERTENSIVE AND ARTERIOSCLEROTIC VASCULAR DISEASE WITH THE RICE DIET*

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THE treatment of heart and kidney disease and of hypertensive and arteriosclerotic vascular disease with the rice diet is either ineffective or dangerous, unless it is done under rigidly controlled conditions. Ineffective, because small or "minimal" additions to the diet may spoil the entire therapeutic result; dangerous, because a strict observance of the diet may lead to a deficiency of vitally important elements unless care is taken that the equilibrium between intake and loss of these substances is maintained. For both reasons, therefore, continuous supervision, over a long period of time, including constant checks of blood and urine chemistry, is essential.

Rigidly controlled conditions are likewise indispensable for the evaluation of the therapeutic results. Claims of positive or negative results based on nothing but blood pressure readings for four to eight weeks before and after treatment and not substantiated by heart films, electrocardiograms, eye-ground photographs and chemical findings do not contribute much to the solution of this problem.

The same authors who a few years ago insisted that the restriction of salt, protein or fat is unwarranted in the treatment of hypertensive and arteriosclerotic vascular disease, now admit the importance of these dietary restrictions. No matter what the value of the restriction of sodium or of chloride or of protein or of cholesterol may be, the fact is: The rice diet contains less sodium and less chloride than any other diet which has been devised to reduce the sodium and chloride intake. It contains less protein than any other diet which has been devised to reduce the protein intake. It contains less cholesterol and other fat than any other diet which has been devised to reduce the cholesterol and fat intake.

The rice diet contains in 2,000 calories less than 5 gm. of fat and about 20 gm. of protein derived from rice and fruit and less than 200 mg. of chloride and 150 mg. of sodium. This does not mean that the patient's caloric intake is restricted to 2,000 calories; it varies according to whether weight gain or weight loss, protein increase or protein decrease is desirable in the individual patient.

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Figure 1 shows a comparison of the most important constituents of the urine on a normal diet and after at least two months on the rice diet. The total nitrogen content has decreased from 15.0 gm. to 2.3 gm.; the urea nitrogen from 12.0 gm. to 1.1 gm.; the uric acid nitrogen from 0.3 gm. to 0.08 gm.; the total creatine nitrogen from 0.6 gm. to 0.4 gm.; the ammonia nitrogen from 0.6 gm. to 0.1 gm.; the sodium from 4.0 gm. to 0.01 gm. The potassium has increased from 2.0 gm. to 3.0 gm. The chloride has decreased from 7.0 gm. to 0.1 gm.; the inorganic phosphate from 1.0 gm.

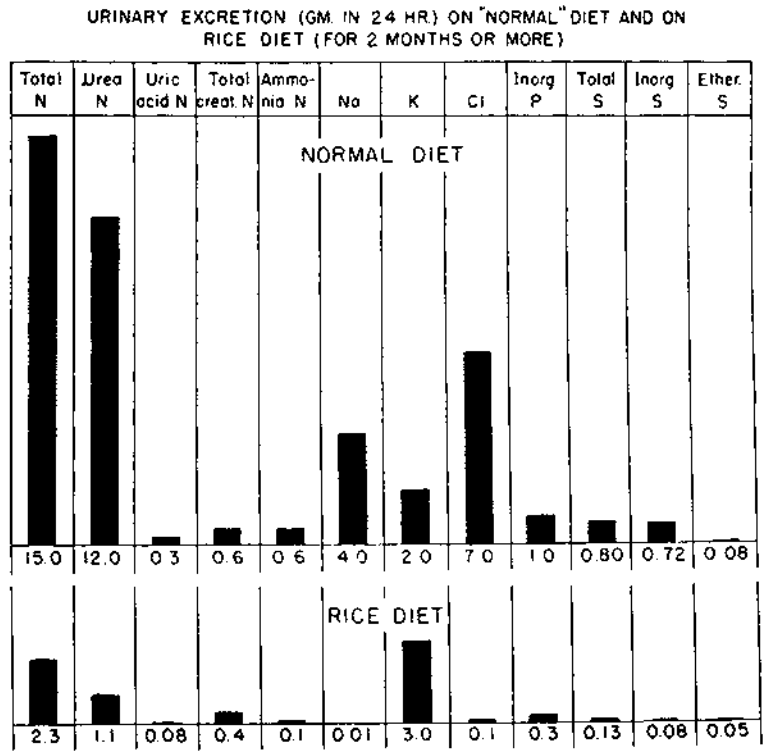

FIG. 1.

to 0.3 gm.; the total sulfate from 0.80 gm. to 0.13 gm.; the inorganic sulfate from 0.72 gm. to 0.08 gm.; the ethereal sulfate from 0.08 gm. to 0.05 gm.

The figures show that the marked decrease in the intake of nitrogen, sodium, chloride, sulfate, etc., on the strict rice diet, is followed by a marked decrease in the excretion of these substances by the kidney. Any deviation from these figures—except in rare cases—indicates that this particular diet has not been followed strictly for any length of time, and also in what way—either deliberately or unintentionally—it has been changed.

A small amount of nitrogen is also excreted through the bowels; a comparison of the daily nitrogen intake with the daily nitrogen output by stool

and urine shows that the nitrogen equilibrium on the rice diet can easily be maintained (table 1).

There are other indications that, because of the protein sparing action of the carbohydrates, the protein part of the rice diet is adequate and that there is no lack of essential amino acids; e.g., the fact that the production of hemoglobin is normal and that anemia does not develop. Also the fact that blood urea and non-protein nitrogen decrease on the rice diet whereas in starvation and in protein deficiency the body uses its own protein and the non-protein nitrogen and the urea nitrogen in the blood increase.

Other differences between starvation and the rice diet are: in starvation, the serum calcium is decreased, on the rice diet unchanged. In starvation, the plasma protein and the A/G ratio are decreased, on the rice diet unchanged or, if low before, often become normal. In starvation, the blood sugar is decreased, on the rice diet unchanged. In starvation, the carbohydrate tolerance is decreased, on the rice diet increased. In starvation, the serum phospholipids are increased, on the rice diet decreased. In starvation, the CO_2 combining power is decreased, on the rice diet increased. In star-

TABLE I

Nitrogen Balance After 60 Days on Rice Diet, gm.N in 24 hrs.
(Averages of 4 consecutive days)

	Intake	Output	Balance
		urine 2.61 stool 1.81	
W. C. m., 59	4.66	4.42	+0.24

vation, the blood volume remains unchanged or—in relation to body weight—increases; on the rice diet, according to Murphy's determinations, it decreases. In starvation, the interstitial fluid remains unchanged or increases; on the rice diet it decreases. (N. B., there is no simple relationship between volume changes and clinical course.) In starvation, the excretion of total creatine bodies in the urine is unchanged; on the rice diet it is decreased. In starvation, the excretion of creatine, ammonia and organic acids is increased, on the rice diet decreased. In starvation, the excretion of total sulfate and inorganic phosphate is decreased, on the rice diet markedly decreased (table 2).

In 490 patients with hypertensive vascular disease and an initial non-protein nitrogen of 20 to 45 mg. per 100 c.c. of blood, there was an average decrease of the non-protein nitrogen from 33 to 28 mg. per 100 c.c. of blood after an average period of 98 days. There was an average decrease of the urea nitrogen from 14 to 8 mg. (table 3). These figures are also interesting in another connection: a decreased salt intake in the diet with ensuing hypochloremia is usually followed by an increase in the blood urea nitrogen,

TABLE II

Chemical Differences between Starvation and Rice Diet

	Starvation	Rice Diet
Blood (or serum)		
Hemoglobin, RBC	Decreased	Unchanged
Calcium	Decreased	Unchanged
Total protein	Decreased	Unchanged (returned to normal if decreased before)
A:G ratio	Decreased	Unchanged
NPN	Increased	Decreased
Urea N	Increased	Decreased
Sugar	Decreased	Unchanged
Carbohydrate tolerance	Decreased	Increased
Phospholipid	Increased	Decreased
Alkali Reserve	Decreased	Increased
Blood volume	Unchanged	Decreased
Interstitial fluid	Unchanged or increased	Decreased
Nitrogen balance	Negative	In equilibrium
Urine		
Total nitrogen	Decreased	Markedly decreased
Urea N	Decreased	Markedly decreased
Creatinine + creatine	Unchanged	Decreased
Creatine	Increased	Decreased
Ammonia N	Increased	Decreased
Organic acids	Increased	Decreased
Total sulfate	Decreased	Markedly decreased
Inorganic phosphate	Decreased	Markedly decreased

and consequently by an increase in the total non-protein nitrogen. On the rice diet the salt *is* limited and the serum chlorides do decrease to a lower level. However, the restriction of the protein in the diet outweighs the effect of salt restriction and usually protects against the azotemia.

It might, perhaps, be well to talk less about the quantity of protein. The important thing is not how much protein is eaten, but how much of what kind of protein. There is actually no such thing as "protein." Proteins differ from each other in regard both to the type and the relative proportions of the various amino acids of which they are composed. They also differ in regard to rate and degree of assimilation. These differences as far as the patient is concerned are indicated by what is termed the biological value of

TABLE III

Average NPN and Urea-N of 490 Patients with Hypertensive Vascular Disease
(Initial NPN 20 to 45 mg. per 100 c.c. Blood)

	Before	After 98 (Average) Days of Rice Diet
NPN (mg./100 c.c. Blood)	33	28
Urea-N (mg./100 c.c. Blood)	14	8

various proteins. It is of no advantage to the patient to receive a large amount of protein with a low biological value which cannot be properly utilized. Moreover, certain patients should use protein only for essential purposes and not merely to supply calories which can just as well be supplied by the oxidation and fermentation of carbohydrates.

The same considerations which apply to protein and essential amino acids are also valid with regard to fat and essential fatty acids. The absolute fat content of rice for instance is small, but the proportion of linoleic acid, an essential fatty acid, is high.

One of the lipids which is supposed to have an important rôle in the development of vascular disease is cholesterol. A high cholesterol concentration in the serum is frequently found in arteriosclerosis, coronary artery disease, exudative vascular retinopathy, hypertensive vascular disease, as well as in diseases of the lens and vitreous body, in uncontrolled diabetes mellitus and in the nephrotic stage of nephritis.

TABLE IV

Total Serum Cholesterol of 511 Patients with Hypertensive Vascular Disease

	Before Rice Diet	After Rice Diet	Average Period of Rice Diet (Days)
148 Patients with initial concentration below 220 mg. per 100 c.c. serum	186	171	120
363 Patients with initial concentration above 219 mg. per 100 c.c. serum	279	205	102

An easy way to produce arteriosclerosis is by feeding cholesterol to rabbits. In dogs it is not so easy. The aging process in the human species seems to be a change from the dog state to the rabbit state. The cholesterol metabolism becomes inadequate and the average serum cholesterol concentration of men of 50 is higher than that of men of 20 who have an identical cholesterol intake. However, if a 20 year old man has a disease which causes a hypercholesterolemia, the same sequelae may occur as in the 50 year old man. The literature describes cases of arteriosclerosis in diabetic children as young as one year.

We have examined the effect of the rice diet on the total serum cholesterol of 511 patients with hypertensive vascular disease (table 4). In 148 patients (29 per cent) who started the rice diet with a normal serum cholesterol, the average decrease was 15 mg. per 100 c.c. of serum after an average period of 120 days. In 363 patients (71 per cent) who had a hypercholesterolemia before the rice diet, the average decrease was 74 mg. after an average period of 102 days.

These figures show that, no matter from what fatty or non-fatty substances the cholesterol in the body is derived, and by what mechanism a high

TABLE V

Total and Free Cholesterol in Serum of 118 Patients with Hypertensive Vascular Disease (Initial total cholesterol 220–463 mg. in 100 c.c. serum)

	Before	After 56 Days (Average) on Rice Diet
Total cholesterol (mg. in 100 c.c. serum)	288	217
Free cholesterol (mg. in 100 c.c. serum)	82.2	65.7
Ratio Free: Total cholesterol (%)	27.8	30.5

serum cholesterol concentration is produced, the serum cholesterol need not necessarily remain high, as has been assumed, but can be decreased by the rice diet.

As Starke has found, both cholesterol fractions, the free and the esterified cholesterol, decrease on the rice diet (table 5). One hundred and eighteen patients with an initial hypercholesterolemia of 220 to 463 mg. per 100 c.c. of serum were examined. The total cholesterol decreased in 113 of the 118 patients. The total cholesterol did not decrease in five of the 118 patients. In the entire group of 118 patients, there was a decrease of the total cholesterol from 288 to 217 (average), of the free cholesterol from 82.2 to 65.7 (average), of the esterified cholesterol from 205.8 to 151.3 (average). In

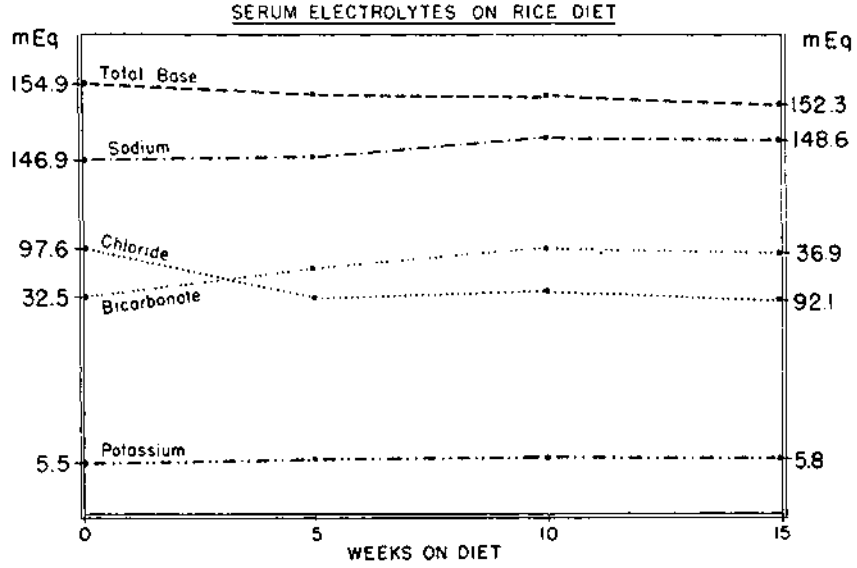

FIG. 2.

TABLE VI

Lipid Phosphorus in Serum of 42 Patients with Hypertensive Vascular Disease
(Mg. lipid P in 100 c.c. serum)

Before	After 78 Days (Average) on Rice Diet
9.91	8.87

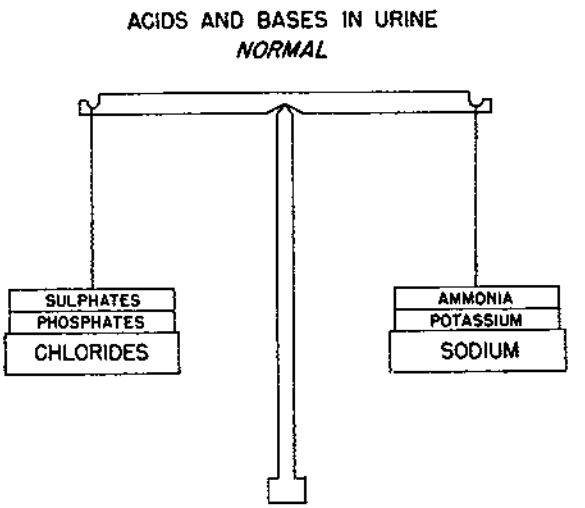

FIG. 3.

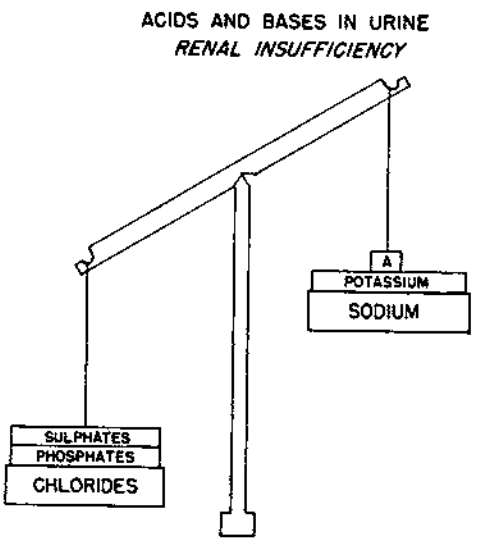

FIG. 4.

42 patients with hypertensive vascular disease, the serum phospholipids were determined. There was a decrease from 9.9 to 8.9 mg. lipid phosphorus per 100 c.c. (table 6).

Figure 2 shows the changes in concentration of sodium, chloride, potassium, bicarbonate, and total base in the serum of 12 patients on the rice diet. After an average period of 15 weeks, the serum chloride showed a definite decrease, the serum bicarbonate a definite increase; the serum sodium, potassium and total base remained relatively constant.

Another change in the mineral metabolism of patients on the rice diet is in the urinary excretion of inorganic sulfates and inorganic phosphates. The inorganic sulfate excretion decreases by 82 per cent, the inorganic phosphate excretion decreases by 62 per cent.

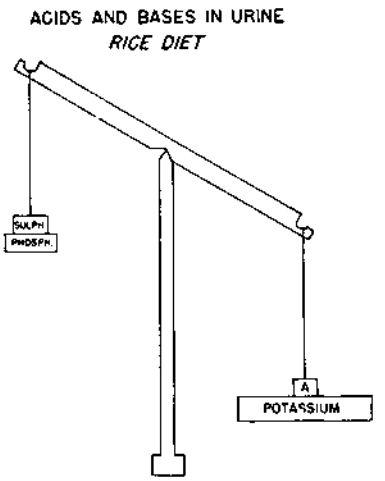

FIG. 5.

These findings are interesting for two reasons: Since phosphates and sulfates are derived mostly from protein, the decreased excretion of phosphorus and sulfur shows again that on the rice diet no endogenous protein is being broken down. Secondly, the sulfate and phosphate metabolism is important because of the acid-base balance. The scales (figure 3) represent this balance in the normal urine. The acids are on one side, the bases on the other side. In kidney insufficiency, the scale goes down on the acid side (figure 4). The kidney has lost one of its main metabolic functions: It is no longer able to form ammonia. On the rice diet, the urine chloride concentration is decreased. This does not affect the acid-base equilibrium because it is counterbalanced by the decrease in the sodium excretion. However, the potassium concentration on the base side is increased, and the sulfate and phosphate concentration on the acid side is decreased, so that even with an insufficient ammonia formation the urine becomes alkaline (figure 5).

Now let me turn from the chemical changes to the clinical changes produced by the rice diet. I will avoid long-winded statistics as much as possible and will try to discuss the main problems by showing you some typical cases as examples of what can be achieved in the individual patient.

The first case is that of a 13 year old school girl in the nephrotic stage of chronic nephritis. It is an example of the disappearance of marked generalized *renal* edema and hypoproteinemia on the rice diet. Early in Jan-

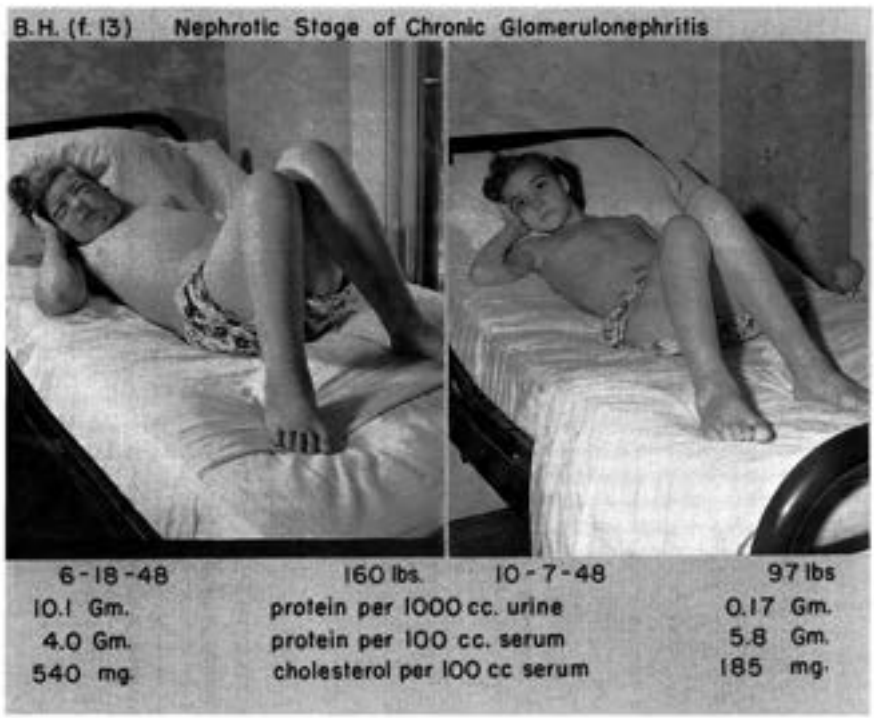

FIG. 6.

uary, 1948, this girl developed swelling of the lower extremities after a sore throat. She was treated by bed rest, salt-poor diet (for part of the time, high protein diet), and penicillin. In February, 1948, massive anasarca developed; a paracentesis was done which resulted in a weight loss of 22 pounds. Later, because of marked dyspnea, a thoracocentesis was necessary and one quart of fluid was removed from the right pleural cavity. During June, the facial edema which had been present since January became worse and the general edema and ascites increased. When the oliguria became serious, the patient was referred to us. The rice diet was started on June 18, 1948. No further paracentesis or thoracocentesis was done. The albuminuria decreased from 10.1 gm. per liter (average during the first 20 days on the rice diet) to 0.17 gm. (average after 111 to 131 days of rice diet). The

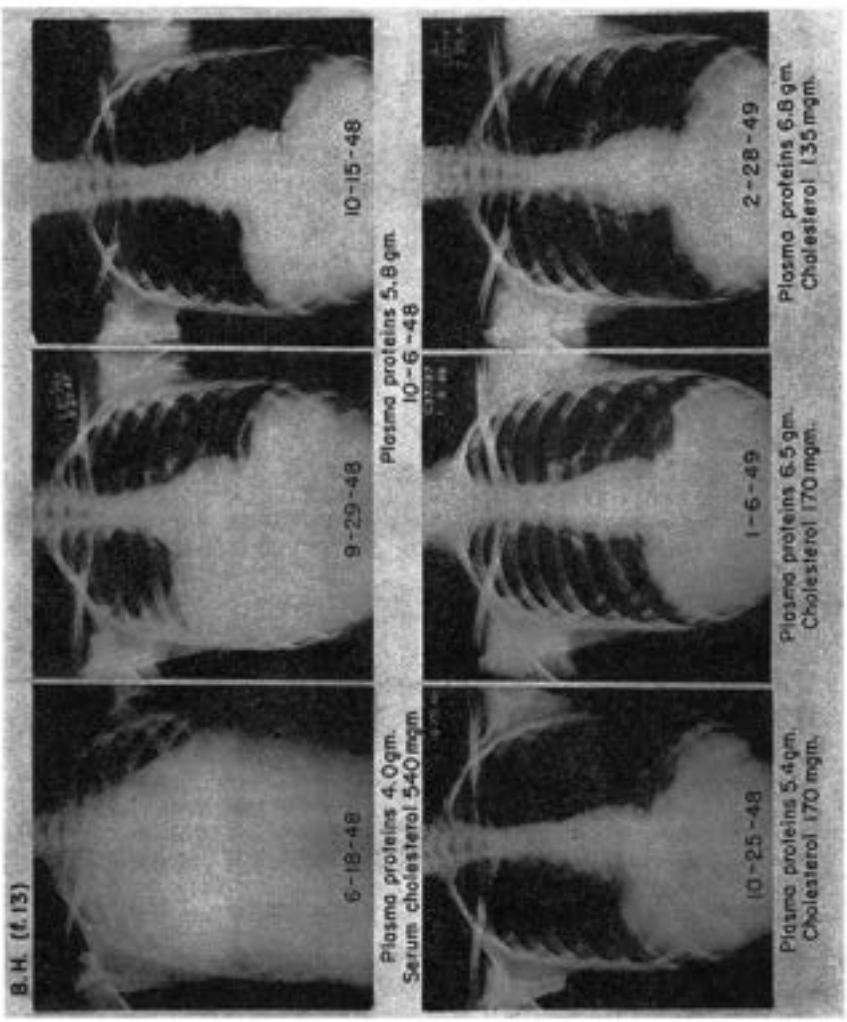
B. H. (f. 13)
6-18-48
9-29-48
10-15-48
Plasma proteins 4.0gm.
Serum cholesterol 540 mgm.
Plasma proteins 5.8 gm.
10-6-48
10-25-48
1-6-49
2-28-49
Plasma proteins 5.4gm.
Cholesterol 170 mgm.
Plasma proteins 6.5gm.
Cholesterol 170 mgm.
Plasma proteins 6.8gm.
Cholesterol 135 mgm.

FIG. 7.

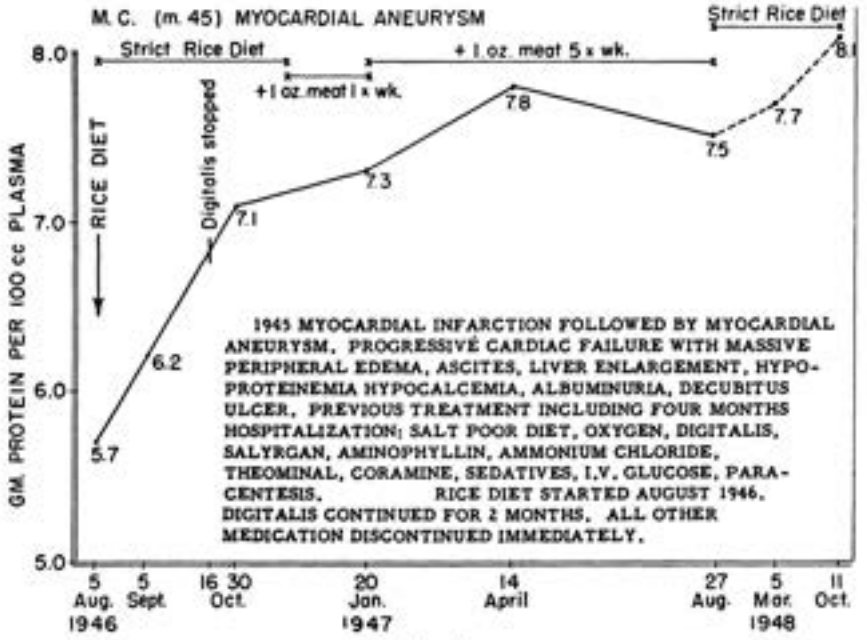

FIG. 8.

plasma protein increased from 4.0 gm. to 5.8 gm. The cholesterol decreased during this period from 540 mg. per 100 c.c. of serum to 185 mg. There was a total weight loss of 63 pounds in 15 weeks with gradual disappearance of ascites and pleural effusion. After eight months on the rice diet, the

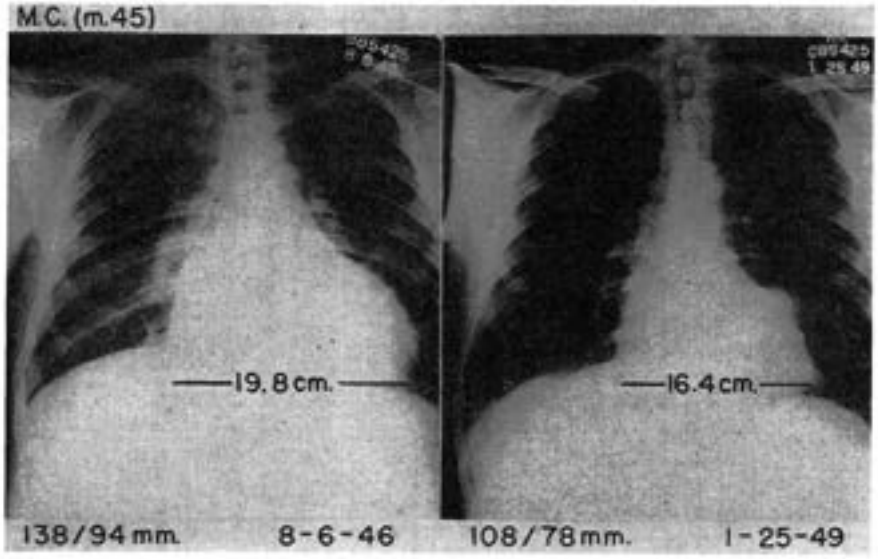

FIG. 9.

plasma protein had increased from 4.0 to 6.8 gm., the cholesterol had decreased from 540 to 135 mg. per 100 c.c. of serum (figures 6 and 7).

Figure 8 shows an example of the effect of the rice diet on the plasma protein of a patient with massive *cardiac* edema and ascites. This patient was a 45 year old man who had had a myocardial infarction in 1945. This

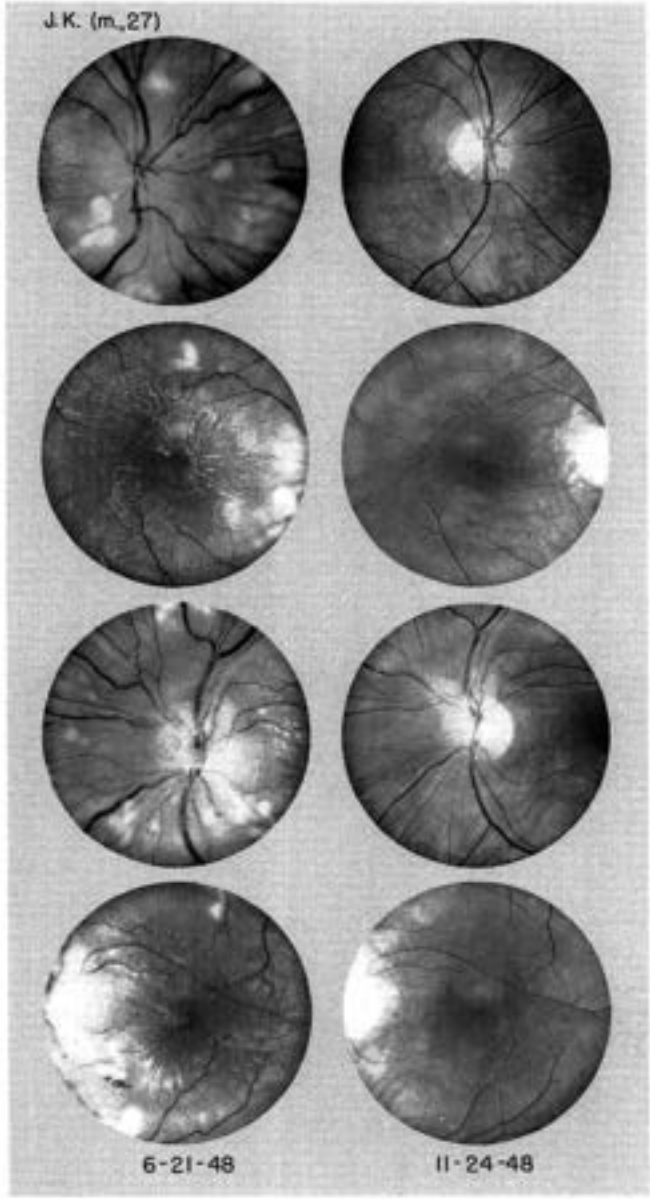

FIG. 10.

was followed by a myocardial aneurysm, progressive cardiac failure with massive peripheral edema, ascites, liver enlargement, hypoproteinemia, hypocalcemia, albuminuria, and decubitus ulcers. Previous treatment, including four months' hospitalization, consisted of salt-free diet, oxygen, digitalis, salyrgan, aminophyllin, ammonium chloride, theominal, coramine, sedatives; i.v. glucose; paracentesis. The rice diet was started August 7, 1946, and was strictly followed; a paracentesis was done August 13. Digitalis was continued for two months, but all other medications were discontinued immediately. There was a loss of weight (edema) of 50 pounds in 10 weeks. Up to the present time (two and one-half years later), the patient has received no medication; he is up and around and completely asymptomatic. The plasma proteins have increased from 5.7 gm. per 100 c.c. to 8.2 gm.

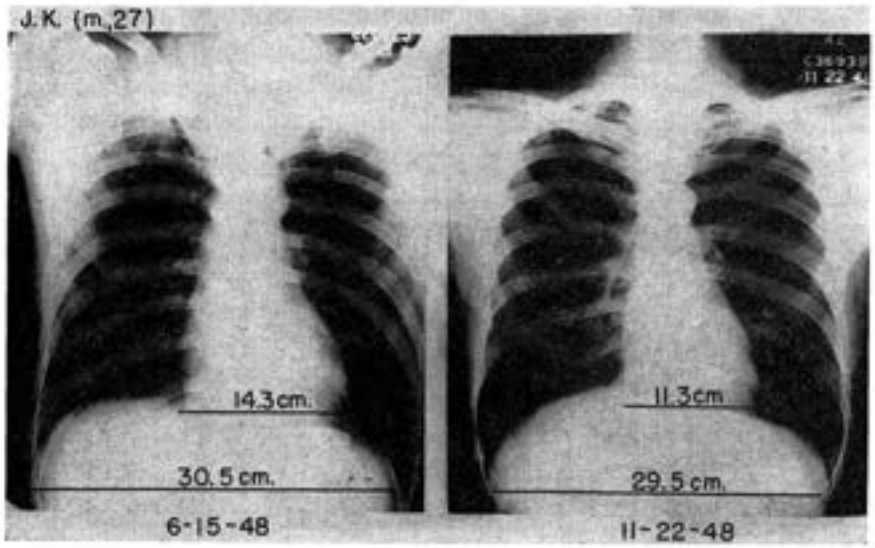

FIG. 11.

The heart is considerably smaller and the aneurysm of the posterior lateral wall of the left ventricle is now clearly visible in the A–P view (figure 9).

The patient, whose eyeground photographs and chest films are shown in figures 10 and 11, is an example of the effect of the rice diet on retinopathy and cardiac enlargement in chronic glomerulonephritis.

The patient was a 27 year old man who two years before admission to Duke Hospital, while in the Navy, had scarlet fever and acute glomerulonephritis, followed by chronic glomerulonephritis. He had been hospitalized for 16 months and treated with rest and various diets. During the month prior to admission, the patient had an exacerbation of his headache, noted blurring of vision and had a generalized convulsion, for which magnesium sulfate was given. At the start of the rice diet the blood pressure was 180

mm. of mercury systolic and 120 diastolic, the heart was enlarged, the vision considerably impaired, with bilateral marked papilledema, many hemorrhages and extensive exudates. The total phenolsulphonephthalein excretion in two hours was 7 per cent. The non-protein nitrogen was 90, the urea N 66.4 mg. per 100 c.c. of blood. The calcium was 7.8, the phosphorus 6.6, the

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FIG. 12.

cholesterol 350 mg. per 100 c.c. of serum. The serum chloride was 99.8 mEq. per liter.

After five months on the rice diet, the total PSP excretion in two hours was still only 10 per cent, but the NPN was 36, the urea N 15.8 mg. per 100 c.c. of blood. The calcium was 8.9, the phosphorus 5.1, the cholesterol 210 mg. per 100 c.c. of serum. The serum chloride was 88.2 mEq. per liter. The blood pressure was 137/99. The patient was asymptomatic; he had

regained his eyesight; papilledema, hemorrhages and most of the exudates had disappeared; the heart had decreased in size with a change in the transverse diameter of 27 per cent.

I have shown you some effects of the rice diet on edema, ascites, heart enlargement and retinopathy in patients with primary kidney disease. I will show you now some characteristic examples of the effect of the rice diet on hypertensive vascular disease without evidence of any primary renal disease. In more than 70 per cent of 777 patients most of whom were seriously ill and had failed to respond to other forms of treatment, the rice diet, given for periods of four to 1,150 days (average 92 days), has proved beneficial; that means that it has produced one or more of the following effects: decrease in the sum of systolic and diastolic blood pressure of at least

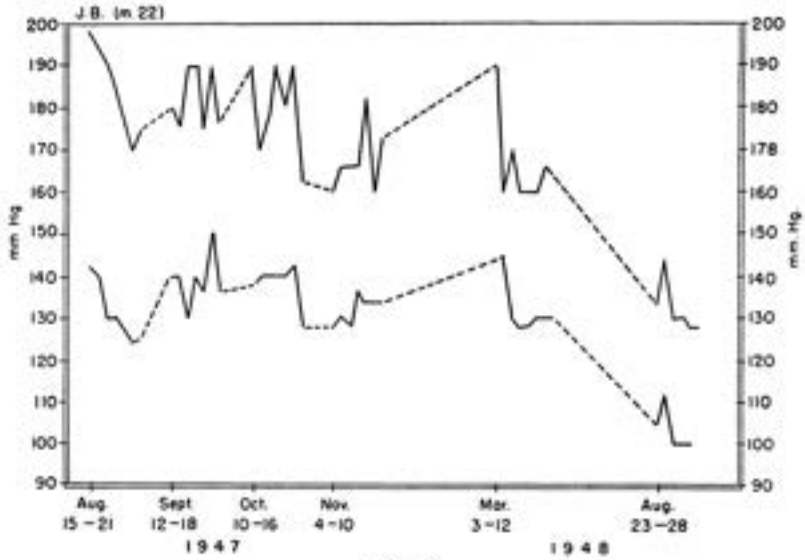

FIG. 13.

40 mm. Hg; reduction in heart size with change in the transverse diameter of 18 per cent or more; change in T_1 from completely inverted to upright; disappearance of severe retinopathy.

I will begin with three typical cases of so-called benign essential hypertension without serious cardiac, renal or retinal complications.

The first one is an example of a satisfactory response to the diet in about four months. It is the case of a 35 year old woman who had had hypertensive vascular disease for 11 years. There was no evidence of any renal excretory involvement. Of two brothers with hypertensive vascular disease, one had died of a stroke at the age of 37. For years, the patient did not feel up to par with increasing fatigue and exhaustion. There was a sensation of pressure and throbbing in the back of the head and in the eyes. From January to April, 1947, because of the appearance of retinal hemor-

rhages, rutin, vitamin K and sedatives were given; all activities had been severely restricted.

The patient began the rice diet in April, 1947. All medication was discontinued. On the first day of the diet, the blood pressure was 202/132; after three weeks of the diet the blood pressure was almost as high as before: 180/132. After 120 days, the blood pressure was 122/95 (figure 12). It has remained at this level until the present time (two years) in spite of the

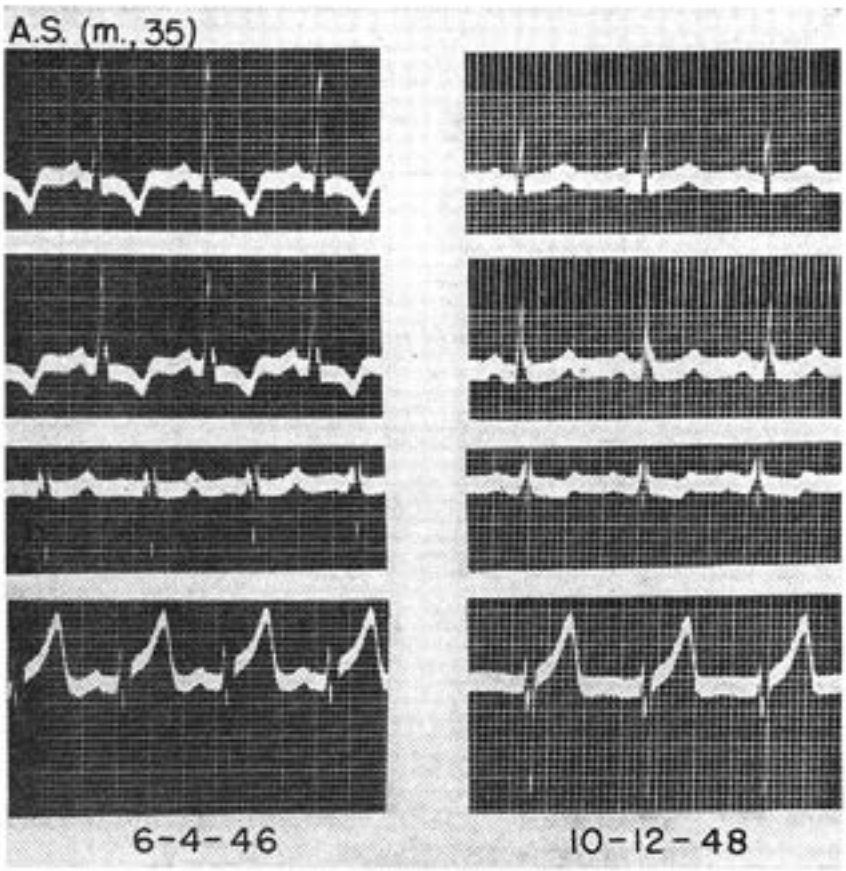

FIG. 14.

fact that two ounces of meat, one potato, 9 oz. of vegetables, one cup of coffee per day and 2 oz. of vegetable oil, 4 oz. of spaghetti per week, have been added to the diet. The patient has resumed her activities and is completely well.

The second case is an example of a rather slow response of hypertension to the diet. It is the case of a 22 year old man with benign essential hypertension without any history of kidney disease or evidence of renal excretory dysfunction. The patient had known about his hypertension for six months.

TREATMENT OF HEART AND KIDNEY DISEASE WITH RICE DIET 837

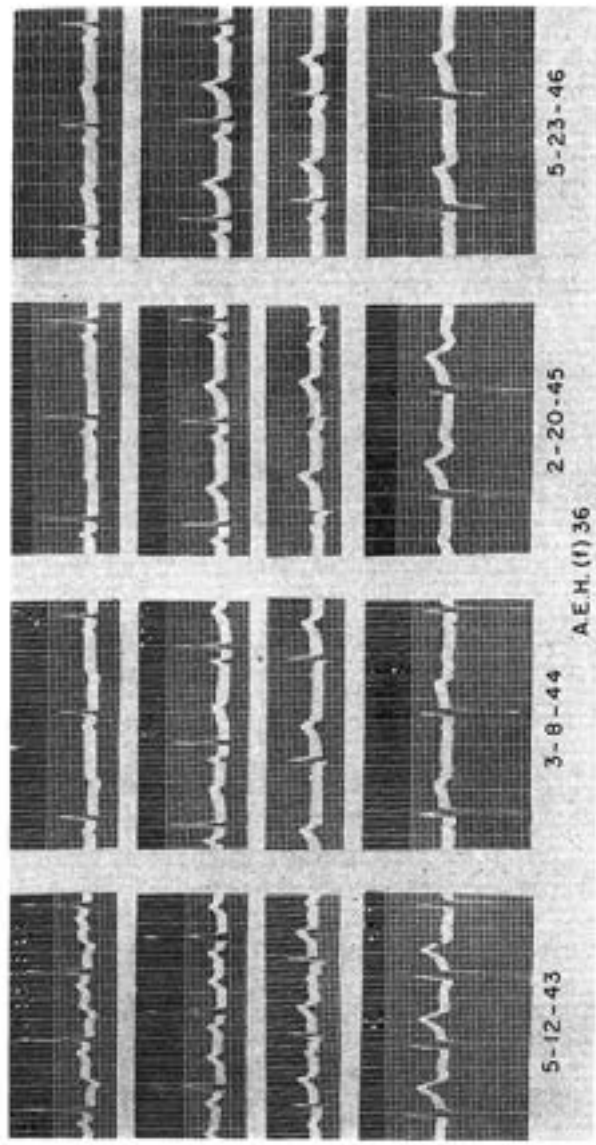

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FIG. 15.

He was asymptomatic except for intense headaches. He was started on the rice diet in New York. Since the blood pressure did not change in seven and one-half weeks, he came to Durham. During August, September and October, 1947, while he was staying in Durham continuously, the blood pressure remained persistently at a level of 170 to 190 systolic and 130 to 145 diastolic; the headache, however, disappeared. When the patient returned for reëxamination in November, 1947, and March, 1948, the blood pressure was as high as before. From June, 1948, on, i.e., *12* months after the rice diet was started, his physician in Alberta noticed that the blood pressure was decreasing. When the patient returned to us in August, 1948, after 14

TABLE VII

Blood Pressure Response According to Length of Time of Treatment

	Number of Patients	Percentage	Average Period on Rice Diet (Days)
4–1150 Days			
Total	777		92
Blood pressure not improved	226*	29%	72
Blood pressure improved	551	71%	101
4–74 Days			
Total	392		37
Blood pressure not improved	151**	38.5%	32
Blood pressure improved	241	61.5%	40
75–1150 Days			
Total	385		149
Blood pressure not improved	75***	19.5%	153
Blood pressure improved	310	80.5%	148

* Including 33 patients who died after 48 days (average).
** Including 25 patients who died after 32 days (average).
*** Including 8 patients who died after 100 days (average).

months on the rice diet, the blood pressure was as low as 128/100 (figure 13).

The shortest time in which we have seen a marked blood pressure decrease on the rice diet was four days. The average time is about three to four months.

Table 7 shows the positive and negative results of treatment in 777 patients with hypertensive vascular disease who followed the rice diet for four to 1150 days (average 92 days). There was a definite decrease of the blood pressure level in 71 per cent of the total group. The average of this decrease was from 198/116 to 150/96 in 101 days. If one differentiates the results according to the length of time the patients have been following the

diet, the importance of the time factor becomes obvious: In 392 patients who followed the diet for four to 74 days (average 37 days), there was a definite lowering of the blood pressure in 62 per cent. In 385 patients who followed the diet for 75 to 1,150 days (average 149 days), there was a definite lowering of the blood pressure level in 81 per cent.

The third case with benign essential hypertension is an example of a satisfactory response to the diet in one month. It is the case of a man now 47 years old who was well until he was 37. In March, 1940, he was seen in the New York Hospital. The blood pressure was 165 to 200 systolic and 105 to 135 diastolic. A diagnosis of hypertensive vascular disease was

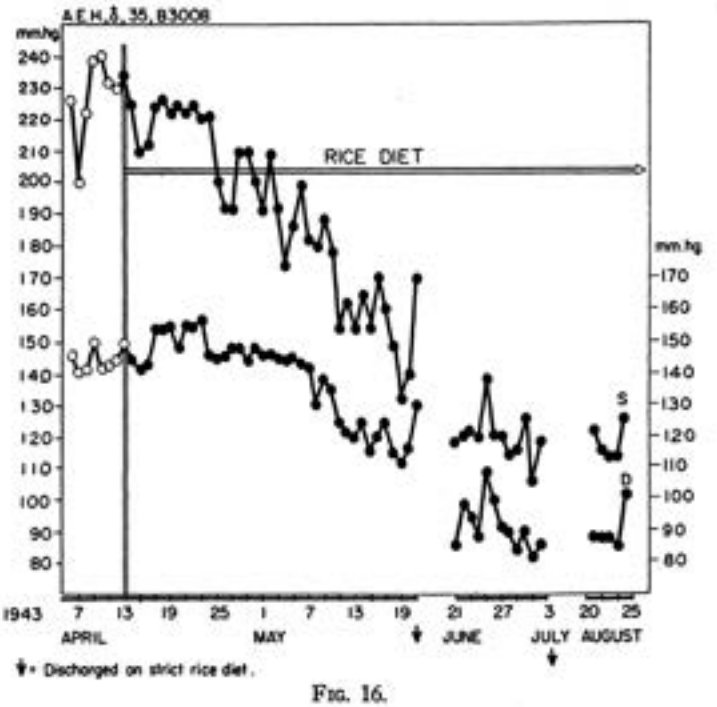

FIG. 16.

made. In January, 1941, he was seen in the Presbyterian Hospital. The blood pressure was found to be 200/140. One month later, the patient was seen in the Rockefeller Hospital with a blood pressure of 200/140. He was treated there by Dr. Henry Schroeder with tyrosinase until this had to be discontinued because of a severe shock-like reaction. As a matter of fact, this was the last patient whom Dr. Schroeder treated with tyrosinase. I like to show his record because Dr. Schroeder in the *American Journal of Medicine* in April of last year made the statement that the control periods preceding the rice diet might be too short to get an accurate base line for studying the effect of the diet. As is true for the majority of my patients, the base line for this patient was recorded by good observers not only over

a period of weeks or months but over a period of years. In this particular case, there are not only the figures of the New York and Presbyterian Hospitals but also those of Dr. Schroeder himself. After the tyrosinase treatment had failed, the patient went to Dr. Smithwick in Boston, where a lumbodorsal sympathectomy was done.

The sympathectomy did not help this patient. The blood pressure figures 14 months after the operation were even slightly higher than before. In 1945, the patient had a therapeutic trial with testosterone with no result. In March, 1945, when he came to us, he had tightness around the heart, headaches and swimming in the head. He had difficulty in walking and complained about a tendency to go toward the left and had at times run into

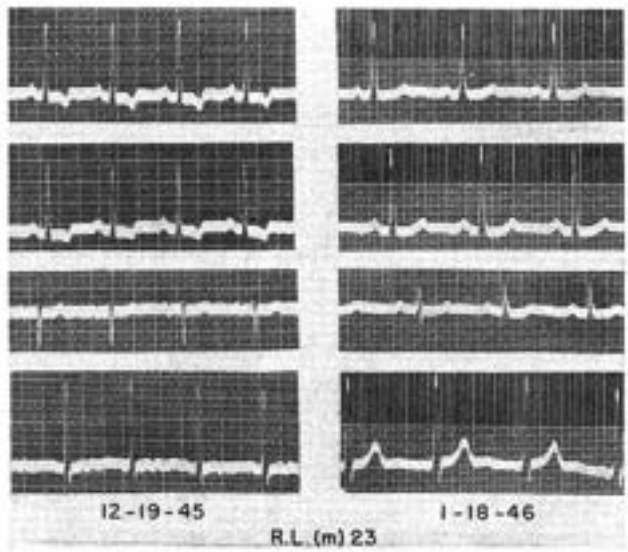

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FIG. 17.

walls. The blood pressure was 220/132. The average of daily blood pressure readings during 20 days while he was in the hospital on a 1,500 calorie diet was 197/129. No evidence of renal excretory dysfunction was found. PSP and urea clearance tests were normal. The rice diet was started on April 20, 1945. The blood pressure after one month of diet was normal and has remained normal to the present time. On February 24, 1949, it was 114/82. The diphasic T_1 in the electrocardiogram reverted to normally upright in seven months, and has remained upright since. The heart became smaller in size with a change in the transverse diameter of 12 per cent. The patient who was a sick man when he came to us in 1945, is now—four years later—well and active.

Patients such as these three, with so-called benign essential hypertension

are frequently told not to be concerned about their disease, unless some complication develops.

I believe the most appropriate time for treatment is before the more incapacitating complications of the disease have developed (cardiac breakdown, cerebral accidents, loss of vision and renal insufficiency). However, I will show you some typical electrocardiograms, chest films and eyeground photographs, which will illustrate that hypertensive vascular disease can be compensated to a great extent even when critical complications are already present.

Figure 14 shows the reversion of an abnormal electrocardiographic pattern to normal in a 35 year old man with hypertensive vascular disease of

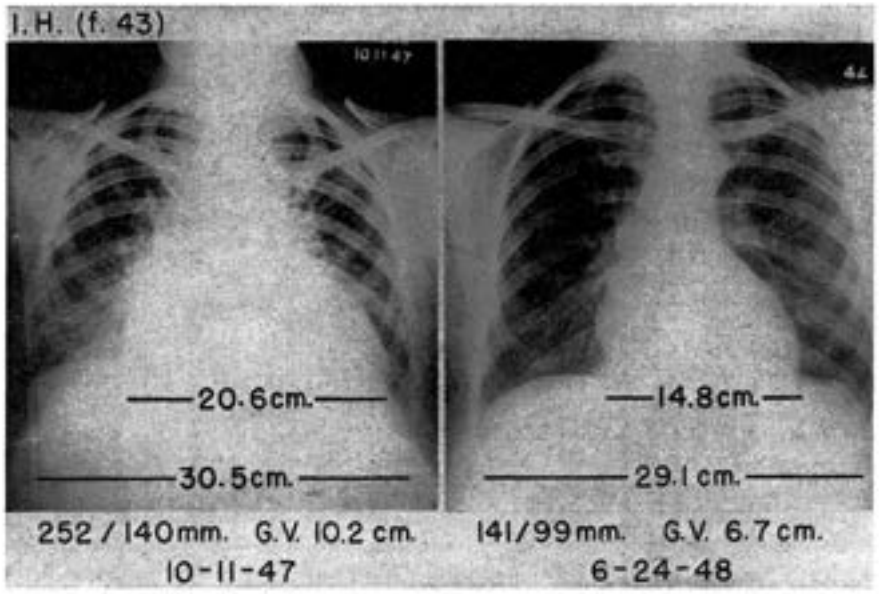

FIG. 18.

less than three years' duration. The change in the electrocardiogram is seen after 26 months on the rice diet. The blood pressure during this time decreased from an average of 205/122 to 150/103. Retinal hemorrhages and exudates disappeared. The deeply inverted T_1 became upright; the electrical axis improved.

Figure 15 illustrates the time factor in the gradual improvement of T_1. The patient was a 35 or 36 year old woman. Hypertension was known to be present for about one year. In May, 1943, T_1 was deeply inverted; in March, 1944, T_1 was low inverted; in February, 1945, low upright; in May, 1946, normally upright. This case also shows that there is neither a simple relationship between blood pressure drop and T_1 improvement nor between reduction in heart size and T_1 improvement. The blood pressure decreased

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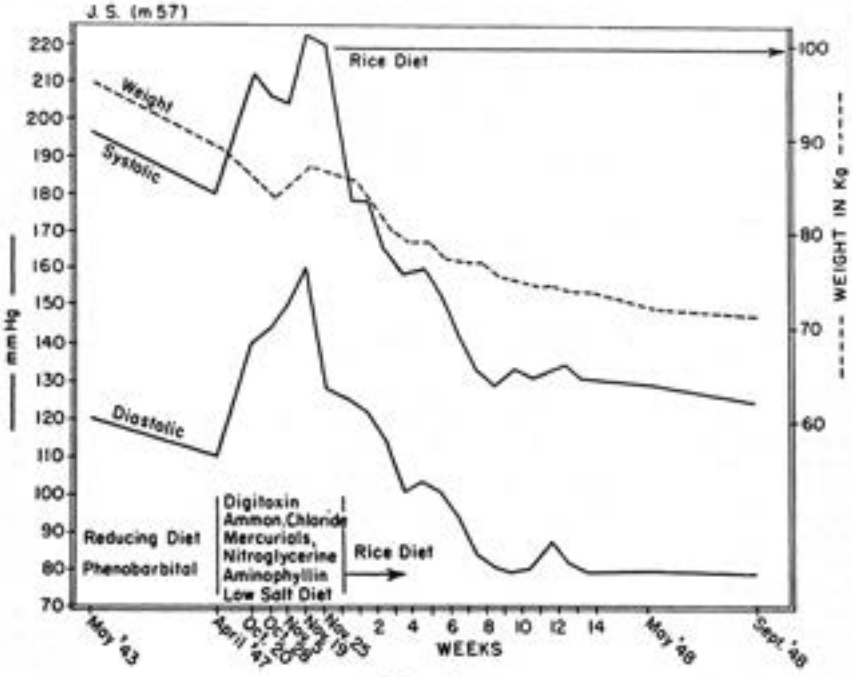

FIG. 19.

TABLE VIII

Changes of T_1 in 520 Patients with Hypertensive Vascular Disease after Rice Diet

Number of Patients	T_1 Before Rice Diet	T_1 After Rice Diet	Period on Rice Diet (Average)
	No Change (388)		
68	Inverted	Inverted	7 months
34	Diphasic	Diphasic	8 months
286	Upright	Upright	11 months
	Change in direction to inverted (10)		
0	Upright	Inverted	
5	Diphasic	Inverted	8 months
5	Upright	Diphasic	4 months
	Change in direction to upright (122)		
38	Diphasic	Upright	9 months
32	Inverted	Diphasic	13 months
52	Inverted	Upright	10 months

from 220/150 to 124/85 (figure 16) and the heart became normal in size within 10 weeks on the rice diet. Three years were required for the inverted T_1 to become normally upright.

Figure 17 shows the reversal of an inverted T_1 in the shortest period of time we have seen, one month. It is the electrocardiogram of a 23 year old man with hypertensive vascular disease, uncomplicated for three years, in the malignant phase with severe neuroretinopathy for three months. During the first month of the rice diet in which T_1 became normal, the blood pressure

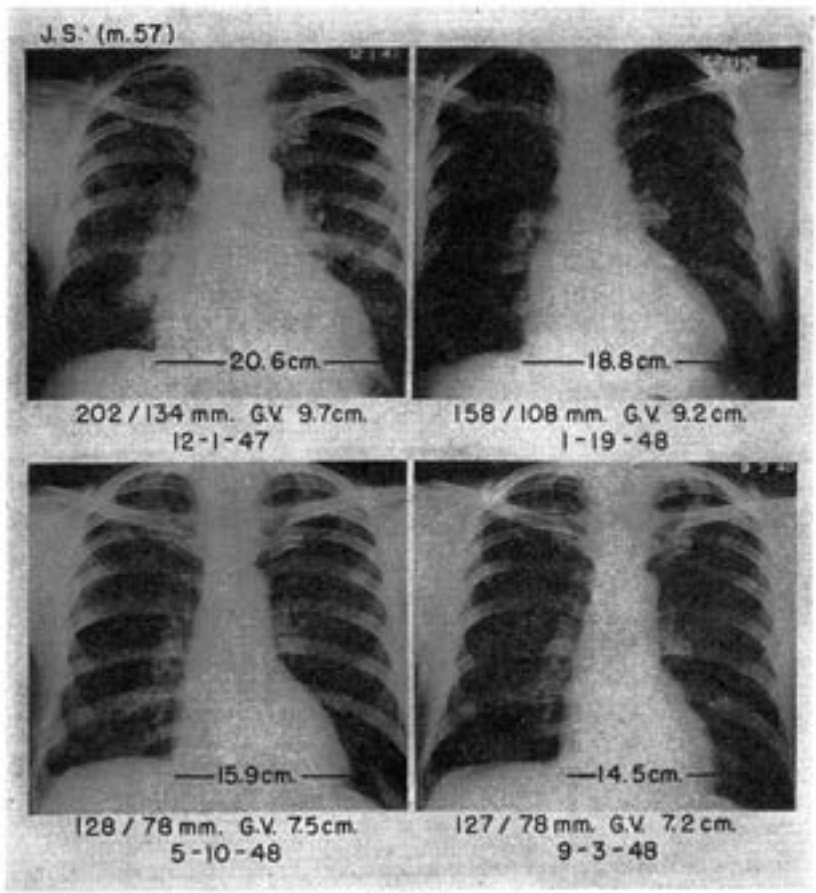

FIG. 20.

level decreased from an average of 222/148 to an average of 153/112. A normal blood pressure was reached only after two more months on the diet.

The T waves in Lead I were evaluated in 520 patients. None of these patients received digitalis or any other drug. All electrocardiograms were made with the patient at rest and in recumbent position. In 286 electrocardiograms which were normal at the start and in 102 electrocardiograms

which were abnormal at the start, no change occurred. In 132 electrocardiograms, a change did occur. In 10 in the direction from normal toward inverted. In 122 in the direction from abnormal to upright (table 8).

Figure 18 shows two chest films as an example of the reduction in heart size produced by the rice diet. It is the case of a 43 year old woman who had had hypertensive vascular disease for 14 years. It remained uncomplicated for 11 years. Then auricular fibrillation and heart failure developed with liver enlargement, edema, dyspnea and substernal pain. The

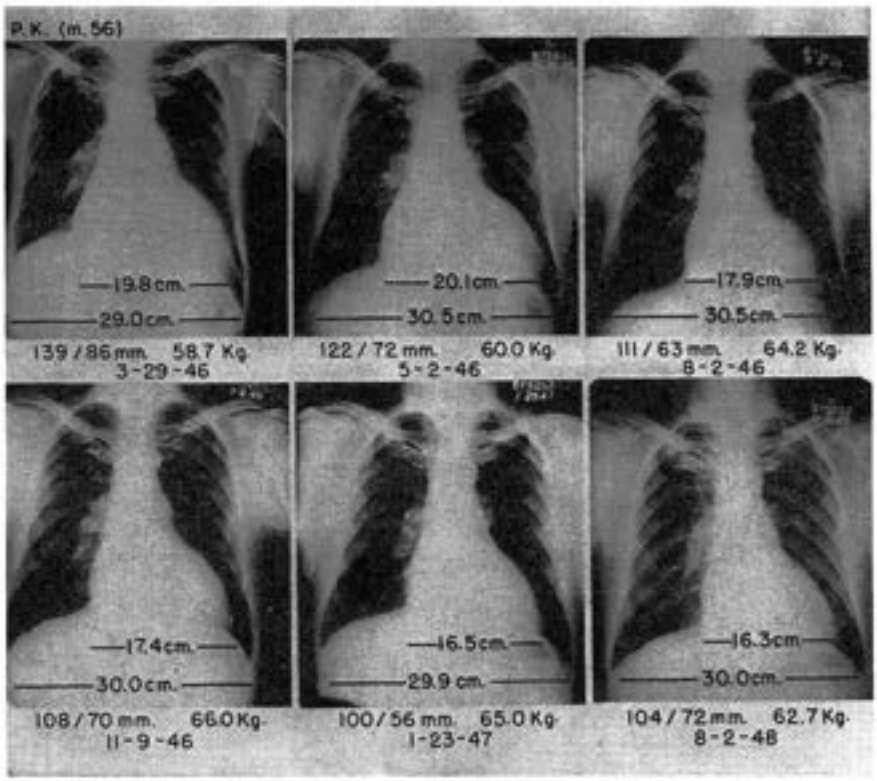

FIG. 21.

usual treatment with dietary restrictions, rest and digitalis was given with no improvement. Within eight months on the rice diet, the blood pressure decreased from 252/140 to 141/99, and the heart became smaller in size with a change in the transverse diameter of almost 40 per cent. The patient became asymptomatic and is now doing rather strenuous work.

The next case is an example of the length of time required for a heart which is enlarged and disfigured by the disease to change its size and shape back towards normal. The patient was a 57 year old man who had known he had hypertensive vascular disease for four years. Hypertensive heart

disease had become apparent in April, 1947. It was treated with digitoxin, ammonium chloride, mercurials, nitroglycerin, aminophyllin, weight reduction, salt-restricted diet. In spite of this medication and a weight loss of 30 pounds, the blood pressure increased and the heart failure became worse. When the patient came to us, the rice diet was started, and all medication including digitalis was immediately discontinued. The edema disappeared in 20 days; the blood pressure returned to normal in two months (figure 19). A decrease in heart size was noted after six weeks with a change in the transverse diameter of 8.7 per cent; after five months there was a change of 29 per cent; after nine months there was a change of 42 per cent (figure 20).

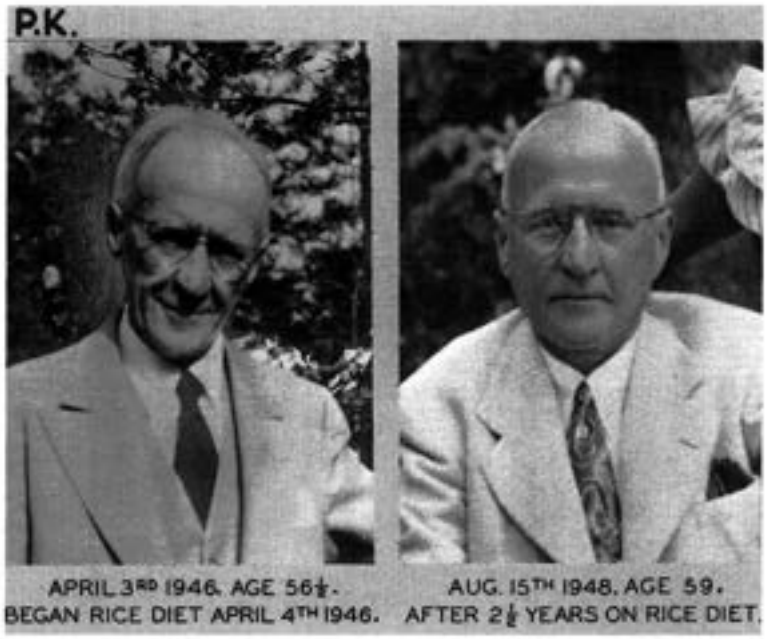

FIG. 22.

The patient became completely asymptomatic and has been without any medication for the past 14 months.

Chest films of 286 patients taken before and after one month or more of dietary treatment were measured for comparison (no digitalis or other drugs were given after the day the first chest film was taken). In 15 of the 286 patients (i.e. in 5 per cent), the heart became larger with an average increase of 2.6 per cent. In 146 patients there was a decrease in heart size with a change in the transverse diameter of 6.2 per cent (average), in 106 patients there was a decrease with an average change of 14.2 per cent and in 19 patients a decrease with an average change of 24.4 per cent (table 9).

I do not think that the improvement in the electrocardiographic pattern or the decrease in heart size or the disappearance of papilledema, hemor-

TABLE IX

Effect of Rice Diet on Heart Size: Average Changes in Transverse Diameter of Heart in 286 Patients with Hypertensive Vascular Disease

	Change		Average Period of Rice Diet (days)
	Diameter of Chest %	Transverse Diameter of Heart %	
15 patients with *increase* of 0–8.0%	+0.8	+ 2.6	184
146 patients with *decrease* of 0–9.9%	−0.7	− 6.2	112
106 patients with *decrease* of 10–19.9%	−0.3	−14.2	114
19 patients with *decrease* of 20% or more	−2.2	−24.4	187

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rhages, and exudates in the eyegrounds occurs as a simple consequence of a decrease in blood pressure. I have seen quite a few patients in whom these improvements have occurred in spite of the fact that the blood pressure remained at exactly the same level as before. They, likewise, occur in the many instances where vascular retinopathy and/or heart enlargement are present without hypertension.

Figure 21 is an example of the compensation of heart failure and the reduction of heart size in a patient who had gone through a fairly complete list of therapeutics. When he came to us in March, 1946, he was 56 years old. He had had nephrolithiasis and had developed hypertension and hypertensive heart disease. Nephrectomy on the left side was done in 1940 in

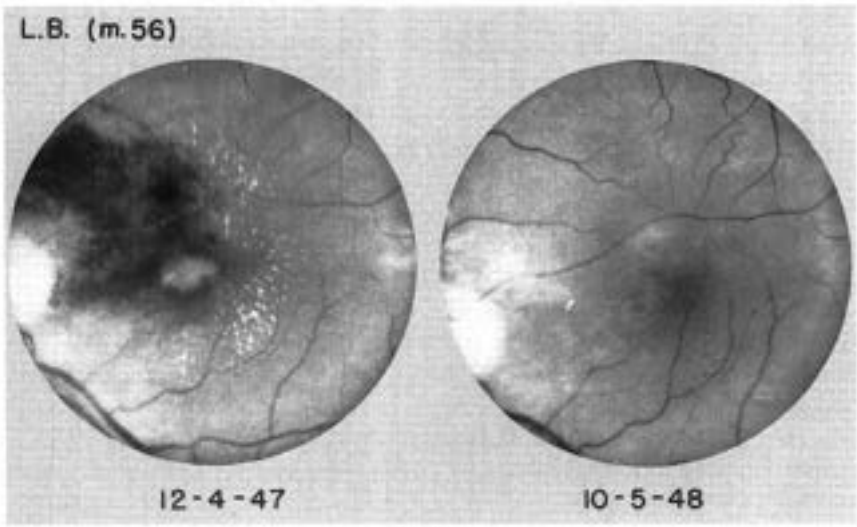

FIG. 23.

the hope of arresting his vascular disease. In spite of this, the disease continued and a left bundle branch block developed. When heart failure gradually increased, digitalis, squill, mercupurin, ammonium chloride, sedatives and salt-poor diet were tried.

The first chest film of March 1946, showed a greatly enlarged heart. There was edema, liver enlargement, and ascites. All medication was immediately discontinued and the rice diet started. Five weeks later the transverse diameter of the heart was 3 mm. larger, but the patient had lost most of his edema and was no longer dyspneic. The patient ate one pound of rice (dry weight) and one pound of dextrose daily and gained over 7 kg. during

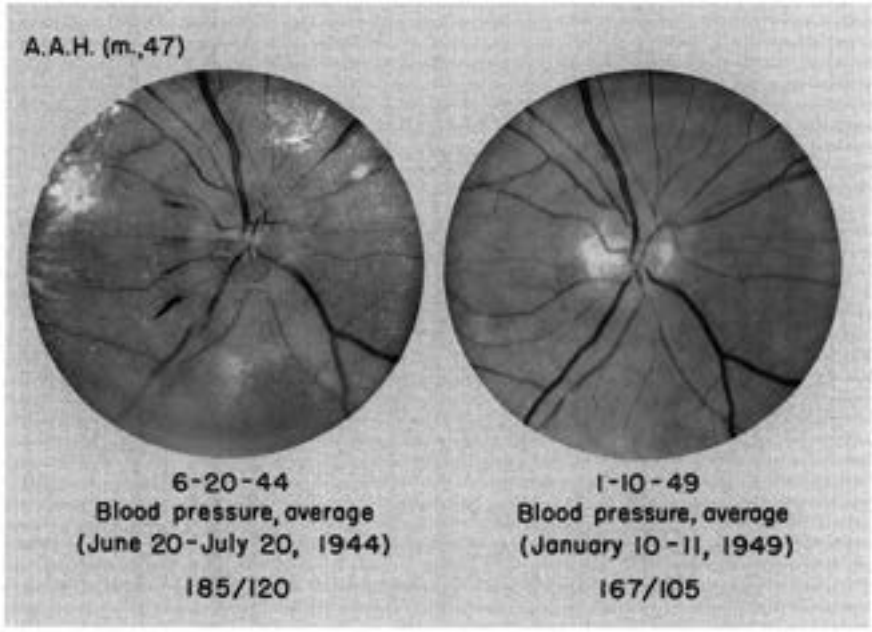

FIG. 24.

seven months in spite of the loss of edema. Four months after the start of the diet the transverse diameter of the heart had decreased from 19.8 to 17.9 cm.; after seven months from 19.8 to 17.4 cm.; after 10 months from 19.8 to 16.5 cm. No medication has been given for the past three years. The patient is feeling well and is completely asymptomatic. The transverse diameter of the heart is now 16.3 cm., which means an overall change of more than 20 per cent. I showed the patient these heart pictures, boasting about the result. In return, the patient sent me a Christmas card with pictures of his face "before and after the rice diet" (figure 22). They are perhaps not uninteresting even from our mechanistic point of view. The first photograph shows the characteristic face of a patient with advanced heart disease,

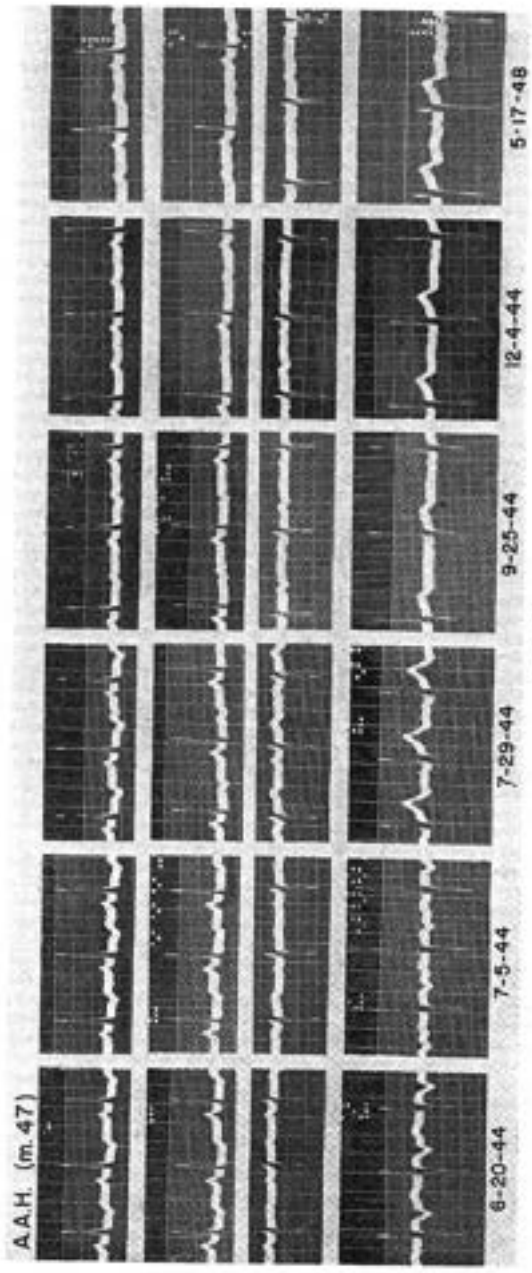

FIG. 25.

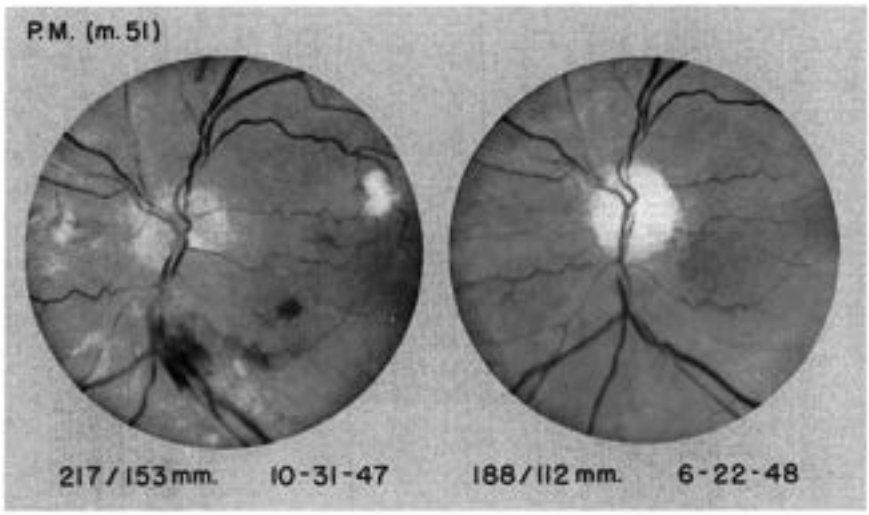

FIG. 26.

drawn, emaciated, prematurely aged, like that of a victim of starvation. The second photograph shows a well nourished, healthy man: one might say that the face has gained what the heart has lost.

Vascular retinopathy responds to the rice diet just as well as myocardial disease. The improvement of the retinopathy occurs no matter whether the blood pressure decreases or not.

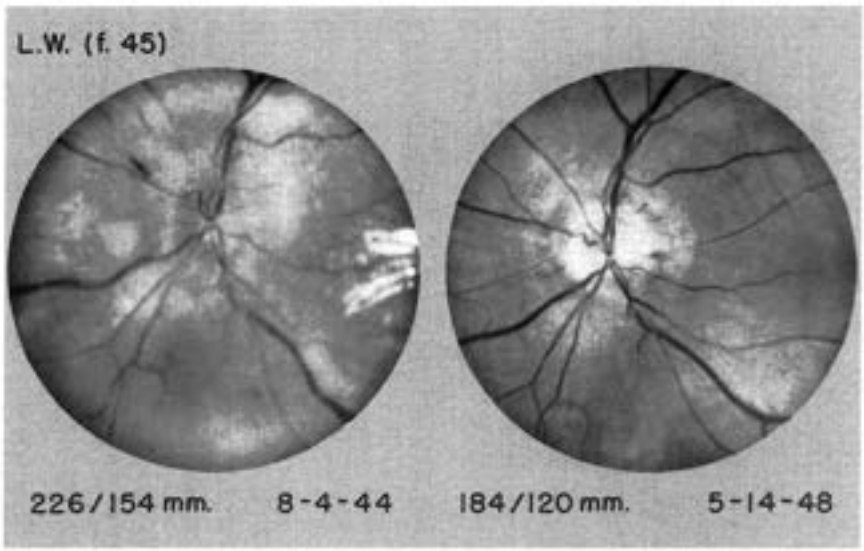

FIG. 27.

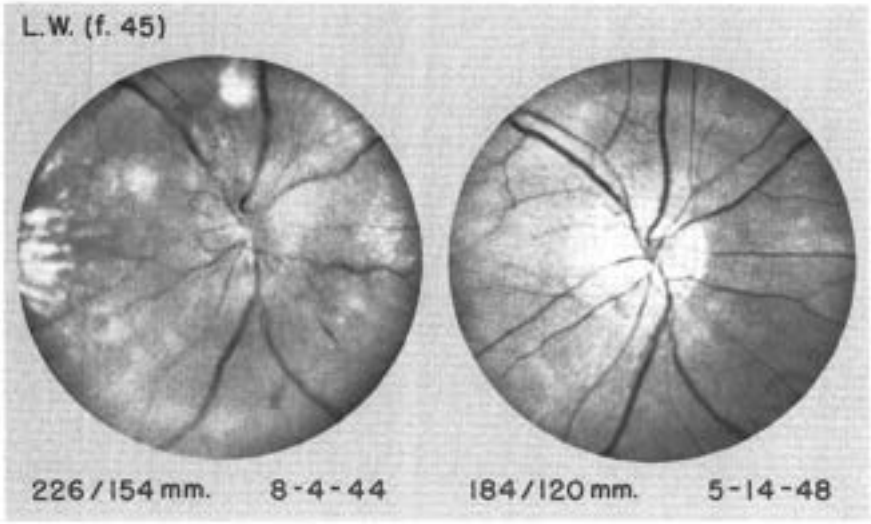

FIG. 28.

The eyeground pictures of three cases are shown as examples of the disappearance of papilledema, exudates, and hemorrhages, in spite of persistent hypertension. The first patient is a 56 year old man with hypertensive vascular disease which had been uncomplicated for 10 to 15 years. One month before he came to us he became blind in his left eye. The pictures (figure 23) show the disappearance of massive hemorrhages and exudates in 10 months on the rice diet. The patient regained his eyesight and is now well and active. The blood pressure has decreased but is still not normal.

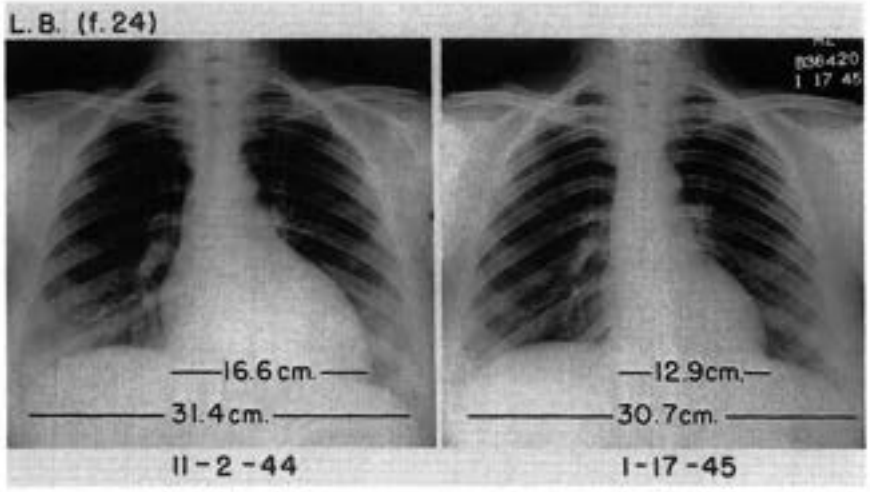

FIG. 29.

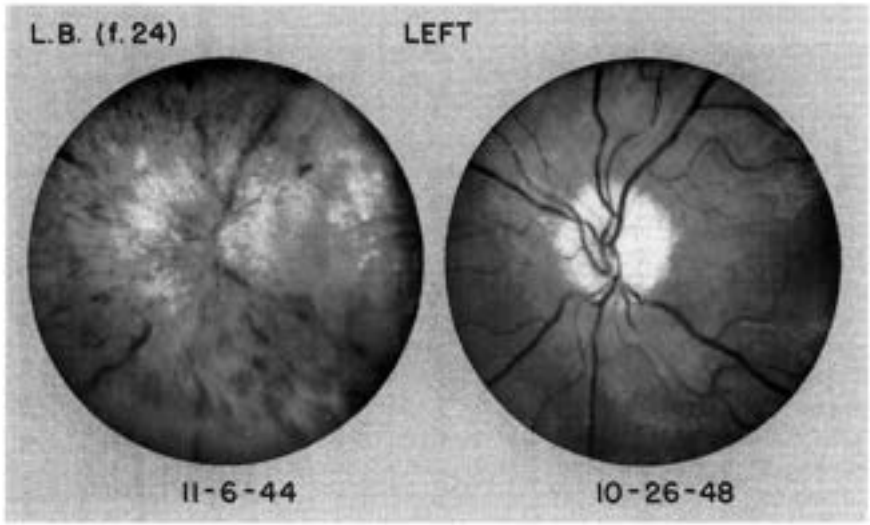

FIG. 30.

The second case is that of a man who was 47 years old when he came to us almost five years ago. He had been suffering from periodic attacks of severe headaches for years, but had known of his hypertension only for three months. He had not been conscious of any impairment of vision until I asked him to close his left eye and he found he was unable to read the headlines of a newspaper with his right eye. In one and one-half years of treatment with the rice diet, the exudates in the macula disappeared. The papilledema and hemorrhages cleared up completely and the eyesight was restored

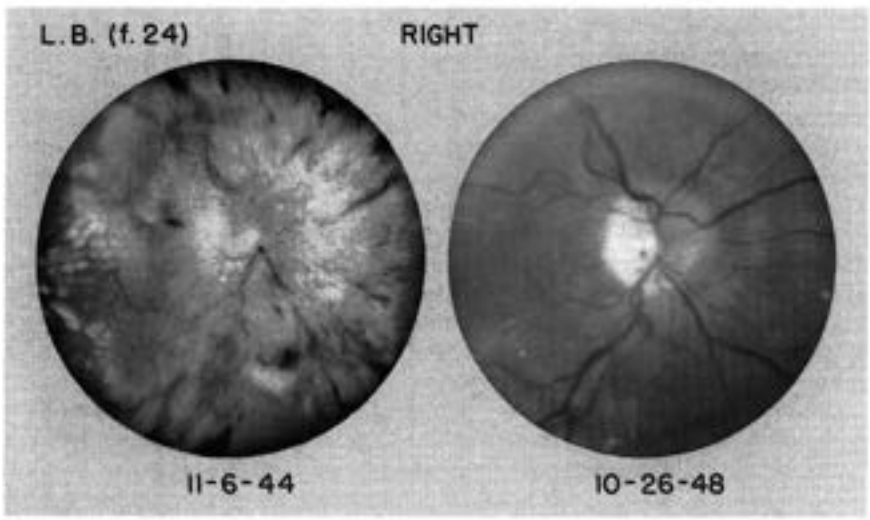

FIG. 31.

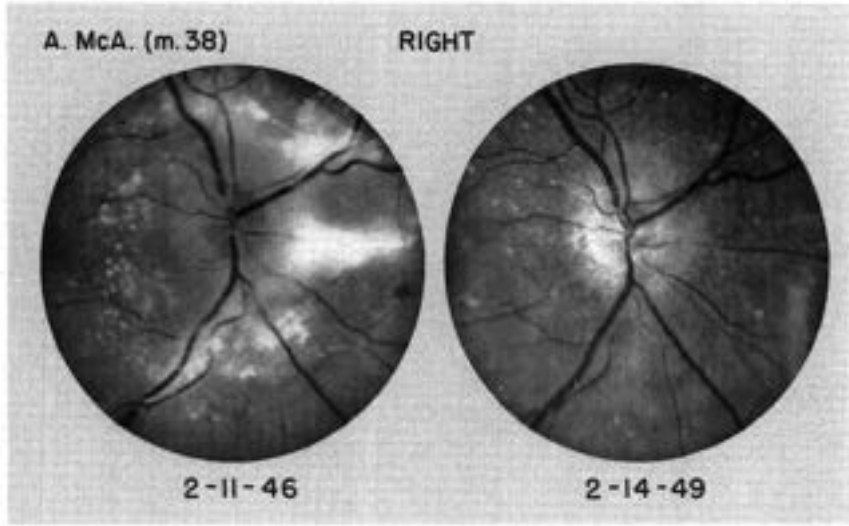

FIG. 32.

(figure 24). The heart, which was involved, also improved; the inverted T_1 in his electrocardiogram became normally upright (figure 25). The blood pressure has decreased but is not normal.

The third patient is a 51 year old man with hypertension known for 10 years. He had had progressive heart failure for seven months. There was hypertensive neuroretinopathy with papilledema, hemorrhages, and exudates, which cleared up in eight months on the rice diet (figure 26). The blood pressure did not become normal, but dropped from 217/153 to 188/112.

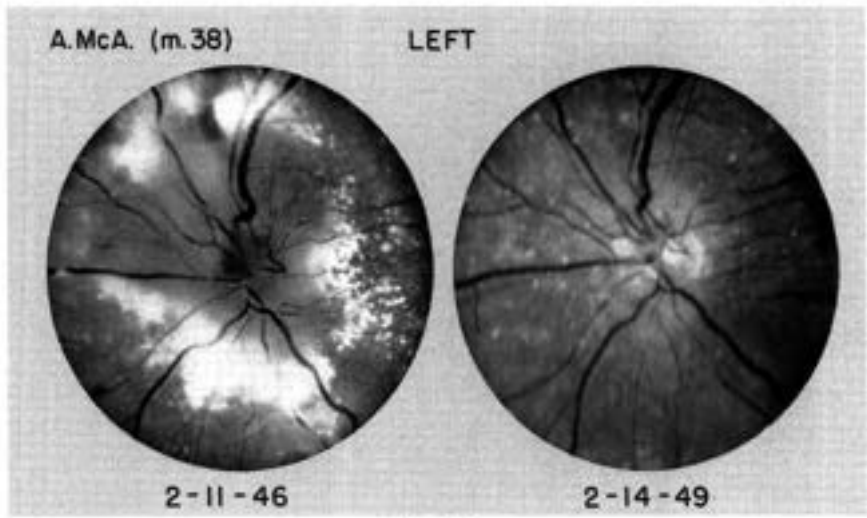

FIG. 33.

I have shown you pictures of patients who had essential hypertension with severe complications. We classify this type of hypertension as benign because of its slow course, although the term benign may lose its sense when the patient becomes blind from retinal disease or when he dies of heart failure, myocardial infarction, cerebral vascular accident or uremia. Moreover, the possibility always exists that any benign vascular disease may suddenly change into the malignant form. The last three patients whose eyeground photographs I showed you presented some of the signs said to be characteristic of malignant hypertension, the high diastolic blood pressure and

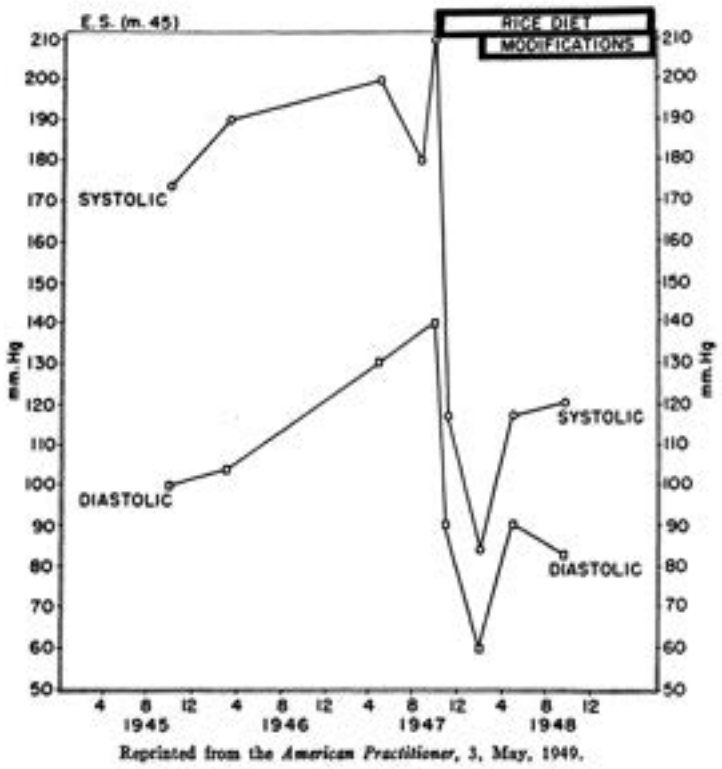

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FIG. 34.

papilledema, hemorrhages and exudates. However, the eyegrounds did not show the picture of the explosive retinopathy which we associate with true malignant hypertension.

The following photographs are shown as examples of the effect of the rice diet on patients with full blown malignant hypertension.

The first case is that of a 45 year old woman who came to us in 1944 with a history of hypertension of four months' duration, apparently malignant from the onset. The eyegrounds show the typical picture of malignant neuroretinopathy. The patient followed the strict rice diet for one

year, then a modified rice diet. The blood pressure decreased from a level of 226/154 to a level of 184/120. The retinopathy healed completely (figures 27 and 28). Not only did the patient not die but after more than four and one-half years she is up and around and has no complaints.

The second patient is a 24 year old woman who had had an uncomplicated hypertension for five years. This benign hypertension had become malignant one month before she came to us (October, 1944). In 24 days on the rice diet, the blood pressure decreased from 233/157 to 118/80. The heart became smaller in size with a change in the transverse diameter of 22 per cent in 11 weeks (figure 29). Papilledema, hemorrhages and exudates disappeared in about three months. As the eyeground pictures of October, 1948, show, the retinopathy did not recur (figures 30 and 31). The

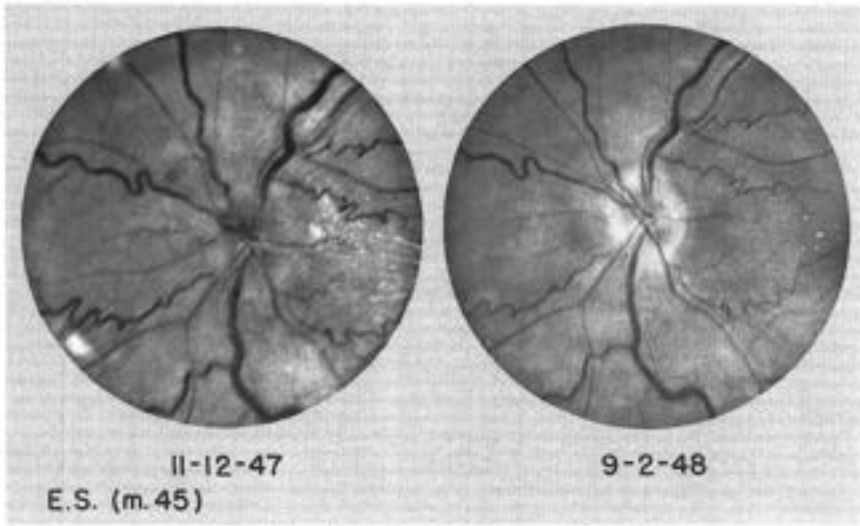

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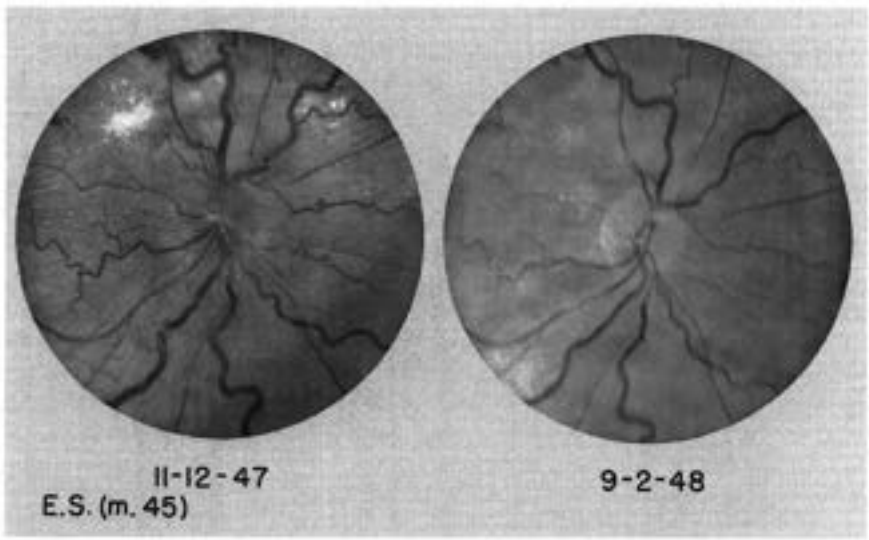
FIG. 35.

patient not only did not die of her malignant hypertension, but after more than four years is now well and doing strenuous work on her farm.

The third patient is a 38 year old man who had had hypertensive vascular disease for one year. The hypertension had been obviously malignant for about three months before he came to us. This case has been chosen as an example of a rather slow response to the rice diet. Definite improvement of the extensive neuroretinopathy was not seen until after one year. The inverted T_1 in the electrocardiogram did not become upright until after two and one-half years, and it took almost three years for the blood pressure to come down to a significantly lower level (figures 32 and 33).

As a kind of summary, let me end with a case which shows not only the success but also the possible dangers of the rice diet. The patient, a busi-

ness man from New York, had had periodic check-ups since 1932 when he was 30 years old. The blood pressure had always been normal until 1941 when a slight elevation was noted. It climbed slowly during the following years. In 1945, it was 170/100, in 1946 190/100, in the Spring of 1947 190/130. In spite of this, the patient was completely asymptomatic. Both family physician and consultant specialist advised treatment with weight reduction, rest, sedatives and restriction of smoking. In September, 1947, the patient suddenly developed a severe headache with visual disturbances and consulted an ophthalmologist who found retinal hemorrhages, exudates, and papilledema and made a diagnosis of retinopathy of malignant hypertension. Another medical specialist was consulted who found a blood pressure of 202/144, confirmed the diagnosis of malignant hypertension and sent



Reprinted from the *American Practitioner*, 3, May, 1949.

FIG. 36.

the patient to a surgeon in the New York Hospital for sympathectomy. The surgeon made the same diagnosis and recorded the same findings. After eight days of observation, a sympathectomy was scheduled for Monday, October 27, 1947. The evening before the operation, the patient decided to try the rice diet first and came to Durham. He presented the typical picture of malignant hypertension. The blood pressure was 210/140, in spite of sedatives; the eyegrounds showed extensive neuroretinopathy. On the rice diet, the blood pressure decreased rapidly. As a matter of fact, it decreased so much that after three months the patient had a blood pressure of 85/58 while lying and 60/30 while standing. A marked hypochloremia with elevation of urea nitrogen and non-protein nitrogen was found and the diet had to be modified greatly by the addition of toast, meat and all kinds of vege-

tables. The blood chemistry returned to normal and the blood pressure was regulated at a level of 110/77 within two weeks (figure 34). All the signs and symptoms of the malignant hypertension have disappeared; papilledema, retinal hemorrhages and exudates have cleared up completely; the engorged and tortuous veins are smaller in caliber and straighter (figures 35 and 36). However, not only the malignant but also the benign hypertension has disappeared. The blood pressure, which had been above normal for six years, is now (one and one-half years after the start of the rice diet) 116/76, although the patient has resumed playing his 18 holes of golf and eats a fairly liberal diet.

Ten years ago, I used to teach, what was generally taught and is still written in textbooks published as late as 1947, that the presence of advanced neuroretinopathy in malignant hypertension is an ominous prognostic sign indicative of the terminal stage of an irreparable disease. My experience with the rice diet has taught me that not only can so-called benign hypertensive vascular disease be effectively treated even when critical complications are present but also that malignant hypertension, in spite of advanced neuroretinopathy, may either be changed into the benign form of hypertension or made to disappear completely. The important result is not that the change in the course of the disease has been achieved by the rice diet but that the course of the disease can be changed.

Treatment of Heart and Kidney Disease and of Hypertensive and Arteriosclerotic Vascular Disease with the Rice Diet

Premier Congrès Mondial de Cardiologie II

TREATMENT OF HEART AND KIDNEY DISEASE AND OF HYPERTENSIVE AND ARTERIOSCLEROTIC VASCULAR DISEASE WITH THE RICE DIET

(This abstract of Dr. Kempner's talk in Paris is reprinted, with permission, from the Proceedings of the First International Heart Congress, Paris, France, 1950.)

SODIUM CHLORIDE intake affects the survival time of rats with experimental hypertension (encapsulation left kidney, nephrectomy right). When the diet consisted exclusively of rice with varying amounts of NaCl, the average survival time of the rats on 100 mg. NaCl was 57 days, on 25 mg. NaCl more than 200 days.

Protein intake affects the survival time of rats with experimental hypertension. On a diet containing a constant amount of NaCl, e.g. 100 mg., the average survival time of the rats when kept exclusively on meat was 17 days, on peas 25 days, on dog chow 28 days, on bread 38 days, on rice 57 days. When the amount of salt was reduced to 25 mg. per day, the survival time on meat was 28 days, on rice more than 200 days.

The "Rice Diet," as used in the treatment of more than 1,500 patients with heart and kidney disease and arteriosclerotic and hypertensive vascular disease, consists of nothing but rice, sugar, fruit and fruit juices. It contains in 2,400 calories less than 150 mg. of sodium, 200 mg. of chloride, 5 Gm. of fat (no cholesterol), and about 25 Gm. of protein derived from rice and fruit. The caloric intake varies according to whether weight gain or weight loss is desirable in the individual patient.

After adaptation to the rice diet, which requires about two months in a "normally regulating" person, the urinary excretion of sodium is decreased by 99.7%, that of chloride by 98.5%, that of total nitrogen by 85%, that of urea by 91%, that of uric acid by 73%, that of creatine bodies by 33%, that of inorganic phosphate by 70%, that of inorganic sulfate by 89%, and that of ethereal sulfate by 37%.

In starvation, hemoglobin, serum calcium, plasma protein, blood sugar, carbohydrate tolerance, CO_2 combining power are decreased; on the rice

diet, they are unchanged or increased. Blood non-protein nitrogen, urea, serum phospholipids, urine creatine, ammonia and organic acids are increased in starvation; on the rice diet, they are decreased. Blood volume and interstitial fluid volume are unchanged in starvation; on the rice diet, they are decreased. The nitrogen balance is negative in starvation, in equilibrium on the rice diet. In patients who are not "salt-losers," serum sodium, potassium and total base remain constant on the rice diet; the chloride decreases; the bicarbonate increases. Constant supervision, however, over a long period of time is essential to detect and to correct by proper dietary modifications any chemical imbalance (hyponatremia, hypochloremia, hyperpotassemia, alkalosis, etc.) which might develop on such a rigid diet, especially in patients with inadequate renal function.

The average NPN of 490 non-uremic patients with hypertensive vascular disease decreased from 33 mg. to 28 mg. per 100 cc. of blood after an average of 98 days, the urea nitrogen from 14 mg. to 8 mg. The cholesterol decreased in 96% of 511 patients from an average of 279 mg. to an average of 205 mg. per 100 cc. of serum after an average of 102 days on the diet.

In patients with subacute and chronic glomerulonephritis and in patients with benign and malignant hypertensive vascular disease and arteriosclerosis, the rice diet produces the following results: disappearance of edema, hydrothorax, ascites, albuminuria, azotemia, hypoproteinemia and hypercholesterolemia; reduction in blood pressure; decrease in heart size; reversion of the inverted T 1 in the electrocardiogram to upright; disappearance of retinal exudates, hemorrhages and papilledema.

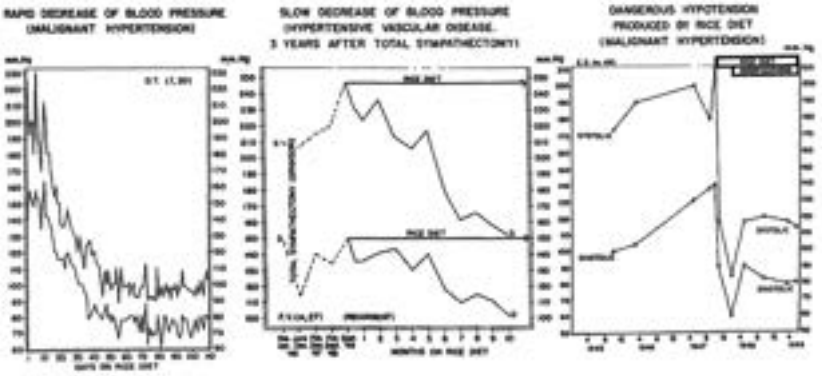
The time factor plays an important role: with an average of 37 days on the rice diet, the blood pressure improved in 61.5% of 392 patients; with an average of 149 days, the blood pressure improved in 80.5% of 385 patients.

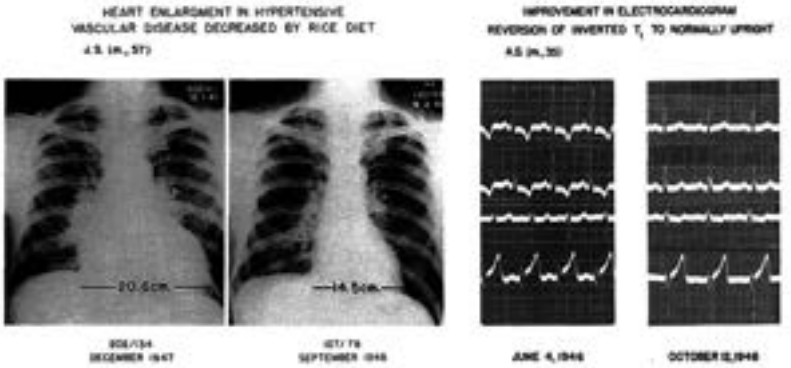
In a series of 286 patients with hypertensive vascular disease (average of 123 days on the rice diet), the heart became larger in 15 patients, the change in the transverse diameter being plus 2.6%. In the remaining 271 patients, the heart became smaller with an average change in the transverse diameter of minus 6.2% in 146 patients, of minus 14.2% in 106 patients, and of minus 24.4% in 19 patients. The decrease in heart size was not dependent on decrease in blood pressure or loss of weight.

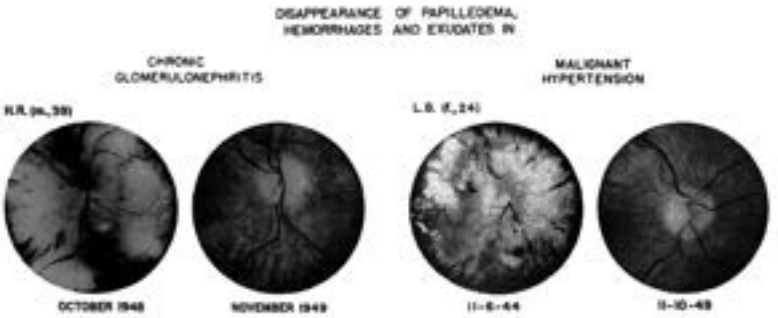
In a series of 120 patients, T 1 was inverted at the start of the rice diet. In 68 patients, it remained inverted (average period 7 months); in 52 patients, T 1 became upright (average period 10 months). In a series of 291 patients, T 1 was upright at the start of the diet. In none, did the upright T 1 become inverted (average period 11 months).

In a series of 225 patients with advanced vascular retinopathy (papil-

KEMPNER: TREATMENT WITH RICE DIET







ledema, hemorrhages or exudates), eyeground photographs were taken before and after 1 to 34 months of the rice diet. Forty-two of the 225 patients had chronic nephritis; 183 had hypertensive vascular disease. Papilledema was present in 54 of the 225 patients when they were started on the diet. In 1, it remained unchanged; in 6, it disappeared partially, in 47 completely. Hemorrhages were present in 173 patients. In 1 patient, they increased; in 9, they remained unchanged; in 44, they disappeared partially, in 119 completely. One patient who had hemorrhages but no exudates before treatment developed an exudate while on the diet. Exudates were present in 180 patients when they were started on the diet. In 3, they increased; in 13, they remained unchanged; in 61, they disappeared partially, in 103 completely.

Nitrogen Balance on Rice Diet

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NITROGEN BALANCE ON RICE DIET[1]

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(Submitted for publication October 7, 1949; accepted, December 5, 1949)

The nitrogen excretion in the urine of 52 patients with hypertensive vascular disease or nephritis who followed the rice diet for one to 14 days, averaged, according to Kempner (1), 4.83 Gm. daily. In 46 patients who followed it for 15 to 30 days, the average was 3.6 Gm., in 26 patients on the diet for one to two months, 2.93 Gm. and in 32 patients on the diet for a period longer than two months, the average was 2.26 Gm. These were all hospital patients.

Schwartz and Merlis (2) determined the nitrogen excretion of five physically healthy persons and of one patient with multiple sclerosis who had followed the rice diet for eight days, and of one patient with severe hypertension who had been on the diet for 90 days. The nitrogen excretion in the urine of these six people after they had been on the diet three to eight days averaged 4.90 Gm. daily: 5.15 Gm. on the third day, 4.86 Gm. on the sixth, and 4.68 Gm. on the eighth day. The patient who followed the diet for 90 days had a urinary nitrogen excretion of 3.81 Gm. on the 90th day. The average nitrogen output in the stool after three to eight days was 1.17 Gm., after 84 to 90 days 1.49 Gm. The caloric intake in each case was 2289 calories; the nitrogen intake, according to analysis, was 2.63 Gm. per day. Schwartz and Merlis found that under these circumstances all their patients were in negative nitrogen balance. The average nitrogen deficit after eight days was 3.22 Gm., the nitrogen deficit after 90 days was 2.67 Gm. N per day.

Currens and his associates (3) reported on nitrogen balance tests in two hypertensive patients who were on the rice diet. The first patient, during the first week on the diet, showed a negative nitrogen balance of 5 Gm. per day; the second, after three months, showed a negative balance of 1 Gm. per day.

We have examined the nitrogen balance in 11 patients with hypertensive vascular disease after 15 to 220 (average 89) days on the rice diet. One patient was examined after a period of 80 days and again after a period of 170 days. Only male subjects were used. Patients who are not able to eat the rice diet, as happens not infrequently in uremia or after cerebral vascular accidents, are not suitable test subjects for this particular problem. Otherwise, the severity of the vascular disease did not play any role in the selection of the patients for the balance test. Ten of the test subjects had been improving on the diet, or at least their disease had not progressed; one patient (test 10 in Table I) had had a fresh myocardial infarction some weeks before the test. None had malignant hypertension.

One patient (test 10 in Table I) was in the hospital during the test, the others were up and around, staying in hotels or private homes but taking their meals at one of two places where the rice diet is prepared under supervision. The patients followed the same diet that they had been on for some weeks. In order to get an unmodified picture of the metabolic state of each patient, individual variations (within the range permitted by the regime) in regard both to diet and to physical activity remained unchanged. This procedure has the theoretical objection that it does not allow continuous observation of food intake and of stool and urine collections. (Check of a complete urine collection by creatinine determination is not reliable. In patients on the rice diet, the excretion of creatinine and total creatine bodies decreases [4].) Additional food intake would influence the result of the balance determination in a negative direction, incomplete stool and urine collections in a positive direction.

These studies were not carried out in a metabolic ward. This nonconventional method of carrying out balance studies seemed practical for the following reasons: *1.* The patients selected for this study were all professional men or business executives. At a considerable financial sacrifice they had moved to Durham for three months to

[1] This work was aided by a grant from the U. S. Public Health Service.

find out whether the rice diet would modify their vascular disease. They were interested in their diet and aware of the fact that the outcome of the test was of decisive importance for the further management of the diet. *2.* The degree of cooperation during the days preceding and following the test was determined by a study of the urinary excreation of Na and Cl. On this diet the excretion of Na and Cl in the urine drops to very low levels. Any additions to the diet are reflected quickly in increased excretion of these electrolytes. The excretion of Na and Cl in these patients before, during, and after the test indicated strict adherence to the diet. *3.* All of these patients had been under careful observation before the test, and all were accustomed to eating a fixed diet and collecting their specimens.

TECHNICAL METHODS

A special technician who was present at every meal and who also collected the specimens, was in charge of each patient. The food for each patient was weighed and an equal amount of the same food or food preparation taken for analysis. Care was taken that non-edible parts such as cores, kernels and fruit skins were weighed and subtracted in both portions. The single items of each meal were combined on a percentage basis. After dilution with an equal amount of 10% NaCl solution which served for rinsing purposes and helped to produce a homogeneous suspension, they were thoroughly blended in a Waring blender. In an aliquot portion of the resulting slurry the nitrogen was determined by a semimicro modification of the Kjeldahl method (5, 6), using a modification of the Arnold-Gunning mixture (7, 8) for digestion and 0.02 Normal hydrochloric acid for titration. All analyses were made at least in duplicate.

Urine nitrogen determinations were made on 24-hour collections started after the first meal of the test period (the bladder having been emptied before the meal) and finished on the morning of the fifth day before breakfast. The urine bottles contained 3 cc. of concentrated nitrogen-free sulfuric acid in order to prevent loss of ammonia. The determinations (using the same method as for the food) were done on each 24-hour collection as soon as it was completed.

The stool collections, starting at midnight after the first day of the test period, were continued through four 24-hour periods. The total food intake of these patients as well as the protein intake had been constant for a long time before the test was started. It was therefore unnecessary to use indicators to mark more closely the connection between the food eaten and the respective stool portions. The stools were deposited in weighed cardboard containers which were kept in large thermos jars. Immediately after being deposited, they were surrounded by dry ice, and thawed only for the determinations. They were weighed, diluted with a known quantity of water and thoroughly treated in a Waring blender. An aliquot amount of the slurry was used for the determination which was done with the same method as that employed for food slurries and urine.

An example of the nitrogen content of a 24-hour intake is given in Table II. The values obtained by our determinations on composites of the single meals were similar to the sum of the values calculated for the individual items from the tables of McCance and Widdowson (9). This was true throughout all the tests. The estimation of the nitrogen balance was based only on our own determinations.

RESULTS

Results and details of the tests are given in Table I. All patients, who were tested in this series, are included.

The result of the 12 tests (11 patients) shows an average positive nitrogen balance of +0.25 Gm. daily. In five patients the balance was negative, in seven positive. The highest negative figure was 0.78 Gm. (intake: 1866 calories); the highest positive figure was 1.43 Gm. (intake: 2475 calories).

The ages of the test subjects ranged from 40 to 66 years. Age was not a significant factor in the results.

The data on weight show no significant weight change in a two-weeks' period before and after the tests. An average weight loss of 5 Kg. had occurred during the first 75 days (average) of the treatment.

Patient 9 was on a modified rice diet of unknown composition for some months before coming under our supervision. In patient 10, "220 days on the rice diet" included one period of two months during which some small additions had been made to the diet. Before the balance test was begun, this patient had again been on the basic rice diet for two months.

The caloric intake varied according to the eating habits of the individual patient. Patient 2 had been asked to restrict the caloric intake during the whole period of treatment, because of marked overweight in the presence of severe coronary disease. Patient 8 had been encouraged to increase the caloric intake. The average intake of the 11 patients during the 12 test periods was 2063 calories, which is close to the figure of 2000 calories frequently quoted from Kempner's papers. A comment on this figure might be made here. Kempner writes: "The rice diet contains in 2000 calories not more than 5 Gm.

NITROGEN BALANCE
In 11 Patients with Hypertensive Vascular Disease
After Several Weeks on Rice Diet

	AGE	DIAGNOSIS	DAYS ON RICE DIET At the Time Of the Test	WEIGHT (Kg.) At Start Of Diet	WEIGHT (Kg.) Two Weeks Before Test	WEIGHT (Kg.) At Time Of Test	WEIGHT (Kg.) Two Weeks After Test	HEIGHT (cm.)	SURFACE AREA At the Time Of the Test (sq.m.)	BASAL CALORIC EXPENDITURE*	CALORIC INTAKE**	TOTAL NITROGEN Gm. N in 24 Hrs. (Averages of 4 Consecutive Days) INTAKE	OUTPUT Urine	OUTPUT Stool	OUTPUT Total	BALANCE
1	60	HCVD.	95	70.6	68.2	68.5	68.9	173	1.81	1586	1875	6.36	2.84	0.96	3.78	+0.58
2	51	HVD. Coronary Thrombosis. Arteriosclerosis. Retinal exudates.	56	83.2	77.9	75.0	74.5	168	1.92	1636	1689	3.24	2.40	1.35	3.51	-0.27
3 a	55	HVD. Cont.	80	72.0	69.8	63.5	64.5	172	1.76	1468	1956	6.12	2.82	1.69	4.58	+0.38
b	55	HVD. Cont.	170	72.0	66.3	64.5	64.6	172	1.75	1454	2345	6.16	2.13	1.90	4.03	+0.13
4	52	HVD.	86	66.8	61.8	61.8	61.8	166.3	1.67	1490	2217	6.36	1.45	1.99	3.44	+0.90
5	66	HVD. Ret. Papilledema. Hem., Exud.	80	78.6	73.1	72.7	73.2	175	1.85	1672	1866	3.91	2.67	2.04	4.69	-0.78
6	66	HVD. Cerebral Vascular Accident.	75	86.0	77.7	78.7	78.1	180.5	1.94	1687	2124	6.91	3.24	1.05	4.29	+0.62
7	59	HVD.	80	56.8	54.5	55.6	55.6	165	1.69	1382	2221	6.66	2.61	1.81	4.42	+0.24
8	56	HVD.	65	70.4	65.0	65.0	67.0	166	1.71	1472	2475	5.37	2.78	3.56	6.34	+1.03
9	59	HVD. Coronary Artery Disease	(15)	66.0	48.8	48.1	47.2	165	1.74	1442	2087	3.86	2.93	1.26	4.19	-0.33
10	64	HVD. Arteriosclerosis. Myocardial Infarction. Ret. Hem., Exud.	(120)	73.3	59.3	58.8	62.3	166	1.61	1378	2096	6.40	2.70	1.87	4.57	-0.17
11	51	HVD. Arteriosclerosis. Cerebr. Vasc. Accid.	95	71.2	72.0	72.0	71.6	174.5	1.85	1698	2084	6.55	3.30	1.21	3.51	+1.04
Av.:	56		89	72.1	67.2	66.6	67.2	169.9	1.76	1519	2063	6.37	2.57	1.55	4.12	+0.25

*calculated from BMR tests
**calculated from McCance-Widdowson, The Chemical Composition of Foods[9]

TABLE I

EXAMPLE OF FOOD INTAKE

(Taken From Test Number 3a)

FOOD	Weight (Gm.)	CALORIES Calculated*	NITROGEN (Gm.) Calculated*	NITROGEN (Gm.) Determined
Breakfast:				
Rice (boiled)	199	243	.74	
Prunes (in syrup)	85	86	.12	
Grapefruit	227	50	.22	
Orange Juice	227	86	.22	
Parched Rice	21	76	.23	
Additional Sugar	35	138	-	
			1.53	1.43
Lunch:				
Rice (boiled)	170	207	.63	
Apricots (in syrup)	28	17	.02	
Pears (in syrup)	170	107	.10	
Peaches (in syrup)	85	56	.05	
Orange Juice	227	86	.22	
Parched Rice	57	206	.62	
Additional Sugar	30	118	-	
			1.64	1.56
Dinner:				
Rice (boiled)	85	104	.31	
Pineapple (in syrup)	114	72	.05	
Apple (baked)	88	34	.04	
Grapes	57	36	.06	
Orange Juice	227	86	.22	
Parched Rice	43	155	.47	
Additional Sugar	35	138	-	
			1.15	1.29
TOTAL		2101	4.32	4.28

*calculated from McCance-Widdowson, The Chemical Composition of Foods[9]

TABLE II

of fat and about 20 Gm. of protein derived from rice and fruit and not more than 200 mg. of chloride and 150 mg. of sodium." This does not mean that the caloric supply is fixed at 2000 calories. It varies according to the varying indications for weight gain or weight loss in the individual patient. The nitrogen and total caloric intake can be controlled by altering the rice and sugar fractions of the diet.

The total nitrogen intake of the 11 patients averaged 4.37 Gm. per day. This represents a protein intake of about 26.4 Gm. if one estimates the protein of all foods except rice by multiplying the total nitrogen by 6.25 and that of rice by multiplying the total nitrogen by 5.95. Since the proteins of cereals contain more nitrogen than is found on the average in other proteins, the nitrogen in the rice protein represents more than the usual 16% (10).

Urine nitrogen excretion averaged 2.57 Gm., stool nitrogen 1.55 Gm. per day. The assumption made by some investigators (11) that there may be an additional nitrogen loss through sweat, skin particles or hair, has been questioned (12). We omit this factor, especially since two of our patients had some intestinal irritation during the time of the test (Patients 5 and 10), which means that the stool nitrogen content in these cases was probably slightly higher than it would have been without this disturbance. (In spite of this, in order to avoid any selection, we did not exclude these patients.)

The basal caloric expenditure of the patients was calculated from BMR tests. The BMR was elevated in Patient 4 (+ 29%), slightly elevated in Patient 2 (+ 5%); it was slightly decreased in all the others, but did not exceed − 10%, (average in nine patients: − 6%).

DISCUSSION

The nitrogen balance of all 11 patients was close to nitrogen equilibrium on either the positive or the negative side. This may fluctuate slightly in individual patients. But since the test subjects were taken at random and had been on the rice diet for different periods of time when the balance tests were done, it may be assumed that these tests give the usual picture of the nitrogen balance after several weeks on the rice diet.

Until an equilibrium is reached, there is a phase of adaptation with definite negative balances which vary considerably with the individual patient. Approximate figures of this nitrogen loss, based on the average nitrogen excretions of 26–52 patients reported by Kempner (1), are: for the first 14 days a total of 27 Gm., for the next 16 days of 11 Gm., for the next 30 days of 1 Gm. This would amount to a loss of 39 Gm. of nitrogen during the first two months. (There was a positive balance of a total of 10 Gm. for the 30 days of the third month which would reduce the total nitrogen loss to 29 Gm. if the third month is included.) Thirty-nine Gm. of nitrogen means less than 2.5% of the total nitrogen content of a 66.6 Kg. person.

Negative nitrogen balances of the degree found in our series are probably of minor importance for the period of time during which the strict rice diet is usually necessary. E. Abderhalden determined the nitrogen balance of a physician (13) who lived for four years on a 25 Gm. protein diet after having been on a 38–40 Gm. protein diet for the previous 15 years. The test subject was feeling well and strong, and during some of the test periods he was extremely active physically (mountain climbing in Switzerland). The balances were close to equilibrium with an average of − 0.07 Gm. nitrogen per day in the seven periods of seven to 13 days each. The strenuous exercise did not influence the nitrogen balance.

A negative balance of − 0.39 Gm. per day after an average of 91 days on the rice diet—the average of the five negative balance values in our series—would mean that in 20 days less nitrogen is lost from the body than in one single day of fasting. (According to Benedict [14] the daily nitrogen loss is relatively constant during a fasting period of 31 days, the average being 8.94 Gm. per day.)

SUMMARY

Twelve nitrogen balance tests on 11 patients after an average period of 89 days on the rice diet showed that nitrogen intake and nitrogen output were close to equilibrium in all 12 test periods. Five balances were slightly negative, seven slightly positive. The average of the five negative balances was − 0.39 Gm., the average of the seven positive balances + 0.70 Gm. per day. The average of the results of all the 12 tests was a positive balance of

+ 0.25 Gm. The significance of a slightly negative balance is discussed.

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Effect of the Rice Diet on the Serum Cholesterol Fractions of 154 Patients with Hypertensive Vascular Disease*

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EITHER hypercholesterolemia or hypertensive vascular disease or a combination of both seems to play an important role in the development of atherosclerosis. Close association between atherosclerosis and a high concentration of cholesterol in the serum has been observed in patients with diabetes mellitus,[1–4] chronic nephritis,[5,6] hypothyroidism[7–9] and xanthomatosis.[10–12] High serum cholesterol concentrations have also been found in patients with coronary artery disease,[13,14] peripheral arteriosclerosis,[15] generalized arteriosclerosis,[16] exudative vascular retinopathy[17] and hypertensive vascular disease.[18–20]

Numerous studies have been made to answer the question whether or not the serum cholesterol concentration can be altered by diet. In fasting, the serum cholesterol rises in men and in animals (swine, cat and guinea pig).[21] Total and esterified cholesterol increase in a roughly parallel way. Following the ingestion of food at the termination of the fast, the cholesterol bound as ester drops more rapidly than does the total cholesterol.

Slightly higher cholesterol values were obtained in four normal women when the diet contained 3.1 gm. of cholesterol per day than when 0.77 gm. of cholesterol per day was given.[22] The values were higher when the cholesterol was administered in egg yolks than in butter containing pure cholesterol. Total serum cholesterol figures as high as 315 mg. per 100 cc. and 600 mg. per 100 cc. were reported in two Arctic explorers who ate a diet very high in fat for twelve months.[23] The serum cholesterol values dropped to 218 mg. per 100 cc. and 200 mg. per 100 cc. when, after their return to a temperate climate, they resumed a diet with a lower fat content.

When egg yolk powder (100 gm. per day) was added to a constant 2,500 calorie diet given to eight patients with arthritis, the serum cholesterol increased by 50 to 170 mg. per 100 cc. within six to ten weeks. In two nephritics who were treated in the same way the serum cholesterol increased by 104 and 218 mg.[24] Rabinowitch[25] found that in diabetics, with the institution of a high-carbohydrate, low-calorie diet, an immediate and sustained decrease of plasma cholesterol occurred.

Steiner[26] reported: "Nine individuals were placed on diets high or low in fat and cholesterol. They were first given a diet containing 300 Gm. of fat for six weeks and then without interruption placed on a diet containing less than 50 Gm. of fat. In five of the nine patients there was no increase in total serum cholesterol during the period of high fat feeding. In four cases a slight rise seemed to occur. Three of the patients subsequently were placed on the high fat diet for a second period but this time 10 Gm. of cholesterol in 200 cc. of milk was added to the regimen. No significant change resulted in the serum cholesterol levels. The serum cholesterol levels of the patients on a low fat diet were no different from those observed during the control period."

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Keys[27] found that young men, aged eighteen to twenty-five, whose diet contained 1.49 gm. of cholesterol per week had the same serum cholesterol concentration as those whose diet contained 4.20 gm. Average serum cholesterol values ranged between 165 and 184 mg. In older men aged forty-five to fifty-five the average range was between 242 and 258 mg. There was no difference in the serum cholesterol concentration when the diet contained 1.62 gm. or 4.81 gm. of cholesterol per week. Keys summarized, "Neither in the younger nor older men is there any relation between blood cholesterol and the habitual intake of cholesterol, in spite of the fact that the differences in the latter are large."

Kempner examined the effect of the rice diet on the serum cholesterol concentration of patients with kidney disease or hypertensive vascular disease. The rice diet contains in 2,000 calories not more than 5 gm. of fat and about 20 gm. of protein derived from rice and fruit, and not more than 200 mg. of chloride and 150 mg. of sodium. A marked reduction of the total[28–30] and esterified[30] cholesterol concentration in the serum of more than 90 per cent of the patients was found.

This paper reports 401 determinations of free and esterified serum cholesterol on 154 patients with hypertensive vascular disease. The effect of the rice diet on the cholesterol fractions was studied after varying periods of time.

METHODS

Total serum cholesterol was determined according to Bloor's method[31] adapted to the photoelectric colorimeter. The Sobel and Mayer[32] modification of the Schoenheimer-Sperry method for free cholesterol was used. All determinations were made in duplicate.

One hundred five patients were male; forty-nine patients were female. Twenty-nine of the women were fifty years of age or older. The ages of the patients ranged from nineteen to seventy years, average fifty-one years.

All patients with nephritis or with fasting blood sugar levels above 115 mg. per 100 cc. were excluded. None of the patients had clinical thyroid disease. Basal metabolic rate was obtained on sixty-nine patients. In fifty-five of these, values were between +15 per cent and −15 per cent of normal. Six had a basal metabolic rate higher than +15 per cent, average +20%; the average total cholesterol of these patients before treatment was 300 mg. per 100 cc. of serum. Eight patients had a basal metabolic rate lower than −15 per cent, average −21 per cent; the average total cholesterol of these patients before treatment was 317 mg. per 100 cc. of serum.

One hundred twenty-two of the 154 patients had cardiac involvement at the time they were first seen. Any one or more of the following is taken as evidence of cardiac involvement: radiologic report of cardiac enlargement, inversion of T_1 or diphasic T_1 in the electrocardiogram, bundle branch block, auricular fibrillation or myocardial infarction.

Fifty-six patients had hemorrhagic vascular retinopathy. Fifty-five had exudative vascular retinopathy. Ten had papilledema. Fifty-six patients had renal involvement. A PSP excretion of less than 50 per cent in two hours, a blood non-protein nitrogen higher than 45 mg. per 100 cc., or proteinuria of more than 0.5 gm. per L. is taken here as evidence of renal involvement. Twenty-one patients had had cerebrovascular accidents or convulsions. Arcus senilis was noted in thirty-four patients.

RESULTS

The mean total cholesterol of 154 patients before treatment was 272 ± 4.4 mg. per 100 cc. of serum. The mean free cholesterol of all 154 patients before treatment was 76.2 ± 1.5 mg. per 100 cc. of serum. The mean esterified cholesterol before treatment was 195.8 ± 3.2 mg. per 100 cc. of serum. The mean ratio of free to total cholesterol before treatment was 28.0 ± 0.25 per cent. One hundred twenty-five patients had a serum cholesterol of more than 220 mg. per 100 cc. of serum before treatment, average 289 mg. per 100 cc. Twenty-nine patients had a serum cholesterol of 220 mg. per 100 cc. or less before treatment, average 199 mg. per 100 cc.

Total and free serum cholesterol was determined in the serum of thirty-six normal individuals whose ages ranged from seventeen to forty-seven years. The mean total

cholesterol was 198 ± 6.2 mg. per 100 cc. of serum. The mean free cholesterol was 54.9 ± 2.1 mg. per 100 cc. of serum. The mean ratio of free to total cholesterol was 27.7 ± 0.6 per cent.

Table I summarizes the changes in total and free cholesterol and in the ratio of free to total cholesterol over varying periods of time. The results of the calculations for significance are shown.

TABLE I

AVERAGE CHANGES IN THE SERUM CHOLESTEROL FRACTIONS AFTER VARIOUS PERIODS OF RICE DIET

	Time in Days	No. of Observations	Mean Serum Cholesterol (mg./100 cc.)		Average Change	Standard Error	t Value for Mean Difference
			Before Treatment	After Treatment			
Total Cholesterol	5–30	60	270 ± 7.9	209 ± 6.2	−61	4.76	12.82
	31–60	80	271 ± 6.1	212 ± 5.9	−59	4.81	12.27
	61–120	73	271 ± 7.0	202 ± 5.8	−69	4.60	15.00
	121–240	34	272 ± 8.0	191 ± 7.2	−81	7.04	11.51
Free Cholesterol	5–30	60	77.2 ± 2.7	64.1 ± 2.4	−13.1	1.57	8.34
	31–60	80	75.7 ± 2.2	64.2 ± 2.1	−11.5	1.81	6.35
	61–120	73	75.6 ± 2.3	59.7 ± 1.8	−15.9	1.56	10.19
	121–240	34	76.7 ± 2.9	55.5 ± 2.2	−21.2	2.60	8.15

	Time in Days	No. of Observations	Mean $\frac{\text{(Free Cholesterol} \times 100)}{\text{(Total Cholesterol)}}$		Average Change	Standard Error	t Value for Mean Difference
			Before Treatment	After Treatment			
Ratio	5–30	60	28.5 ± 0.4	30.4 ± 0.4	+1.9	.47	4.04
	31–60	80	28.0 ± 0.4	30.2 ± 0.4	+2.2	.47	4.68
	61–120	73	28.0 ± 0.3	29.7 ± 0.4	+1.7	.50	3.40
	121–240	34	28.2 ± 0.8	29.0 ± 0.4	+0.8	.84	0.95

It appears from these data that the total cholesterol decreases rapidly and that the decrease is maintained when the patient follows the rice diet, that the free cholesterol decreases at a slower rate than does the total cholesterol so that the ratio of free to total cholesterol rises accordingly.

However, there is a difference in the rate of decrease in free cholesterol between those patients who initially had hypercholesterolemia and those whose initial total cholesterol was normal. In the patients who had an initial total cholesterol of 220 mg. or less per 100 cc. of serum the ratio of free to total cholesterol did not change. In those patients who had an initial total cholesterol of 221 mg. or more per 100 cc. of serum there was a definite rise in the ratio of free to total cholesterol. (Table II.)

COMMENT

We do not know all the sources from which cholesterol is derived. It has been shown that cholesterol can be synthesized[33–35] and destroyed[35] in the animal body. Bloch, Borek and Rittenberg[36] found with the Warburg apparatus that intact liver cells under

aerobic conditions produced cholesterol from acetate containing D_2O and C^{13}. Cholesterol can also be synthesized from acetone.

We do not know the mechanism by which the normal cholesterol level in the serum is maintained and why, in the process of aging and in certain diseases, the serum concentration rises. Neither do we know under what conditions hypercholesterolemia causes atherosclerosis.

Further studies will be needed to show why hypercholesterolemia is reduced by the rice diet. It may be due to the low fat or to the low cholesterol content of the diet, or to both. The low protein content of the diet may be of importance. The change in fluid balance, or the low sodium or low chloride content, or the relative alkalinity of the diet may possibly play a role. The slight but definite rise in the ratio of free to total cholesterol on the rice diet calls attention to the liver. There could be decreased blood flow through the liver, decreased excretion of free cholesterol by the liver or decreased production of cholesterol or impairment of esterification.

It is known that feeding of cholesterol causes hypercholesterolemia and atherosclerosis in rabbits.[37–39] Atherosclerosis which sometimes is found "spontaneously" in chickens can be accelerated by cholesterol feeding.[40] Recently Steiner and Kendall[41] have produced hypercholesterolemia and atherosclerosis in dogs by combined feeding of thiouracil and cholesterol. McMeans and Klotz[42] have found regression of the fatty streaks in the arteries of rabbits when the cholesterol was removed from the diet. A low fat diet can retard atherosclerosis in the chicken.[43] Leary[44] has stated that cholesterol deposits in the atheromatous lesions in man may undergo lysis. Wilens[45] has observed a relative absence of atherosclerosis in persons dying of wasting diseases and concludes that "significant resorption of previously formed atheromatous lesions may occur during periods of marked weight loss."

So far there are no figures available which show to what extent lowering of the serum concentration of free and esterified cholesterol in man prevents, retards or arrests atherosclerosis or causes a regression of lesions already present. However, of all the diets used in the treatment of hypertensive vascular disease the rice diet is the lowest in fat and in cholesterol, and has reduced hypercholesterolemia in 98.4 per cent of the 125 patients whose initial total serum cholesterol was more than 220 mg. per 100 cc. In eighty-two of these patients (65.6 per cent) the serum cholesterol fell to normal values (220 mg. per 100 cc. or less).

TABLE II

EFFECT OF RICE DIET ON SERUM CHOLESTEROL FRACTIONS IN TWENTY-NINE PATIENTS WITH AN INITIAL "NORMAL" CHOLESTEROL CONCENTRATION AND 125 PATIENTS WITH AN INITIAL CHOLESTEROL LEVEL ABOVE "NORMAL"

Initial Total Cholesterol (mg. per 100 cc. of serum) No. of Patients	150–220 mg. 29	221–463 mg. 125	150–463 mg. 154
Total Cholesterol (mg. per 100 cc. of serum)			
Before treatment	199 ± 3.17	289 ± 4.07	272 ± 4.41
After treatment	166 ± 4.85	209 ± 3.99	201 ± 3.63
Free Cholesterol (mg. per 100 cc. of serum)			
Before treatment	57.2 ± 1.76	80.6 ± 1.56	76.2 ± 1.50
After treatment	47.4 ± 1.55	62.5 ± 1.39	59.7 ± 1.26
Ratio $\frac{(\text{Free Cholesterol} \times 100)}{(\text{Total Cholesterol})}$			
Before treatment	28.7 ± 0.77	27.9 ± 0.26	28.0 ± 0.25
After treatment	28.7 ± 0.49	29.8 ± 0.27	29.6 ± 0.24

CONCLUSIONS

The rice diet causes a decrease in total, free and esterified serum cholesterol in patients with hypertensive vascular disease.

Of the 154 patients studied, 125 had a total serum cholesterol concentration greater than 220 mg. per 100 cc. before the rice diet was started. Twenty-nine patients had a serum cholesterol of 220 mg. per 100 cc. or less.

The total cholesterol and the esterified cholesterol decreased in 149 of the 154 patients. The free cholesterol decreased in 140 patients. There was no change in the mean ratio of free to total cholesterol in those patients whose initial total cholesterol was 220 mg. per 100 cc. of serum or less. There was an increase in the mean ratio of free to total cholesterol in those patients whose initial total cholesterol was 221 mg. per 100 cc. or more.

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The Treatment of Retinopathy in Kidney Disease and Hypertensive and Arteriosclerotic Vascular Disease with the Rice Diet

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THE TREATMENT OF RETINOPATHY IN KIDNEY DISEASE AND HYPERTENSIVE AND ARTERIOSCLEROTIC VASCULAR DISEASE WITH THE RICE DIET

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Advanced retinopathy with papilledema, hemorrhages or exudates is supposed to be in nephritis, hypertensive vascular disease and arteriosclerosis, an ominous sign indicative of irreparable damage to the blood vessels. This is true unless radical treatment is begun in time to be effective before the terminal cerebral, cardiac or renal break-down occurs. The rice diet has proved to be effective not only in arresting hemorrhagic and exudative retinopathy and neuroretinopathy but in reversing these pathological processes to such a degree that even patients who could no longer distinguish any objects have later been able to read fine print.

The rice diet is an unpleasant and monotonous diet. It consists of nothing but rice, fruit and sugar. It must be followed for many months before its full effects are obtained. It may become ineffective if it is modified by so-called "minimal" additions. It is dangerous and may cause serious electrolyte imbalance unless the patient is carefully supervised and frequent checks of blood and urine chemistry are made. It contains less sodium, less chloride, less protein and less fat than any other salt, protein or fat restricted diet. This is reflected by the changes in the urinary excretion of patients on the rice diet; there is a decrease in sodium chloride, total nitrogen, urea, uric acid, creatine bodies, inorganic phosphate, inorganic sulfate and ethereal sulfate. After about two months on the diet, the urinary excretion of total nitrogen is decreased by 85 per cent, that of urea by 90 per cent, that of chloride by 96 per cent, and that of sodium by 99 per cent. (The sodium chloride concentration per 100 cc. of urine is less than 15 mg.; on an ordinary diet it is about 600 mg.).

There are fundamental chemical differences between the effects of starvation and of the rice diet: Hemoglobin, red bloods cells, calcium and to-

tal protein, A/G ratio, sugar, carbohydrate tolerance and CO_2 combining power in the blood are decreased in starvation. On the rice diet, they are unchanged or increased. The blood non protein nitrogen and urea nitrogen are increased in starvation. On the rice dier, they are decreased. Blood volume and interstitial fluid volume are unchanged or increased in starvation. On the rice diet, they are decreased. The nitrogen balance is negative in starvation. On the rice diet, it is in equilibrium.

The rice diet causes a marked decrease in abnormally elevated serum cholesterol. A high cholesterol concentration in the serum is frequently found in arteriosclerosis, coronary artery disease, hypertensive vascular disease and exudative vascular retinopathy, as well as in disease of the lens and vitreous body, in uncontrolled diabetes mellitus and in the nephrotic stage of nephritis. In about 150 patients who started the rice diet with a normal serum cholesterol, the average decrease was 15 mg. per 100 cc. of serum after an average period of 120 days. In 360 patients with a hypercholesterolemia before the rice diet, the average decrease was 74 mg. after an average period of about 100 days.

The acid base equilibrium is changed on the rice diet. Sodium and chloride are excluded to about an equal degree, but the acid metabolites, phosphate and sulfate, are markedly reduced, and the basic element, postassium, is increased, as compared to an ordinary diet.

Any of the following criteria were used to determine whether or not the diet was beneficial: decrease in the sum of systolic and diastolic blood pressure of at least 40 mm. Hg.; reduction in heart size with change in the transverse diameter of 18 per cent or more; change in the T wave of the electrocardiogram from inverted to upright; disappearance of papilledema, hemorrhagic and exudative retinopathy.

The diet proved beneficial in about 60 per cent of the patients with hypertensive vascular disease or with primary kidney disease who followed it for an average of about 40 days and in about 80 per cent of those patients who followed it for an average of about 150 days.

It is generally assumed that cardiac enlargement ans T_1 inversion in hypertensive vascular disease and chronic glomerulonephritis are caused by the high blood pressure. However, marked reduction in heart size reversion of the inverted T_1 to normally upright has occurred in patients on the rice diet in spite of the fact that the blood pressure remained at a constant high level or was only insignificantly reduced.

Advanced retinopathy is a not infrequent manifestation of severe nephritis, arteriosclerosis arn hypertensive vascular disease. For instance, of 1000 patients with hypertensive vascular disease treated by the rice diet, 310 had papilledema, hemorrhages or exudates, either singly or in combination.

A few histories will be reported briefly. They were not chosen from the point of view of the best management of the diet nor of the most favorable therapeutic results, but because they are instructive in the discussion of the question: Is there any direct relation between the appearance and disappearance of vascular retinopathy and the appearance and disappearance

of any of the other manifestations of hypertensive vascular disease, arteriosclerosis and nephritis?

The first patient (H. R.) was a 39 year old man in the terminal stage of chronic glomerulonephritis. In 1919, at the age of 10, he had proteinuria and hematuria. Proteinuria (1+ to 2+) persisted. He felt perfectly well, but at a routine examination at the University, when he was 18 or 19, 4+ proteinuria was found and he was advised to leave college and rest. He rested for the next two years and since that time has led a moderately active life without physical strain.

In January, 1948, he was hospitalized because of headache and high blood pressure. "His heart was enlarged and his kidneys were not good" He was treated with theobromine, ascorbic acid and nicotinic acid. In the summer of 1948, he had had a hemorrhage. A few weeks later, he "bumped his head against a door", one night, and was unconscious for a few minutes. After that time, he had severe headaches with nausea and vomiting. The blood pressure continued to go up and there was progressive blurring of vision in both eyes. Because of this, the patient was sent to our clinic on October 1, 1948.

The blood pressure on admission was 240/140. The **right** eye showed massive papilledema and retinal edema, extensive hemorrhages and exudates. The arteries were narrow; the veins were full (Plate 1). The **left** eye showed massive papilledema; because of extensive hemorrhages and exudates, the continuity of the blood vessels was lost. The veins were full. No detail of the arteries could be made out (Plate 2).

The transverse diameter of the heart was 11.4 cm.; the chest diameter was 29.5 cm. T_1 in the electrocardiogram was upright; the angle of the electrical axis was +65° Hemoglobin was 14.3 Gm.; non protein nitrogen 114 mg., urea nitrogen 82 mg., sugar 92 mg. per 100 cc., blood; chlorides 107m Eq. per 1000 cc. serum; cholesterol 320 mg. per 100 cc. serum; plasma protein 6,8 Gm. per 100 cc.; urine protein 4.5 Gm. per 1000 cc.; occasional hyaline casts and 10-12 red blood cells were seen per high power field. The total PSP excretion in two hours was 10 per cent. The concentration-dilution test showed a range from 1.010 to 1.011.

The patient was started on the rice diet October 2, 1948. He followed the basic rice diet for 3½ months. Then the diet was gradually modified to include small amounts of vegetables and vegetable oil. The average urine chloride concentration (as NaC_l per 100 cc.) was: 10 mg., October 15-28, 1948; 9 mg., December 25 to January 14; 41 mg., February 21 to June 13 and 26 mg., July 10 to November 21, 1949.

Headache nausea and vomiting disappeared. The blood pressure, which at first (October 1-11,1948) averaged 225/143, decreased gradually. March 23-25, 1949, it averaged 186/117. November 21, 1949, it was 180/114. At that time, the tranverse diameter of the heart was 10.5 cm.; the chest diameter was 29.7 cm.. T_1 in the electrocardiogram was upright; the angle of the electrical axis was +79°. The non protein nitrogen was almost as high as it had been on admission: 90 mg. per 100 cc. blood, urea nitrogen 55 mg. per 100 cc. blood. The chloride was 96 mEq. per 1000 cc. serum; the

cholesterol 100 mg. per 100 cc. serum. The plasma protein remained unchanged: 6.8 Gm. per 100 cc. The urine protein had decreased from 4.5 Gm. to 0.16 Gm. per 1000 cc. An occasional red blood cell was seen per high power field. The total PSP excretion in two hours was 7 per cent.

There was continuous improvement of the retinopathy. The eyeground photographs taken November 22, 1949, 13 months after the start of the rice diet, show the **right** disc well outlined. Papilledema, retinal edema hemorrhages and exudates have disappeared. The veins are less engorged and less tortuous; the arteries are still narrow and irregular in caliber. Choroidal pattern is prominent (Plate 1). There is some residual blurring along the temporal border of the **left** disc and revascularization at the upper nasal margin of the disc. Papilledema, retinal edema, hemorrhages and exudates have disappeared. The veins are less engorged and less tortuous. The arteries are still narrow and irregular in caliber, especially the inferior temporal artery. There is sheathing of one branch of the superior nasal artery. Choroidal pattern is prominent (Plate 2).

The second patient (F. H.) was a 33 year old man in the terminal stage of chronic glomerulonephritis. From the age of 8 to 26, he had osteomyelitis for which 10 or 12 operations were performed. The osteomyelitis had been clinically inactive since 1943. In 1946, he was accepted for life insurance. In September, 1947, he had a severe epistaxis for which he was admitted to the Michael Reese Hospital. Blood pressure at that time was 240/140. The electrocardiogram showed left axis deviation. Serum creatinine was 2.7 mg. per 100 cc.; serum protein 6.7 Gm.; albumin 4.5 Gm.; globulin 2.2 Gm. Hemoglobin was 13.8 Gm.; RBC 4,500,000. The urine contained from 2+ to 4+ protein, 8-10 hyaline casts, 18-20 red blood cells, 4-5 white blood cells per high power field. The urine culture was positive for staphylococcus aureus, the same organism as cultured from the osteomyelitis. The intravenous pyelogram showed slow excretion. The patient was given a salt-poor diet with unrestricted protein, and a course of penicillin following which urine cultures were negative. The blood pressure remained approximately 220/140. In December, 1947, he went on a rice diet; the blood pressure dropped to 180/140. After that, he followed a rice diet at some times, at other times an ordinary diet. From November, 1948, on, he had periodic headaches which subsided on resuming a rice diet. The blood pressure most of the time was around 200/140. In the spring of 1948, the vision in his right eye diminished rather suddenly. Eyeground changes were found. From the fall of 1948, he noticed some swelling of the eyelids on awakening. Because of the progressive loss of vision, the patient came to our clinic on March 21, 1949.

The blood pressure on admission was 244/152. The **right** eye showed papilledema. Large and small hemorrhages and hard exudates were present around the disc and the macular area. There was a partial star-figure in the macula. The arteries showed focal spasm and the light reflex was increased (Plates 3 and 4). The **left** eye showed papilledema and peripapillary edema, large and small hemorrhages and hard exudates below the disc and in the nasal and temporal area. The was perivascular shea-

thing of the artery passing inferiorly and nasally from the disc. The veins were tortuous (Plates 5 and 6).

The transverse diameter of the heart was 13.8 cm.; the chest diameter was 29.5 cm. T_1 in the electrocardiogram was upright; the angle of the electrical axis was +31°. Hemoglobin was 9.8 Gm.; non protein nitrogen 70 mg., urea nitrogen 43 mg. per 100 cc. blood; chlorides 102 mEq. per 1000 cc. serum; cholesterol 165 mg. per 100 cc. serum; plasma protein 7.3 Gm. per 100 cc.; urine protein 4 Gm. per 1000 cc.; occasional hyaline casts and 6-8 red blood cells were seen per high power field. The total PSP excretion in two hours was 9 per cent. The concentration-dilution test showed a range from 1.007 to 1.010.

The patient was started on the rice diet for 3 months. Then the diet was gradually modified to include small amounts of vegetables, vegetable oil, nuts and oatmeal. The average urine chloride concentration (as NaCl per 100 cc.) was: 33 mg., April 12 to May 1, 1949; 14 mg., June 5 to June 22 and 17 mg.; July 30, 1949 to January 30, 1950.

The headache disappeared. The blood pressure, which at first (March 21-28, 1949) averaged 229/142, decreased gradually. June 20-30, 1949, it averaged 157/117; eleven months later, 141/106 (average of 10 readings in January and February, 1950). On February, 1950, the transverse diameter of the heart was 10.9 cm.; the chest diameter was 28.4 cm. T_1 in the electrocardiogram was upright; the angle of the electrical axis was +66° Hemoglobin was 12.4 Gm.; non protein nitrogen 42 mg., urea nitrogen 15 mg. per 100 cc. blood; chlorides 90 mEq. per 1000 cc. serum; cholesterol 200 mg. per 100 cc. serum,; plasma protein 7.4 Gm. per 100 cc.; urine protein 0.3 Gm. per 1000 cc.; no red blood cells were seen in the sediment. The total PSP excretion in two hours was 21 per cent.

There was continuous improvement of the retinopathy. The eyeground photographs taken February 3, 1950, 11 months after the start of the rice diet, show the **right** disc well outlined, except along the inferior margin. The arterial light reflex persists; arteries show less spasm. There are still a few hard exudates. The star-figure, the hemorrhages and the papilledema have disappeared (Plates 3 and 4). The **left** dis is well outlined. The veins are less tortuous. The perivascular sheating is unchanged. There is focal spasm of the superior nasal vessel. The hemorrhages and most of the exudates have disappeared (Plates 5 and 6).

The third patient (S. V.) was a 22 year old man with advanced chronic glomerulonephritis. In 1936, at the age of 9, he had purpura. This recurred in 1941, at the age of 14; he had a great deal of abdominal pain; proteinuria was noted. He was hospitalized for four months and treated with a diet from which milk, eggs and wheat, to which he had been found sensitive, were omitted. The proteinuria persisted and the blood pressure remained "slightly elevated" The patient attended highschool and college and was asymptomatic until Christmas, 1948, when he noted blurring of vision in the right eye. Within a few days, he developed bilateral temporal headaches which continued for about two weeks. He was hospitalized for four weeks and treated with a low calorie, salt-poor diet. Because of progres-

sive less of vision, the patient was transferied to our clinic on February 11 1949

The blood pressure on admission was 200/112. The **right** eye showed blurring of the disc along the nasal border, no papilledema. A large hemorrhage near the disc and small scattered hemorrhages and numerous hard exudates were present. The veins were tortuous and distended; arterio-venous compression was present; the arteries were attenuated. There was focal spasm of the arteries with focal sclerosis in the superior and inferior temporal arteries (Plates 7 and 8). The **left** eye showed blurring of the disc along the superior, inferior and nasal borders. There were numerous small hard exudates and several small hemorrhages. The veins were distended and tortuous (Plate 9).

The transverse diameter of the heart was 13.0 cm.; the chest diameter was 28.5 cm. (Figure 1). In the electrocardiogram, ST_2 and ST_3 were slight ly depressed; the angle of the electrical axis was + 74°. Hemoglobin was 14.6 Gm.; non protein nitrogen 64 mg., urea nitrogen 39 mg, sugar 112 mg. per 100 cc. blood; chlorides 101 mEq. per 1000 cc. serum; cholesterol 265 mg. per 100 cc. serum; plasma protein 6.9 Gm. per 100 cc.; urine protein 0.55 Gm. per 1000 cc.; 8-10 red blood cells were seen per high power field. The total PSP excretion in two hours was 26 per cent.

The patient was started on the rice diet on February 11, 1949. He followed the basic rice diet for 3½ months. Then the diet was gradually modified to include small amounts of nuts, vegetables, vegetable oil and homemade butter. The average urine chloride concentration (as NaCl per 100 cc.) was: 36 mg., Februray 25 to March 10, 1949; 15 mg., May 6-19 and 14 mg., June 15, 1949, to January 9, 1950.

The blood pressure decreased gradually. May 10-19, 1949, it averaged 128/86, November 1-5, 140/93. The heart decreased in size (Figure 1). November 2, the transverse diameter was 10.5 cm.; the chest diameter was 28.8 cm. The ST changes in the electrocardiogran disappeared; the angle of the electrical axis was +81°.Hemoglobin was 16.0 Gm. The non protein nitrogen and urea nitrogen were: February 11, 1949, 64 and 39; April 7,58 and 28; November 2,44 and 10 mg. per 100 cc. blood. November 2, the chlorides were 89 mEq. per 1000 cc. serum. The cholesterol concentration in the serum decreased: February 11, 265; April 7, 185; July 12, 120; November 2 (after the addition of vegetable oil and butter), 160 mg. per 100 cc. serum. The plasma protein increased: February 11, 6.9; April 7, 7.5; July 12, 8.5; November 2, 8.0 Gm. per 100 cc. The urine protein decreased from 0.55 Gm. (average February 11-23, 1949) to 0.06 Gm. per 1000 cc. (average November 1-5). Three to 4 red blood cells were seen per high power field. The total PSP excretion in two hours was: February 11, 26 per cent; May 18, 18 per cent; July 12, 16 per cent; November 2,21 per cent.

There was continuous improvement of the retinopathy. The eyeground photographs taken November 4 1949, 9 months after the start of the rice diet, show the **right** disc more clearly outlined. The veins are less tortuous and less engorged; arterio-venous compression as before; less arteriolar spasm.

The hemorrhages have disappeared. Very few hard exudates remain (Plates 7 and 8). The **left** disc is more clearly outlined. The veins are less engorged. The hemorrhages and hard exudates have disppeared (Plate 9).

The fourth patient (N. W.) was a 40 year old woman with advanced chronic nephritis. She had always been well until 1942, when at the age of 37, she had an attack of renal colic, characterized by dysuria, frequency, chills, blood in the urine and right flank pain. For some time, she was asymptomatic, but in 1943, a second attack of renal colic occurred, and she had the same symptoms again. She had no further trouble until early in 1945 when bilateral frontal headaches associated with nausea and vomiting began. She had no appetite, felt very weak and lost a good deal of weight. Three months later, the vision became impaired and scotomata were noticed. A month after that, hypertension, 200 plus systolic, was found. Pus and protein were present in the urine. Medication was given which decreased the intensity of the headaches, but nausea and vomiting persisted and became progressively worse so that from February till August, 1945, she lost 30 pounds. Since June, 1945, dyspnea on exertion had been present and since the beginning of July, she had been on digitalis. In the middle of July, she had a sore throat, pain in the right flank, a swollen face and neck and a fever of 102 degrees F. There was no dysuria or frequency. She was treated with quinine and atabrine. The fever subsided. Because of persistent weakness and progressive loss of vision, the patient was sent to our clinic on August 8, 1945.

The blood pressure on admission was 180/100. The **right** eye showed papilledema, retinal edema, hard and soft exudates (Plate 10). The **left** eye showed papilledema and retinal edema. There were hard and soft exudates, a partial star-figure and a few hemorrhages. The veins were engorged and tortuous (Plates 11 and 12).

The transverse diameter of the heart was 13.8 cm.; the chest diameter was 27.9 cm. The electrocardiogram showed inversion of T_1 and diphasic T_2; the angle of the electrical axis was $+30°$. Hemoglobin was 85 Gm; non protein nitrogen 84 mg., urea nitrogen 57 mg., sugar 107 mg. per 100 cc. blood; chlorides 99 mEq. per 1000 cc. serum; cholesterol 180 mg. per 100 cc. serum; plasma protein 6.9 Gm. per 100.; A/G ratio 1.0. The urine protein was 1+. The total PSP excretion in two hours was 18 per cent. The patient had profuse vaginal bleeding for which a curettage was done on August 23, 1945. The histological diagnosis was estrogenic endometrium; no malignancy.

The patient was started on the rice diet August 10, 1945. She followed the basic rice diet for 5 weeks. For the next 5 months, she was on a modified rice diet. The average chloride concentration (as NaCl per 100 cc. of urine) was: 13 mg., August 28 to September 8, 1945, and 28 mg., November 15 to January 25, 1946.

The blood pressure decreased within a few weeks. August 8-14, 1945, it averaged 160/92; August 15-21, 144/90; August 22-28, 142/94; August 29-September 4, 133/89; September 12-15, 130/87. Headache, nausea and vomiting disappeared. The dyspnea subsided although digitalis was discontinued. The non protein nitrogen and urea nitrogen decreased gradually.

The plasma protein increased. November 15-17, 1945, the blood pressure averaged 144/99. The transverse diameter of the heart was 11.7 cm.; the chest diameter was 28.5 cm. T_1 and T_2 in the electrocardiogram were upright; the angle of the electrical axis was +58°. Hemoglobin was 12.1 Gm.; non protein nitrogen 35 mg, urea nitrogen 13.2 mg. per 100 cc. blood; chlorides 101 mEq. per 1000 cc. serum; cholesterol 155 mg. per 100 cc. serum; plasma protein 7.7 Gm. per 100 cc. The urine protein was 3+. The total PSP excretion in two hours was 24 per cent. .

After January, 1946, the patient no longer followed the modified rice diet well. The urine chloride concentration May 28, 1946, and March 17, 1947, averaged 147 mg. (as NaCl per 100 cc.).

The blood pressure increased again. In March, 1947, it was 193/117. The transverse diameter of the heart was 13.2 cm.; the chest diameter was 28.1 cm. T_1 an T_2 remained upright; the angle of the electrical axis decreased to +23°. Hemoglobin was 12.6 Gm.; non protein nitrogen 51 mg., urea nitrogen 28.8 mg. per 100 cc. blood; chlorides 98 mEq. per 1000 cc. serum; cholesterol 155 mg. per 100 cc. serum; plasma protein 7.1 Gm. per 100 cc. The urine contained a heavy trace of protein. The total PSP excretion in two hours was 13 per cent.

In spite of the fact that the diet was not followed well and the blood pressure increased again, there was continuous improvement of the retinopathy. The eyeground photographs taken March 19, 1947, 19 months after the start of the rice diet, show the **right** disc moderately well outlined. Papilledema, retinal edema and hard exudates have disappeared (Plate 10). The **left** eye shows the disc well outlined. The veins are straighter. Star-figure, papilledema, hemorrhages and exudates have disappeared (Plates 11 and 12).

The fifth patient (D. K.) was a 19 year old girl with hemorrhagic exudative retinopathy. The primary disease was either malignant hypertension or advanced chronic glomerulonephritis. She came to the clinic on March 8, 1949 with the chief complaint of failing vision of 12 days duration. She had always been well. When she entered a school of nursing in 1946, her blood pressure was 120/80, but a trace of protein was present in the urine. In July, 1948, on a routine examination, her blood presure was 190/120. This was attributed to emotional excitement and phenobarbital was given. During the fall of 1948, the blood pressure was checked several times; it was about 130/90. She said she had had some arguments with the head nurse and was almost dismissed from the school. There were several weeks when she was "always worried and excited". During this time, she began to have headaches, chiefly behind the eyes, occurring practically every day after breakfast and lasting all day. They were not severe. On her days off, the headaches did not occur. With the headaches, she frequently had pounding of the heart and when she was excited she noticed that it was beating very rapidly. Occasionally, after January 1, 1949, she had nausea and vomiting. On February 24, her vision became blurred. She went to an ophthalmologist who referred her to the medical service; she was put to bed. The blood pressure in the arms fluctuated between 170 and 200 systolic and 120 and 150 diastolic. A diastolic reading of 170 was obtained twice.

The blood pressure in the legs was 260/170. Advanced retinopathy was found. The heart was enlarged to the left. The transverse diameter was 13.4 cm. the chest diameter was 25.8 cm. A loud blowing systolic murmur was heard. Cystoscopy showed the bladder to be inflamed. The impression was acute cystitis. Retrograde pyelograms were negative. The treatment consisted of complete bed rest, a sodium poor diet (5 Gm. daily), 120 mg. of rutin daily, and emperin for the headache. Since there was no improvement, the patient was sent to our clinic on March 8, 1949.

The blood pressure on admission was 204/138. The **right** eye showed the disc markedly blurred. There was slight papilledema and retinal edema. There were scattered cottony exudates and hemorrhages, hard exudates or edema residue below and medial to the disc. The macular area showed masive exudates and edema. The veins were engorged; arterio-venous compression was present; there was a slight increase in the light reflex on the arteries (Plates 13 and 14). The **left** eye showed papilledema. Edema, hemorrhages,cottony and hard exudates were in the macular area. There was venous engorgement and tortuosity, and general attenuation and focal spasm of the arteries (Plates 15 and 16).

The heart was enlarged, chiefly to the left. The transverse diameter was 11.2 cm. There was a gallop rhythm and a loud blowing systolic murmur at the apex. T_1 in the electrocardiogram was upright; the angle of the electrical axis was +68°. Hemoglobin was 14.1 Gm.; non protein nitrogen 44 mg., urea nitrogen 19 mg., sugar 103 mg., per 100 cc. blood; chlorides 98 mEq per 1000 cc. serum; cholesterol 233 mg. per 100 cc. serum; plasma protein 6.5 Gm. per 100 cc.; urine protein was 2.0 Gm. per 1000 cc. The total PSP excretion in two hours was 20 per cent.

The patient was started on the rice diet immediatelly. She followed the basic rice diet for 4 months Then the diet was gradually modified to include small amounts of vegetables, vegetable oil and nuts. The average urine chloride concentration (as NaCl per 100 cc.) was: 35 mg., March 28 to April 11, 1949; 14 mg., June 24 to July 10, and 25 mg., August 8 to January 17, 1950.

The blood pressure, which at first (March 8-9, 1949) averaged 191/134, decreased gradually. July 6-15, it averaged 158/111, September 21-23, 145/100. Headache, nausea and vomiting disappeared. September 21, 1949, the transverse diameter of the heart was 10.2 cm.; the chest diameter was 25.2 cm. T_1 in the electrocardiogram was upright; the angle of the electrical axis was + 72°. Hemoglobin was 13.0 Gm.; chlorides 92 mEq., per 1000 cc. serum; cholesterol 215 mg. per 100 cc. serum. The plasma protein increased from 6.5 to 7.5 Gm. per 100 cc. The urine protein decreased from 2.0 Gm. to 0.72 Gm. per 1000 cc. However, the total PSP excretion in two hours decreased from 20 to 15 per cent, the non protein nitrogen increased from 44 mg. to 64 mg., the urea nitrogen from 19 mg. to 39 mg.

There was continuous improvement of the retinopathy. The eyeground photographs taken September 21, 1949, 6 months after the start of the rice diet, show the **right** disc well outlined. The veins are less engorged and straighter. Arterio-venous compression is still present. There is still

increased light reflex on the arteries, but they are less tortuous. Hemorrhages, cottony exudates and nearly all of the edema residue have disappeared (Plates 13 and 14). The **left** eye shows the disc well outlined. There is less arteriolar constriction. Hemorrhages, cottony exudates and edema residue have disappeared (Plates 15 and 16).

The sixth patient (W. H.) was a 40 year old man with hypertensive and arteriosclerotic vascular disease. Early in 1940, when he was 36, he developed headaches and dizziness. Blood pressure readings were 180 to to 200 systolic. An abnormal electrocardiogram was found. He was kept in bed for six weeks and then resumed his activities. A few months later he was re-examined and was advised to rest for another twelve weeks. His nervous tension improved, but the systolic blood pressure remained between 180 and 205. He was almost asymptomatic between 1941 and 1944 but because of the persistent blood pressure elevation, he came to our hospital in July, 1944.

The blood pressure on admission was 220/148. The **right** eye showed a well-outlined disc, increased light reflex on the arteries, arterio-venous compression, no hemorrhages or exudates. The **left** eye showed a well-outlined disc, increased light reflex on the arteries, arterio-venous compression and tortuosity of the veins, no hemorrhages or exudates.

The transverse diameter of the heart was 16.8 cm.; the chest diameter was 31.0 cm. The aorta was tortuous. T_1 in the elctrocardiogram was inverted; the angle of the electrical axis was — 55° (Figure 2). Hemoglobin was 15.3 Gm.; non protein nitrogen 34 mg. per 100 cc. blood. There was no proteinuria. The total PSP excretion in two hours was 60 per cent

The patient was started on the rice diet September 4, 1944. The blood pressure, which at first (July 24-September 4, 1944) averaged 203/131, decreased gradually. October 24, 1944, it was 168/112. At that time, the transverse diameter of the heart was 13.8 cm.; the chest diameter was 31.7 cm. During 1945, he was seen on seven occasions. The blood pressure average was 163/108. He followed the rice diet fairly well for one year. Then, although he continued to eat some rice and fruit, he also took other food and gradually resumed a "normal" diet. He was not seen in the clinic between January, 1947, and September, 1948. During these twenty months, he felt well and was asymptomatic except that in March, 1948, he had a severe epistaxis.On awakening on September 10, 1948, he noticed that the vision of his right eye was blurred, but he was still able to identify large objects. He immediately resumed the strict rice diet, and a week later on September 17, 1948, he returned to our clinic.

The blood pressure on this admission was 200/114. In the **right** eye, there was a thrombosis of the superior temporal vein. The disc was blurred. Hemorrhages and exudates covered the superior half of the retina. There was increased light reflex on the arteries, tortuosity of the veins and arterio-venous compression. The veins were engorged. The **left** eye showed a well-outlined disc, increased light reflex on the arteries, and tortuosity of the veins.

The transverse diameter of the heart was 14.0 cm.; the chest diameter was 31.7 cm. T_1 in the electrocardiogram was inverted; the angle of the electrical axis was — 39° (Figure 2). Hemoglobin was 16 Gm.; non protein nitrogen 26 mg., urea nitrogen 6.6 mg. per 100 cc. blood; chlorides 99 mEq. per 1000 cc. serum; cholesterol 175 mg. per 100 cc. serum; plasma protein 6.3 Gm. per 100. cc.; urine protein 0.1 Gm. per 1000 cc. The total PSP excretion in two hours was 62 per cent.

The patient was again started on the rice diet September 17, 1948. He followed the basic rice diet for 3 months, a slightly modified diet for 3 months, and then he again deviated from his diet. The average urine chloride concentration (as NaCl per 100 cc.) was: 11 mg., September 24 to October 10, 1948; 13 mg., December 11 to December 17; 16 mg., January 11 to March 3, 1949, and 76 mg., July 13, 1949, to February 2, 1950.

Eyegound photographs were not taken until November 8, 1948, because of the danger of increased intraocular tension. The **right** eye shows hemorrhages and exudates covering the supramacular area, tortuosity of the veins and sheathing of a branch of the superior temporal vein (Plate 17).

The blood pressure, which averaged 196/123 (September 17-22, 1948), decreased gradually. December 10-19, 1948, it averaged 141/98. March 3, 1949, it was 128/90; July 13, 1949, 140/100; February 2, 1950, 142/96. The vision improved. The T_1 in the electrocardiogram, which had been inverted since July, 1944, was diphasic in July, 1949, and upright in February, 1950 (Figure 2). The angle of the electrical axis in February, 1950, was — 25° The transverse diameter of the heart was 12.7 cm.; the chest diameter was 31.7 cm. Hemoglobin was 15.5 Gm.; non protein nitrogen 31 mg., urea nitrogen 11.0 mg. per 100 cc. blood; chlorides 104 mEq per 1000 cc. serum; cholesterol 210 mg. per 100 cc. serum; plasma protein 6,0 Gm. per 100 cc.; there was no proteinuria. The total PSP excretion in two hours was 66 per cent.

There was continuous improvement of the retinopathy. The eyeground photographs taken February 2, 1950, 17 months after the patient resumed the rice diet, show perivascular sheathing of a branch of the superior temporal vein and extensive revascularization in the **right** eye; the hemorrhages and exudates have disappeared (Plate 17). The **left** disc is well-outlined. The tortuosity of the veins is still present. There are no exudates or hemorrhages.

The seventh patient (M.G.) was a 48 year old woman with so-called "benign" essential hypertension. In 1928, at the age of 28, she had toxemia during her first pregnancy. For the next 7 years, her systolic pressure varied between 130 and 170. Of 5 subsequent pregnancies, two terminated spontaneously in the third and sixth month; two were interrupted during the third month because of severe headaches and blood pressure elevation. Several operations were done between 1935 and 1947: cholescystectomy, appendectomy, hemorrhoidectomy, removal of "a lump in the left side of the abdomen" and repair of a bladder stricture. During this time, the blood pressure was 160 to 170 systolic. In 1942, she had "some kind of hormone therapy" and gained in weight to 270 pounds. Then she followed a re-

duction diet and lost about 90 pounds. During 1946, 1947 and 1948, the patient felt tired, was easily upset and sometimes cried without much reason. One day in 1947, she had a "black out" and "blurred vision for a few hours". Because of fatigue, nervousness and "visual disturbances", the patient was sent to our clinic on December 30, 1948.

The blood pressure on admission was 280/160. The weight was 205 pounds, with a height of 5 2".

In both eyes, the discs were well-outlined. The arterial light reflex was widened. The arteries were attenuated. Focal arterial spasm and sclerosis were present. The veins were tortuous. In the **right** eye, there were no hemorrhages or exudates. In the **left** eye, there were hemorrhages and cotton wool patches above the macula — probably due to thrombosis of the branch of the superior temporal vein — and several small hemorrhages below the disc (Plate 18). .....

The transverse diameter of the heart was 12.7 cm.; the chest diameter was 27.0 cm. The ST segments in leads 1 and 2 of the electrocardiogram were depressed. T_1 was diphasic; the angle of the electrical axis was +20°. Hemoglobin was 12.6 Gm.; non protein nitrogen 34 mg. urea nitrogen 16 mg.; sugar 93 mg. per 100 cc. blood; chlorides 103 mEq. per 1000 cc. serum; cholesterol 285 mg. per 100 cc. serum; plasma protein 7.0 Gm. per 100 cc.; urine protein 0.1 Gm. per 1000 cc. The total PSP excretion in two hours was 51 per cent. The concentration-dilution test showed a range from 1.003 to 1.024.

The patient was started on the rice diet January 6, 1949. She followed the basic rice diet with some exceptions for 4 months (December, 1948, to April, 1949), during which time she lost 40 pounds; a diet modified by the addition of small amounts of vegetables, vegetable oil and nuts for 5 months, during which time she lost an additional 32 pounds, and the basic rice diet for another 4 months during which time she lost 15 pounds. The average urine chloride concentration (as NaCl per 100 cc.) was: 22 mg., January 20, 1949, to February 4; 68 mg., April 11 - 19; 45 mg., May 19 to September 13; 27 mg., October 12 - 25, 1949, and 8 mg., January 24 to February 6, 1950.

The blood pressure, which at first (December 30, 1948, to January 10, 1949) averaged 241/136, decreased gradually. February 11-21, it averaged 199/124; March 11-21, 202/119; April 11-21, 195/119; June 15-16, 171/106; October 4-14, 170/103; January 24-February 3, 1950, 163/100. The weight decreased: December 30, 1948, it was 205 pounds; April 20, 1949, 166 pounds; October 9, 132 pounds and January 21, 1950, 117 pounds. The cholesterol decreased: December 30, 1948, it was 285 mg.; April 13, 1949, 235 mg.; June 15, 155 mg.; December 30, 165 mg. per 100 cc. serum. The transverse diameter of the heart decreased from 12.7 cm. (December, 1948) to 11.4 cm. (January, 1950); the chest diameter measured 27.0 and 27.5 cm. respectively. The diphasic T_1 became upright; the angle of the eletrical axis remained +20° Hemoglobin was 11.3 Gm.; non protein nitrogen 25 mg., urea nitrogen 6.0 mg. per 100 cc. blood; chlorides 93 mEq. per 1000 cc. serum; cholesterol 170 mg. per 100 cc. serum; plasma protein

6.1 Gm, per 100 cc. There was no proteinuria. The total PSP excretion in two hours was 50 per cent (February 10, 1950).

There was continuous improvement of the retinopathy. The photograph of the macular area of the **left** eye taken January 25, 1950, 12½ months after the start of the rice diet, shows increased light reflex and perivascular sheathing of the superior temporal vein and its branches. Revascularization is present. The smaller veins, especially branches of both superior and inferior temporal veins, are less tortuous and less engorged. Hemorrhages and exudates have disappeared (Plate 18).

The eighth patient (A. H.) was a 45 year old woman with malignant hypertension. She had always been well until 1950 when at the age of 42 she developed headaches; they occurred daily and were most severe in the morning At first, they were relieved by aspirin. In 1946, because of the intensity of the headaches, she consulted a physician. Hypertension, 225 to 240 systolic, was found. It is not certain whether or not proteinuria was present. She rested more and did less housework. Salt was restricted. Because there was only slight improvement, her physician started her on a rice diet which she "followed with some cheating for three months". The headaches continued. The blood pressure remained above 200 systolic. "Because she did not have the will-power" to follow the diet, it was discontinued. In April, 1948, when the systolic reading was almost 300, a modified rice diet was tried again. In June, the blood pressure was 210 systolic, and the eyegrounds were reported to be normal. In September, after a vacation, the blood pressure was 210 systolic. Early in November, 1948, a reading of 240 systolic was obtained and on November 23, 1948, she was sent to our clinic.

The blood pressure on admission was 300+/150. The **right** eye showed massive papilledema and peripapillary edema; masses of hard exudates and scattered hemorrhages. The veins were engorged and very tortuous, the arteries narrow with localized areas of marked constriction (Plate 19). The **left** eye showed massive papilledema and peripapillary edema, masses of hard exudates and scattered hemorrhages. The veins were engorged, the arteries narrow with localized areas of marked constriction (Plate 20).

The transverse diameter of the heart was 12.4 cm.; the chest diameter was 23.7 cm. The electrocardiogram showed a diphasic T_1; the angle of the electrical axis was -16°. Hemoglobin was 13 Gm.; non protein nitrogen 36 mg., urea nitrogen 16 mg., sugar 140 mg. per 100 cc. blood; chlorides 102 mEq. per 1000 cc. serum; cholesterol 270 mg. per 100 cc. serum; plasma protein 7.2 Gm. per 100 cc.; urine protein 0.8 Gm. per 1000 cc. Twenty-two to 24 white blood cells were seen per high power field, no red blood cells or casts. The total P S P excretion in two hours was 88 per cent. The concentration-dilution test showed a range from 1.005 to 1.020.

The patient was started on the rice diet November 27, 1948; she followed it strictly until March. The headache disappeared completely. The blood pressure decreased. November 23-30, 1948, it averaged 256/135; February 23-March 3, 1949, 179/102. The transverse diameter of the heart decreased from 12.4 cm. to 11.1 cm.; the chest diameter measured 23.7

and 23.8 cm. respectively. The diphasic T_1 became upright; the angle of the eletrical axis increased to-5°. Hemoglobin was 13.3 Gm.; non protein nitrogen 23 mg., urea nitrogen 6 mg., sugar 81 mg. per 100 cc. blood; chlorides 100 mEq. per 1000 cc. serum; cholesterol 185 mg. per 100 cc. serum; plasma protein 7.1 Gm. per 100 cc. The urine protein decreased from 0.8 Gm. to .08 Gm, per 1000 cc. The urine sediment showed 4-6 white blood cells and 16-17 red blood cells per high power field From March on, the patient did not follow the diet strictly but did"some cheating". The urine chloride concentration (as NaCl per 100 cc.), which from February 1 to March 1, 1949, had averaged 15 mg., averaged 145 mg. between March 31, 1949, and February 20, 1950. February 20-24, 1950, the blood pressure averaged 220/123. The transverse diameter of the heart was 10.7 cm.; the chest diameter was 23.5 cm. T_1 in the electrocardiogram remained upright; the angle of the electrical axis was -9°. Hemoglobin was 13.2 Gm.; non protein nitrogen 28 mg., urea nitrogen 10.4 mg., sugar 96 mg. per 100 cc. blood; chlorides 100 mEq. per 1000 cc. serum; cholesterol 185 mg. per 100 cc. serum; plasma protein 6.7 Gm. per 100 cc.; urine protein 0.16 Gm. per 1000 cc. One to 3 red blood cells were seen per high power field.

There was continuous improvement of the retinopathy. Eyeground photographs taken February 25, 1950, 15 months after the start of the rice diet, show the **right** disc well-outlined; no retinal edema. The veins are less engorged and less tortuous; variation in the caliber of the arteries is still present. The hard exudates have decreased in size and number; the hemorrhages have disappeared (Plate 19). The **left** disc is well-outlined; the retinal edema has disappeared; the veins are less engorged and less tortuous. The arteries show increased light reflex and variation in caliber; an artery passing to the nasal side shows perivascular sheathing. The hard exudates have decreased in size and number. The hemorrhages have disappeared (Plate 20).

The ninth patient (D. T.) was a 20 year old woman with malignant hypertension. She had always been well until April, 1948, when during the fifth month of her first pregnancy, she had a severe cold. She was treated - for the first time in her life - with a sulfonamide (3 tablets daily for about 10 days). On the third day, a skin rash appeared which was thought to be due to poison ivy. The skin rash persisted for one month. Then joint and muscular pain developed and she had mild urinary frequency. In May, the patient was hospitalized for 5 days and had a course of penicillin. In June, a systolic blood pressure of 180 was found, and the pregnancy (during the seventh month) was terminated by a Cesarian section. The blood pressure remained high, and she developed headaches. Three weeks after the delivery, she had two convulsions. The blood pressure was 220/140. She was again hospitalized. In the hospital, she had one more convulsion. A lumbar puncture was done. She was given sedatives, two tablets of veratrin every four hours and intravenous magnesium sulfate on three occasions. Following the convulsions, the vision became blurred, and she had attacks of paroxysmal dyspnea. Since the headache became more severe with progres-

sive loss of vision and the blood pressure continued to rise, the patient was transferred to our hospital on August 6, 1948.

The blood pressure on admission was 225/140. The temperature was normal. The heart was normal in size. T_4 in the electrocardiogram was upright; the angle of the electrical axis was +66°. Hemoglobin was 18.3 - 16.2 Gm.; non protein nitrogen 30 mg., urea nitrogen 9.7 mg., sugar 110 mg. per 100 cc. blood; chlorides 82 mEq. per 1000 cc. serum; cholesterol 380 mg. per 100 cc. serum; plasma protein 7.2 Gm. per 100 cc.; urine protein 4.5 Gm. per 1000 cc. One to 2 red blood cells were seen per high power field, no white blood cells, no casts. The total PSP excretion in two hours was 47 per cent. The concentration-dilution test showed a range from 1.003 to 1.014.

Because the patient was too ill, eyeground photographs could not be taken until 20 days after admission. The **right** disc was blurred along the superior margin. There was retinal edema. There were numerous hemorrhages and soft exudates, and a star-figure in the macula. The terminal segments of small venous branches appeared markedly dilated, the arteries very much attenuated (Plates 21 an 22). The **left** disc was well-outlined. There was retinal edema. There were numerous hemorrhages and large soft exudates and an incomplete star-figure near the macula. The veins were very much engorged and varied markedly in caliber. A branch of the superior temporal vein running toward the macula was very twisted (Plates 23 and 24).

The patient was started on the rice diet on August 6, 1949. She followed the basic rice diet for 55 days; then the diet was gradually modified to include small amounts of vegetables, vegetable oil, nuts, oatmeal and macaroni. However, it was not strictly followed. The average urine chloride concentration (as NaCl per 100 cc.) was: 16 mg., August 15 to September 2; 9 mg., November 1-18, and 83., mg., December 10, 1948, to October 24, 1949.

The blood pressure decreased rapidly (Figure 3). August 6-12, 1948, it averaged 205/151; August 13-19, 190/148; August 20-26, 160/124; August 27 -September 2, 139/115; September 10-16, 121/88; September 17-23, 104/81; September 24-30, 101/77; October 1-7, 99/77; October 8-14, 1948, 96/78. In October, 1948, the blood pressure was 128/88. The transverse diameter of the heart was 9.7 cm.; the chest diameter was 24.3 cm. Hemoglobin was 14.7 Gm.; non protein nitrogen 30 mg., urea nitrogen 6.0 mg. per 100 cc. blood; chlorides 103 mEq. per 1000 cc. serum. The total PSP excretion in two hours was 54 per cent. The cholesterol decreased from 380 mg on August 7, 1948, to 285 on August 17, to 225 on August 30, to 190 on November 20, to 160 on October 24, 1949. The plasma protein increased from 7.2 Gm. (August 7, 1948) to 8.2 (February 28, 1949); in October, 1949, it was 7.5 Gm. The urine protein decreased. The averages were: August 6-13, 1948, 2.0; August 20-26, 0.68; September 10-16, 0.46; October 8-14, 0.17; January 27 -February 28, 1949, 0.08 Gm. per 1000 cc.; in October, 1949 it had increased to 0.36 Gm. per 1000 cc. There were rare white cells but no red blood cells or casts in the urinary sediment.

There was continuous improvement of the retinopathy. The photographs taken October 24, 1949, 14 months after the start of the rice diet, show the

right disc well-outlined and pale. The retinal edema has disappeared. The veins are less engorged; there is less spasm of the inferior nasal and inferior temporal arteries. In the macular area, a small amount of edema residue is still present. Star-figure, cottony exudates and hemorrhages have disappeared (Plates 21 and 22). The **left** disc is well-outlined and pale. The retinal edema has disappeared. The veins are not engorged. There is perivascular sheathing of a branch of the superior nasal artery. Star-figure, cottony exudates and hemorrhages have disappeared (Plates 23 and 24).

The tenth patient (L. B.) was a 24-year old woman with malignant hypertension. She had always been well until 1939 when at the age of 19 her first pregnancy was complicated by severe headache and edema of the feet. A systolic blood pressure of 210 was found. There were no symptoms of urinary tract disease and, as far as the patient knows, no proteinuria. The systolic blood pressure between the first and second pregnancy was "always over 200" She had headaches three or four times a week on awakening in the morning. At 23, she became pregnant again and was not seen by a physician until the end of the fifth month (August 18, 1944). Her systolic blood pressure then was above 260. On September 1, 1944, she was seen in the Obstetrical Clinic of our hospital; the blood pressure was 260/145. Ophthalmoscopic examination at that time showed arterio-venous compression and narrowing of the arterioles, but no exudates or hemorrhages. There was slight ankle edema and proteinuria. The urinary sediment showed only occasional white blood cells. Hysterotomy was advised but refused by the patient. On September 5, 1944, the blood pressure was 248/140. On September 26, after bed rest, a "low salt, high protein, low calorie diet with limited fluids" and sedation with phenobarbital, it was 190/135. There was marked proteinuria; occasional red blood cells and hyaline casts were seen per high power field On October 2, 1944, she was admitted to the Obstetrical Ward because of vaginal bleeding. The blood pressure was 260/170. On October 5, a stillborn infant was delivered. Blood pressure readings (Twice daily) October 6-11 averaged 224/147. After discharge on October 11, she had headache and progressive dimness of vision. She was sent to our Medical Ward on October 30, 1944.

The blood pressure on admission was 233/157. The weight was 172 pounds. The height was 158.5 cm. Both eyes showed marked papilledema, extensive retinal edema, engorged veins, many hemorrhages and hard and soft exudates. Arteries could not be seen because of the edema (Plates 25 and 26).

The transverse diameter of the heart was 16.6 cm.; the diameter of the chest was 32.0 cm. The electrocardiogram showed an upright T_1; the angle of the electrical axis was $+18°$. Hemoglobin was 14.7 Gm.; non protein nitrogen 26 mg.; urea nitrogen 9.5 mg.; sugar 93 mg. per 100 cc. blood; chlorides 96 mEq. per 1000 cc. serum; cholesterol 240 mg. per 100 cc. serum; plasma protein 7.2 Gm. per 100 cc.; urine protein 0.67 Gm. per 1000 cc. Two to 3 white blood cells were seen per high power field; no red blood cells,, no casts. The total

PSP excretion in two hours was 61 per cent. The concentration-dilution test showed a range from 1.010 to 1.030.

The patient was started on the rice diet on October 30, 1944. She followed it well for 4 months. The average urine chloride concentration (as NaCl per 100 cc.) was: 13 mg. The headaches disappeared completely. The blood pressure decreased rapidly, averaging 155/105 the second week, 138/96 the third week and 130/92 the fourth week (Figure 4). It averaged 120/87 December 18-20, 1944, and January 15-18, 1945.

February 20-23, 1945, the average blood pressure was 121/87. The transverse diameter of the heart was 12.9 cm.; the chest diameter was 30.5 cm. T_1 in the electrocardiogram was upright; the angle of the electrical axis was+58°. The hemoglobin was 12.7 Gm.; non protein nitrogen 25 mg., urea nitrogen 3.0 mg. per 100 cc. blood; chlorides 91 mEq. per 1000 cc. serum; cholesterol 110 mg. per 100 cc. serum; plasma protein 7.1 Gm. per 100 cc. urine protein 0.28 Gm. per 1000 cc. The total PSP excretion in two hours was 47 per cent. The weight was 141 pounds.

There was continuous improvement of the retinopathy. Papilledema, hemorrhages and cottony exudates disappeared. Only a few hard exudates were still present.

After February; 1945, the rice diet was not strictly followed. The average urine chloride concentration (as NaCl per 100 cc.) was 83 mg. The average blood pressure was: May 7-9, 1945, 126/88; August 6-9, 1945, 119/78; December 10-13, 1945, 143/92. The weight was 139 pounds Early in 1946, the patient resumed an ordinary diet and during the next three years gained 87 pounds. She was not seen again until October 25, 1948. The average blood pressure October 25-27 was 191/131. The eyegrounds showed no papilledema, hemorrhages or exudates. The patient was urged to resume the rice diet and to lose weight. However, she did not do so.

She returned to the hospital on November 5, 1949, because she was theree months pregnant. She had felt perfectly well during the intervening year except for recent recurrence of headaches. On admission, the blood pressure was 225/135. The weight was 222 pounds. The transverse diameter of the heart was 17.1 cm.; the diameter of the chest was 31.6 cm. The T_1 in the electrocardiogram was low upright; the angle of the electrical axis was +45°. Hemoglobin was 14.0 Gm.; non protein nitrogen 32 mg. per 100 cc. blood; chlorides 103 mEq. per 1000 cc. serum; cholesterol 180 mg. per 100 cc. serum; plasma protein 7.1 Gm. per 100 cc.; there was no proteinuria. Two to 3 red blood cells and 2-3 white blood cells were seen per high power field. The total PSP excretion in two hours was 60 per cent.

The eyeground photographs taken November 10, 1949, 5 years after the rice diet was started for the first time, show both discs well-outlined but pale; there are no hemorrhages and exudates. The light reflex on the arteries is increased and vaso-constriction is present (Plates 25 and 26).

From November 5-21, she followed the rice diet strictly. The blood pressure again decreased rapidly. November 14, it was 142/100. The preg-

nancy was interrupted on November 15. The average blood pressure November 19-21 was 143/94. The patient was urged to continue the diet. However she gave it up as soon as she left the hospital (November 23). December 12, she returned for a gynecological check-up; the blood pressure averaged 177/110.

The eleventh patient (J. R.) was a 47 year old man with malignant hypertension. He had had scarlet fever, uncomplicated, at the age of 6. At the age of 16, he had migratory joint pains with swelling and shortness of breath. At the age of 17, he had pleurisy. He was told that his heart was enlarged. After the age of 15, he frequently had a sore throat and on 5 occasions peritonsillar abscesses were drained. In 1942, tonsillectomy was done. In December, 1948, a nonradiating dull left flank pain developd. The urine was rusty-colored. For two weeks, the patient had nocturia 4 to 5 times a night passing a small amount of urine at each voiding. Oliguria, first noted then, persisted. About the first of January, 1949, he was given some white tablets for five days (? sulfonamide). At the same time, his vision suddenly became blurred. He was told by an ophthalmologist that he had papilledema and that his systolic blood pressure was 230. Early in March, he was hospitalized and treated with bed rest and a low salt diet. X-rays failed to reveal any kidney stones. He continued the diet at home and stayed in bed for three weeks. Since the blurring of vision persisted, the patient was sent to our clinic on March 25, 1949.

The blood pressure on admission was 230/130. The **right** eye showed papilledema, retinal edema, massive hemorrhages and cotton wool patches, venous engorgement and tortuosity, attenuation of the arteries (Plate 27). The **left** eye showed papilledema, retinal edema, massive hemorrhages and cotton wool patches, venous engorgement and tortuosity, attenuation of the arteries. There were hard exudates near the macula (Plate 28).

The transverse diameter of the heart was 11.9 cm. T_1 in the electrocardiogram was upright; the angle of the electrical axis was $+30°$. Hemoglobin was 12.2 Gm.; non protein nitrogen 48 mg., urea nitrogen 29 mg. per 100 cc. blood; chlorides 97 mEq. per 1000 cc. serum; cholesterol 230 mg. per 100 cc. serum; plasma protein 7.5 Gm. per 100 cc.; urine protein 0.9 Gm. per 1000 cc. Six to 8 white blood cells were seen per high power field. The total PSP excretion in two hours was 48 per cent. The concentration-dilution test showed a range from 1.016 to 1.021.

The patient was started on the rice diet March 28, 1949. He followed the basic rice diet for 3 months. Then the rice diet was modified to include small amounts of vegetables and vegetable oil. The average urine chloride concentration (as NaCl per 100 cc.) was: 13 mg., April 21 to May 12; 13 mg., June 19-30; 14 mg., July 28 to September 14, and 44 mg., October 10, 1949, to January 11, 1950.

The blood pressure, which at first (March 25-April 8, 1949) averaged 208/126, decreased gradually. June 21-July 1, it averaged 153/95. Nine months later (January 11-12, 1950), it had risen again; the average was 187/114. The transverse diameter of the heart was 10.9 cm.; the chest

diameter was 29.5 cm. T_1 in the electrocardiogram was upright; the angle of the electrical axis was +69°. Hemoglobin was 14.3 Gm.; non protein nitrogen 32 mg., urea nitrogen 12 mg. per 100 cc. blood; chlorides 94 mEq. per 1000 cc. serum; cholesterol 200 mg. per 100 cc. serum; plasma protein 7.3 Gm. per 100 cc.; urine protein 0.1 Gm. per 1000 cc. Occasional white blood cells were seen in the sediment. The total PSP excretion in two hours was 40 per cent.

There was continuous improvement of the retinopathy. The eyeground photographs taken January 12, 1950, 10 months after the start of the rice diet, show the **right** disc well-outlined. The veins are less engorged and less tortuous; the arteries remain attenuated. There is straightening of a branch of the inferior nasal artery. Papilledema, retinal edema, hemorrhages and exudates have disappeared (Plate 27). The **left** disc is not quite sharply outlined. The veins are less tortuous and less engorged; the arteries remain attenuated. Papilledema, retinal edema, cottony patches, hard exudates and hemorrhages have disappeared (Plate 28).

The twelfth patient (P. K.) was a 39 year old man with malignant hypertension. He had always been well, but during the course of a routine examination in 1942, his blood pressure was found to be too high. He was examined in the Mayo Clinic in 1943, and a diagnosis of hypertension, Group II, was made. The systolic blood pressure was between 154 and 190 and the diastolic between 110 and 120. Examination of the eyegrounds showed a moderate degree of narrowing and sclerosis of the retinal arterioles. Chest film and intravenous urograms showed nothing pathological. Thiocyanate was given but since the blood pressure did not change, it was discontinued after two or three months. Although he had no complaints, he was checked by his physician every six months. In January, 1949, while feeling perfectly well, he noticed blood in his urine. Because of this and a rather high blood pressure, he was hospitalized and treated with Priscol, Vitamin K and bed rest. The hematuria cleared up, but the patient developed shortness of breath on exertion. On February 10, 1949, he noticed a "blind spot in his left eye" and was therefore sent to our clinic on February 12.

The blood pressure on admission was 215/143. The **right** eye showed papilledema, small hemorrhages and cottony exudates. The veins were engorged (Plate 29). The **left** eye showed papilledema, a large cottony exudate just temporal to the disc, small hemorrhages and soft exudates. The inferior temporal artery and a branch of the inferior nasal artery showed focal constriction. Perivascular sheathing was present along a small branch of the superior temporal artery (Plate 30).

The heart was enlarged to the left (Figure 5). The transverse diameter of the heart was 14.5 cm.; the chest diameter was 33.0 cm. The electrocardiogram showed an inverted T_1; the angle of the electrical axis was -22° (Figure 6). Hemoglobin was 14.1 Gm.; non protein nitrogen 38 mg., urea nitrogen 16.2 mg., sugar 80 mg. per 100 cc. blood; chlorides 100 mEq. per 1000 cc serum; cholesterol 350 mg per 100 cc. serum; plasma protein 6.7 Gm. per 100 cc.; urine protein 1.1 Gm. per 1000 cc. One to 2 granular

casts were seen per high power field, no red blood cells. The total P S P excretion in two hours was 31 per cent. The concentration-dilution test showed a range from 1.008 to 1.016.

The patient was immediately started on the rice diet. He followed the basic rice diet for 3 months. Then the diet was gradually modified to include small amounts of vegetables, vegetable oil and nuts. The average urine chloride concentration (as NaCl per 100 cc.) was: 22 mg., February 28 to March 17; 11 mg., May 2-15, and 41 mg., June 13 to November 1, 1949.

The blood pressure decreased gradually. February 12-21, it averaged 210/140; May 10-19, 189/124; July 12-13, 168/118; November 1-2, 147/110. The heart became smaller in size (Figure 5). The transverse diameter decreased from 14.5 cm. to 12.2 cm.; the chest diameter was the same (33.1 cm.). The inverted T_1 became upright (Figure 6); the angle of the electrical axis increased to $+5°$. Hemoglobin was 15.0 Gm.; non protein nitrogen 41 mg., urea nitrogen 18.7 mg. per 100 cc. blood; chlorides 96 mEq. per 1000 cc. serum. The cholesterol decreased from 350 to 225 mg per 100 cc. serum. The plasma protein increased from 6.7 to 7.0 Gm. per 100 cc. The urine protein decreased from 1.1 Gm. to. 11 Gm. per 1000 cc. There were no longer any granular casts in the urine. The total PSP excretion remained constant: the total excretion in two hours was 30 per cent.

There was continuous improvement of the retinopathy. The eyeground photographs taken November 2, 1949, 9 months after the start of the rice diet, show the **right** disc fairy well-outlined. Papilledema, hemorrhages and exudates have disappeared. The veins are less engorged and less tortuous; the arteries are less tortuous (Plate 29). The **left** disc is not quite sharply outlined along the nasal and superior margins. Papilledema, hemorrhages and exudates have disappeared (Plate 30).

All of the 12 patients, whose histories have just been given, had advanced vascular retinopathy and in every case the retinopathy showed marked improvement on the rice diet.

All of these patients had hypertension at the time of admission (Table 1). The degree of hypertension varied from 180/100 to 280/160. There was no direct relation between the degree of retinopathy and the degree of hypertension. In fact, in this series it happens that the retinopathy in patient 7 whose initial blood pressure was 280/160 was much milder than that of patient 4 whose blood pressure was 180/100.

The blood pressure of all these patients decreased on the diet. However, there was no direct relation between the lowering of the blood pressure and the disappearance of the retinopathy. In some instances, the process of healing continued even after the patient had discontinued the diet prematurely and the blood pressure had risen again, in one patient to a level higher than that on the first admission.

Chest films, taken on admission and at the same time as the last eyeground picture, are available for comparison in 11 of the 12 patients. There was no direct relation between enlargement and the degree of retinopathy nor

between the decrease in heart size and the disappearance of the retinopathy. In 10 instances, the transverse diameter of the heart was smaller in the last than in the first film (Table 2). One patient had had a marked reduction in heart size after three months on the rice diet, but after having given up all dietary restrictions for three years, the heart had become even larger than it had been at the time of the first admission. The retinopathy, however, did not recur.

Five of the 12 patients had an abnormal T_1 in the electrocardiogram at the time of admission (Table 3). (In one instance, a digitalis effect cannot be ruled out). In 2, T_1 was diphasic, in 3 inverted. At the time when the last eyeground photographs were taken, the T_1 in the electrocardiograms of all of the patients was normal. However, there was no direct relation between the degree of T_1 abnormality and the degree of retinopathy nor between the disappearance of the T_1 abnormality and the disappearance of the retinopathy.

Nine of the 12 patients had at the time of admission proteinuria ranging from 0.67 to 4.5 Gm. protein per 1000 cc. (Table 4). There was no direct relation between the degree of proteinuria and the degree of retinopathy. The proteinuria of all these patients decreased on the diet. At the time when the last eyeground photographs were taken, the proteinuria ranged from 0.06 to 0.72 Gm. per 1000 cc. However, there was no direct relation between the decrease of the proteinuria and the disappearance of the retinopathy.

In 9 of the 12 patients the renal function as measured by the phenolsulfonphthalein test, was impaired (Table 5). The total PSP excretion in two hours at the time of admission was: 10 per cent or less in 2 patients, 18 to 26 per cent in 3, and 31 to 51 per cent in 4. Only 3 patients had a PSP excretion of more than 60 per cent. There was no direct relation between the degree of retinopathy and the degree of renal impairment. In fact, the retinopathy in patient 8, who had a PSP excretion of 88 per cent with an initial blood pressure of 300+/150, was much more severe than that of patient 7, who had a PSP excretion of 51 per cent with an initial blood pressure reading of 280/160. There was no direct relation between the change in the PSP excretion and the disappearance of the retinopathy. In all 12 patients, the retinopathy improved. When the last eyeground photographs were taken, the PSP figures of 6 patients were lower than on admission: of 3 patients higher than on admission and of 3 patients practically constant.

Four of the 12 patients had a non protein nitrogen above 60 mg. per 100 cc of blood at the time of admission (Table 6). There was no direct relation between the degree of retinopathy and the level of the non protein nitrogen. The protein nitrogen decreased in 7 of the 12 patients; in one it remained constant; in 4, it increased.

In the 4 patients with an initial non protein nitrogen above 60 mg. it decreased from an average of 83 mg. per 100 cc. blood to an average of 57 mg. In 4 patients with an initial non protein nitrogen below 50 mg., it decreased from an average of 38 mg. to an average of 29 mg. In one, it remained constant. In 2 patients, it increased from an average of 32 mg. to an

average of 37 mg., in 1 patient from 4 mg. to 64 mg. There was no direct relation between the improvement in the retinopathy and the changes in non protein nitrogen.

Nine of the 12 patients had hypercholesterolemia at the time of admission (Table 7). Their initial cholesterol concentrations were between 230 mg and 380 mg. per 100 cc, serum. There was no direct relation between the degree of retinopathy and the degree of hypercholesterolemia. The cholesterol concentration of all 9 patients decreased on the diet. At the time when the last eyeground photographs were taken the cholesterol concentrations were between 100 and 225 mg. per 100 cc. serum. However, there was no direct relation between the decrease in the cholesterol concentration and the disappearance of the retinopathy.

It is true that hypertension, heart enlargement, T_1 inversion, proteinuria, decreased PSP excretion, azotemia and hypercholesterolemia are often associated with retinal hemorrhages, exudates and papilledema. On the other hand, very oftenl no papilledema, hemorrhages or exudates are found in patients with severe or even terminal nephritis, arteriosclerosis and hypertensive vascular disease.

No matter what role hypertension, proteinuria, hypercholesterolemia, renal insufficiency or a combination of these or other factos play in the production of retinopathy or how these factors may be influenced by treatment, the fact remains that in the majority of these patients treated by the rice diet, papilledema, hemorrhages and exudates disappear.

In a series of 225 patients with advanced vascular retinopathy (papilledema, hemorrhages or exudates), eyeground photographs taken before and after 1 to 34 months of the rice diet are available for comparison. Forty-two of the 225 patients had chronic nephritis; 183 had hypertensive vascular disease (Table 8).

Papilledema was present in 15 of the 42 patients with chronic nephritis. In 1, it disappeared partially, in 14 completely. Hemorrhages were present in 38 of the 42 patients. In 5, they remained unchanged; in 7, they disappeared partially, in 26 completely. Two of the 42 patients who had no exudates at the start of the diet developed exudates while on the diet. In 37 of the 42 patients, exudates were present on admission. In 1, they increased; in 3, they remained unchanged; in 13, they disappeared partially, in 20 completely.

Thirty-nine of the 183 patients with hypertensive vascular disease had papilledema. In 1 patient it remained unchanged; in 5 patients, it disappeared partially, in 33 completely. Hemorrhages were present in 135 of the 183 patients. In 1 patient, they increased; in 4 patients, they remained unchanged; in 37, they disappeared partially, in 93 completely. Exudates were present in 143 of the 183 patients. In 2 patients, they increased; in 10 patients, they remained unchanged; in 48, they disappeared partially, in 83 completely.

Table 1
BLOOD PESSURE

PATIENT	ON ADMISSION (mm. Hg.)	MINIMUM ON STRICT DIET (mm. Hg.)	(Cl.)*	AT TIME OF LAST PICTURE (mm. Hg.)	(Cl.)*
1	240/140	152/94	(4)	188/114	(13)
2	244/152	146/110	(14)	140/101	(7)
3	200/112	110/70	(14)	140/93	(17)
4	180/100	124/78	(9)	193/117	(137)
5	204/136	120/90	(17)	165/100	(24)
6	200/114	122/90	(5)	142/96	(132)
7	280/160	140/90	(15)	163/100	(9)
8	300/150	162/92	(14)	220/123	(177)
9	225/140	90/62	(8)	128/88	(105)
10	233/157	120/84	(13)	225/135	(500+)
11	230/130	138/80	(7)	187/114	(85)
12	215/143	162/120	(9)	147/110	(52)

*Chloride (as mg. NaCl) per 100 cc. of urine.

Table 2
HEART SIZE

PATIENT	TRANSVERSE DIAMETER OF HEART (cm.) AT TIME OF ADMISSION	TRANSVERSE DIAMETER OF HEART (cm.) AT TIME OF LAST PICTURE	DIAMETER OF CHEST (cm.) AT TIME OF ADMISSION	DIAMETER OF CHEST (cm.) AT TIME OF LAST PICTURE	TIME BETWEEN ADMISSION AND LAST PICTURE (months)
1	11.4	10.5	29.5	29.7	13
2	13.8	10.9	29.5	28.4	11
3	13.0	10.5	28.5	28.8	9
4	13.8	13.2	27.9	28.1	19
5	11.2	10.2		25.2	6
6	14.0	12.7	31.7	31.7	15
7	12.7	11.4	27.8	27.5	12 1/2
8	12.4	10.7	23.7	23.5	15
9		9.7		24.3	14
10	16.6	17.1	32.0	31.6	60
11	11.9	10.9		28.4	10
12	14.5	12.2	33.0	33.1	9

Table 3
ELECTROCARDIOGRAM

PATIENT	T_1		ELECTRICAL AXIS (°)		TIME BETWEEN ADMISSION AND LAST PICTURE (months)
	AT TIME OF ADMISSION	AT TIME OF LAST PICTURE	AT TIME OF ADMISSION	AT TIME OF LAST PICTURE	
1	Upright	Upright	+ 65	+ 79	13
2	Upright	Upright	+ 31	+ 66	11
3	Upright	Upright	+ 74	+ 81	9
4	Inverted	Upright	+ 30	+ 23	19
5	Upright	Upright	+ 68	+ 72	6
6	Inverted	Upright	- 39	- 25	15
7	Diphasic	Upright	+ 20	+ 20	12 1/2
8	Diphasic	Upright	- 16	- 9	15
9	Upright	Upright	+ 66	+ 58	14
10	Upright	Upright	+ 18	+ 45	60
11	Upright	Upright	+ 30	+ 69	10
12	Inverted	Upright	- 22	+ 5	9

Table 4
PROTEINURIA

PATIENT	AT TIME OF ADMISSION (Gm. per 1000 cc.)	AT TIME OF LAST PICTURE (Gm. per 1000 cc.)	TIME BETWEEN ADMISSION AND LAST PICTURE (months)
1	4.5	0.16	13
2	4.0	0.3	11
3	0.55	0.06	9
4	1+	trace	19
5	2.0	0.72	6
6	0.1	0	15
7	0.1	0	12 1/2
8	0.8	0.16	15
9	4.5	0.36	14
10	0.67	0	60
11	0.9	0.1	10
12	1.1	0.11	9

Table 5
PHENOLSULFONPHTHALEIN TEST

PATIENT	AT TIME OF ADMISSION Total Excretion in 2 Hours (%)	AT TIME OF LAST PICTURE Total Excretion in 2 Hours (%)	TIME BETWEEN ADMISSION AND LAST PICTURE (months)
1	18	7	13
2	9	21	11
3	26	21	9
4	18	13	19
5	20	16	6
6	62	66	15
7	51	50	12 1/2
8	88	60	15
9	47	54	14
10	61	60	60
11	48	40	10
12	31	30	9

Table 6
NON PROTEIN NITROGEN

PATIENT	AT TIME OF ADMISSION (mg. per 100 cc. of blood)	AT TIME OF LAST PICTURE (mg. per 100 cc. of blood)	TIME BETWEEN ADMISSION AND LAST PICTURE (months)
1	114	90	13
2	70	42	11
3	64	44	9
4	84	51	19
5	44	64	6
6	26	31	15
7	34	25	12 1/2
8	36	28	15
9	30	30	14
10	26	32	60
11	48	32	10
12	38	41	9

Table 7
CHOLESTREROL

PATIENT	AT TIME OF ADMISSION (mg. per 100 cc. of blood)	AT TIME OF LAST PICTURE (mg. per 100 cc. of blood)	TIME BETWEEN ADMISSION AND LAST PICTURE (months)
1	320	190	13
2	165	200	11
3	265	160	9
4	180	155	19
5	233	215	6
6	175	210	15
7	265	170	12 1/2
8	270	195	15
9	380	160	14
10	240	180	60
11	230	200	10
12	350	225	9

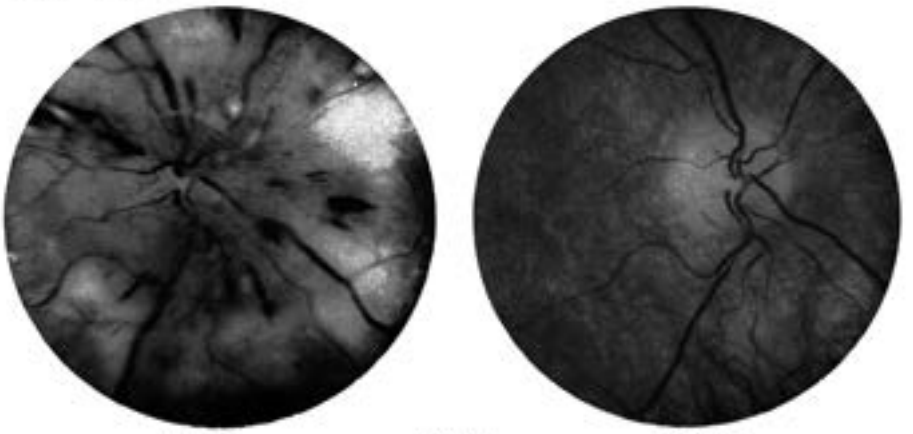
Tab'e 8

EFFECT OF RICE DIET ON RETINOPATHY

(225 Patients Where Eyeground Phtographe Are Available Before And After 1 To 34 Months Of Diet)

	PRESENT BEFORE TREATMENT	INCREASED	REMAINED UNCHANGED	DISAPPEARED	
				PARTIALLY	COMPLETELY
CHRONIC NEPHRITIS (42 Patients)					
PAPILLEDEMA	15	–	–	1	14
HEMORRHAGES	38	–	5*	7	26*
EXUDATES	37	1	3	13	20
*One of these patients who had hemorrhages but no exudates before developed exudates while on the diet.					
HYPERTENSIVE VASCULAR DISEASE (183 Patients)					
PAPILLEDEMA	39	–	1	5	33
HEMORRHAGES	135	1	4	37	93
EXUDATES	143	2	10	48	83

H. R. (m., 39)



10-2-48 RIGHT 11-22-49

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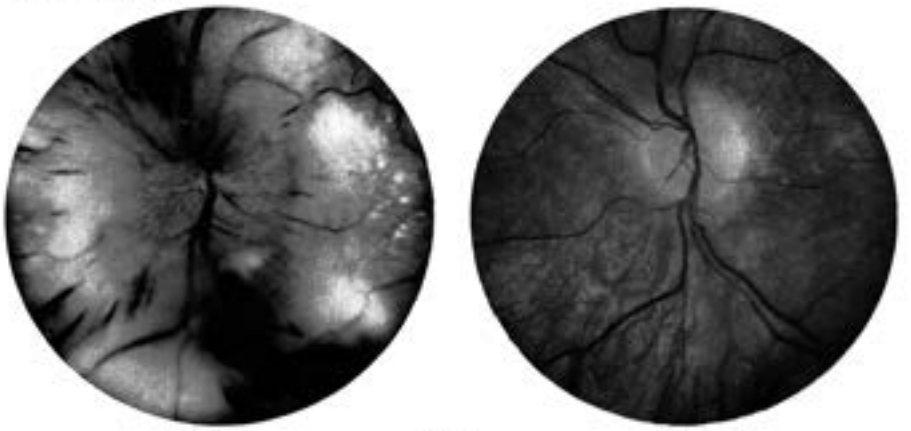

10-2-48 LEFT 11-22-49

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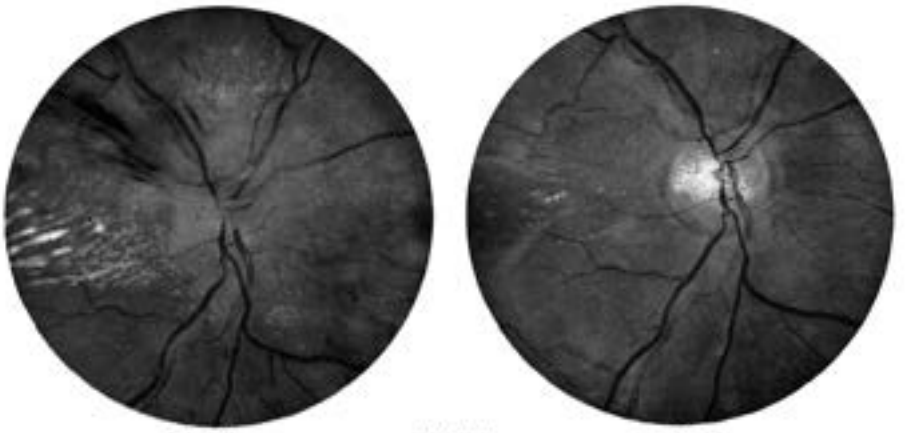

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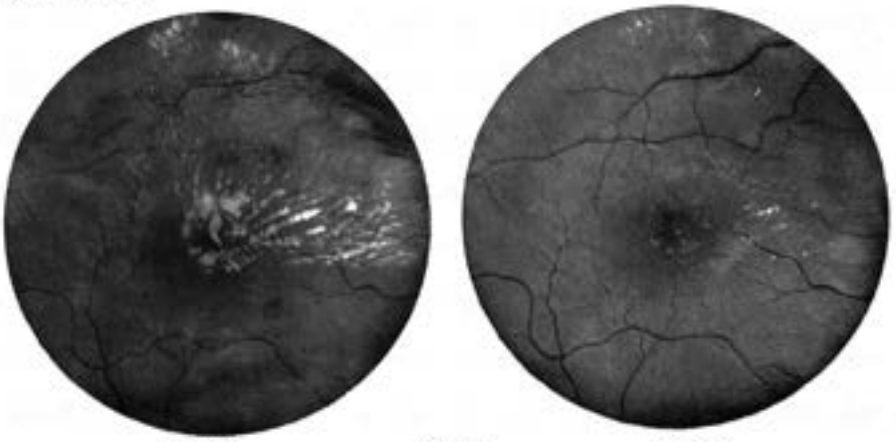

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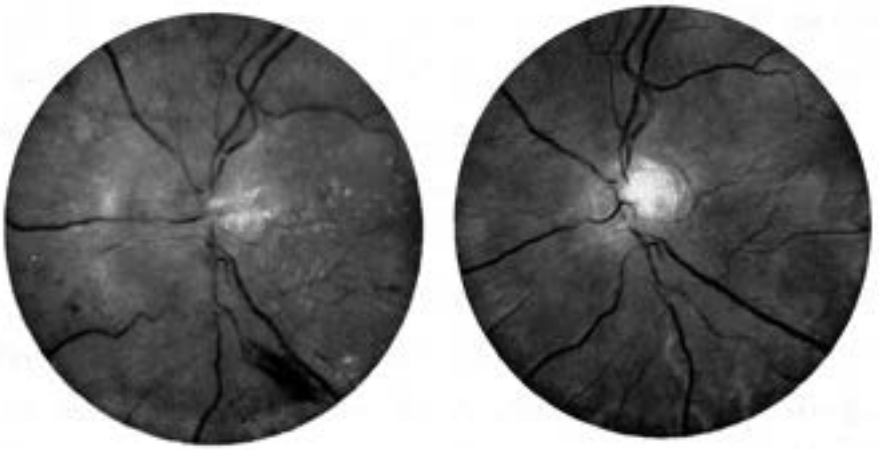

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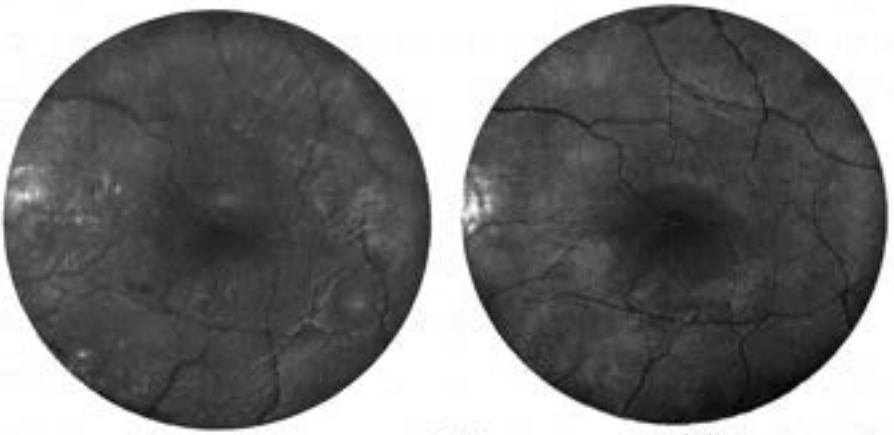

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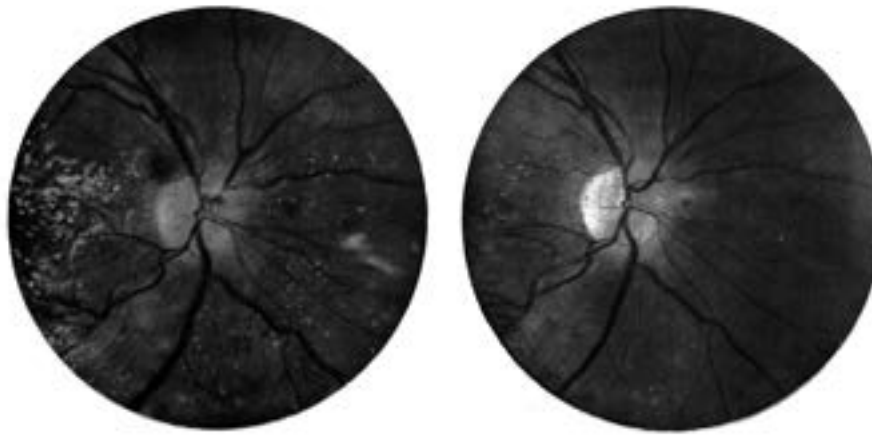

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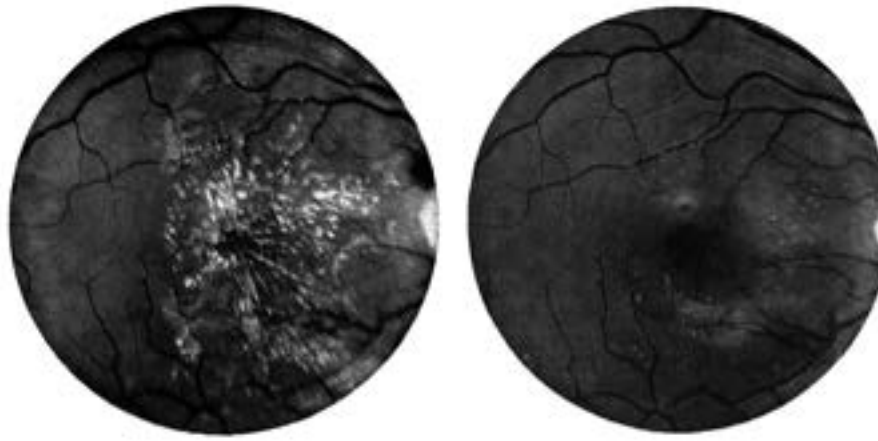

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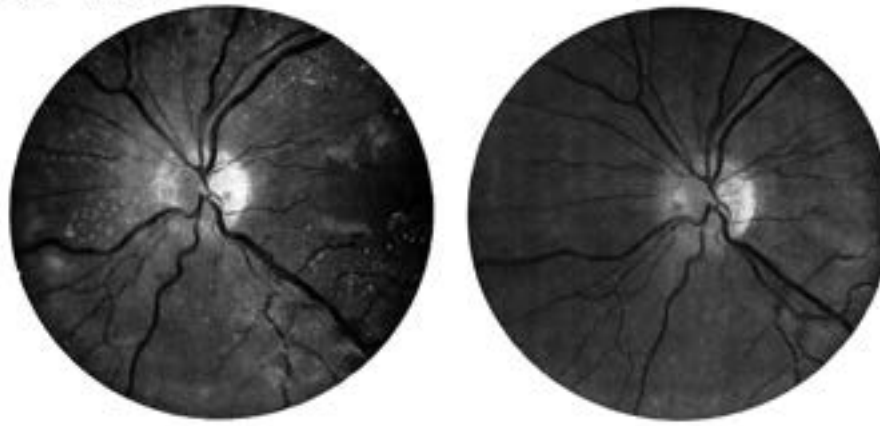

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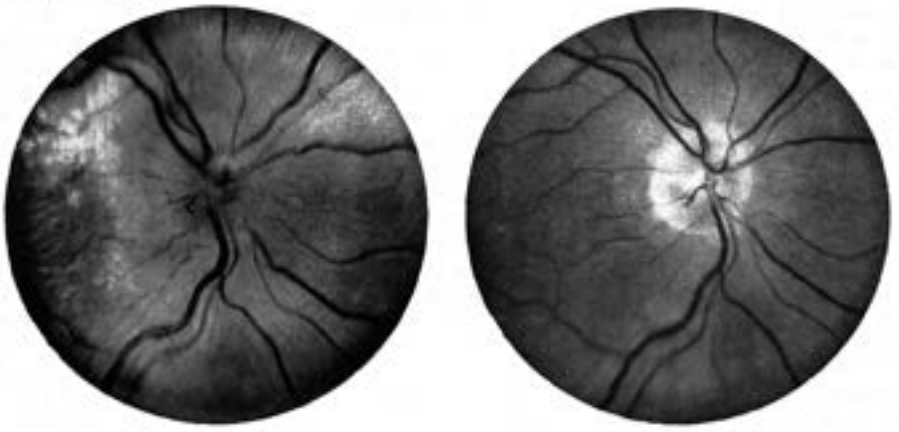

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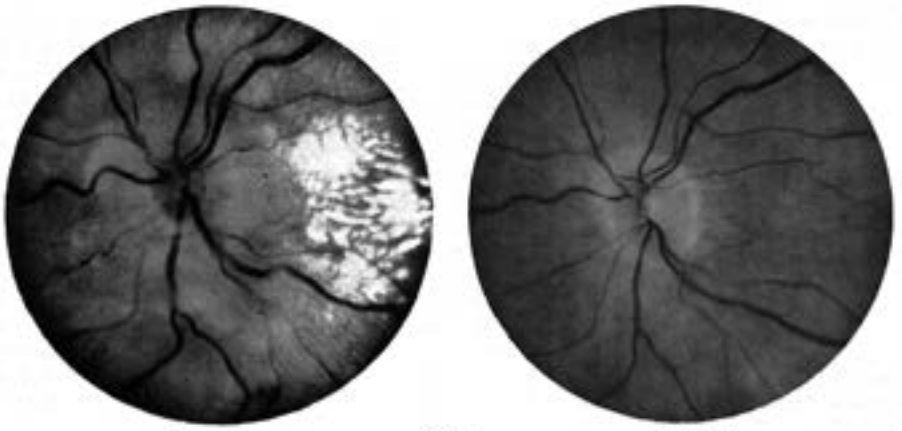

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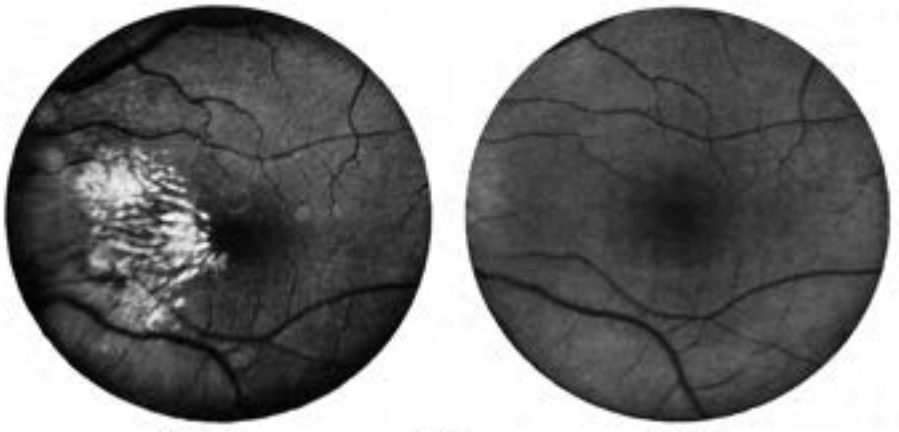

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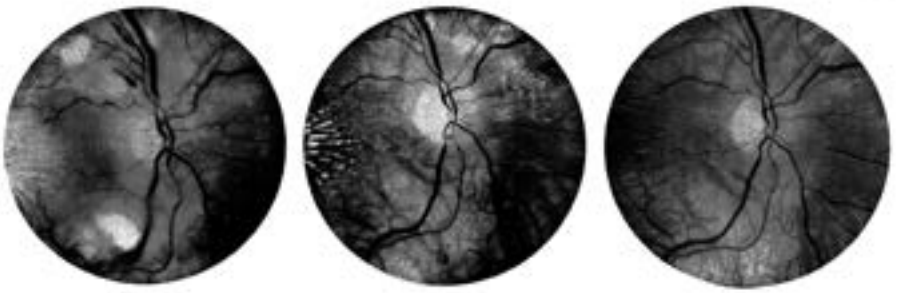
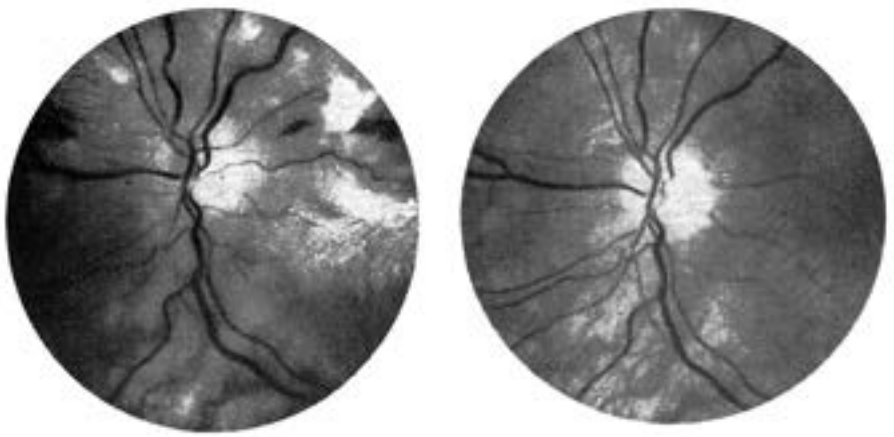


3-11-49 5-12-49 9-21-49

D. K. (f., 19) RIGHT

3-11-49 5-12-49 9-21-49

D. K. (f., 19)



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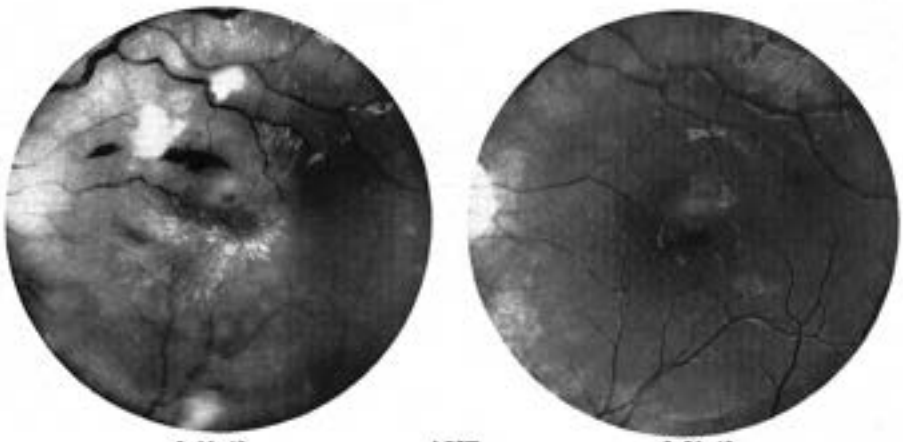

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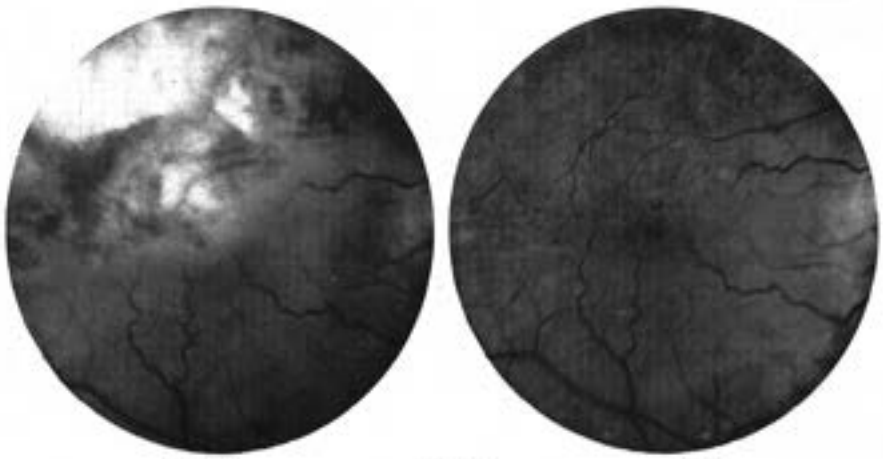

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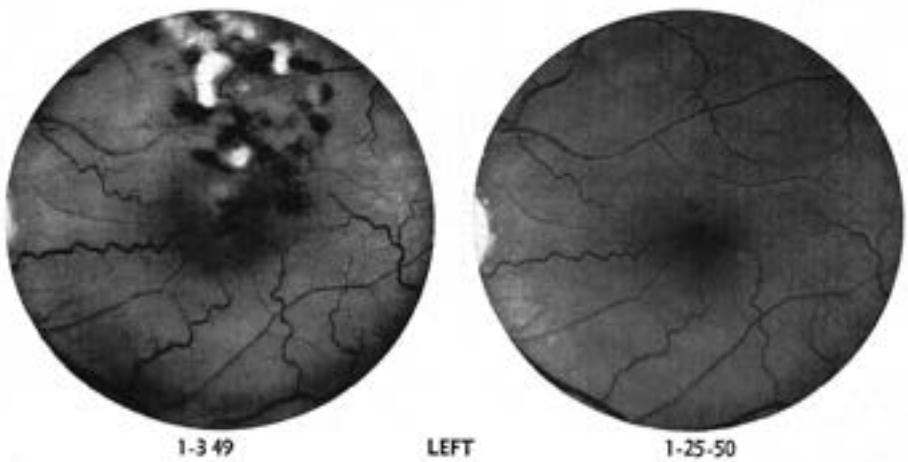

1-3 49 LEFT 1-25-50

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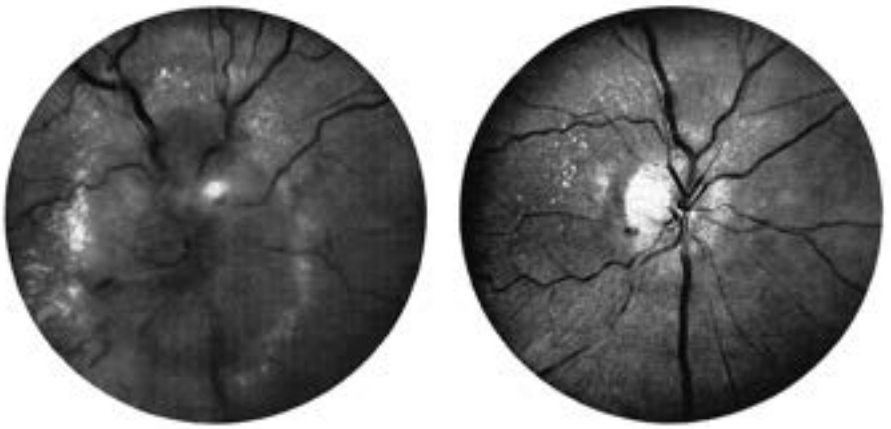

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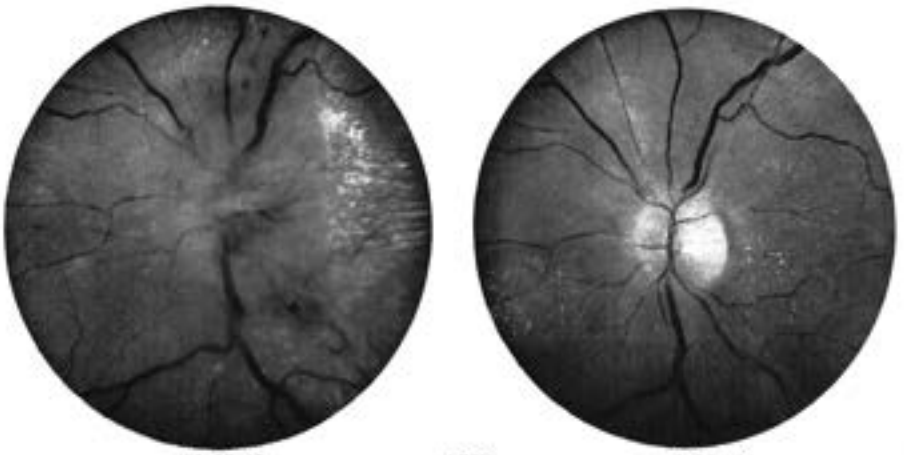

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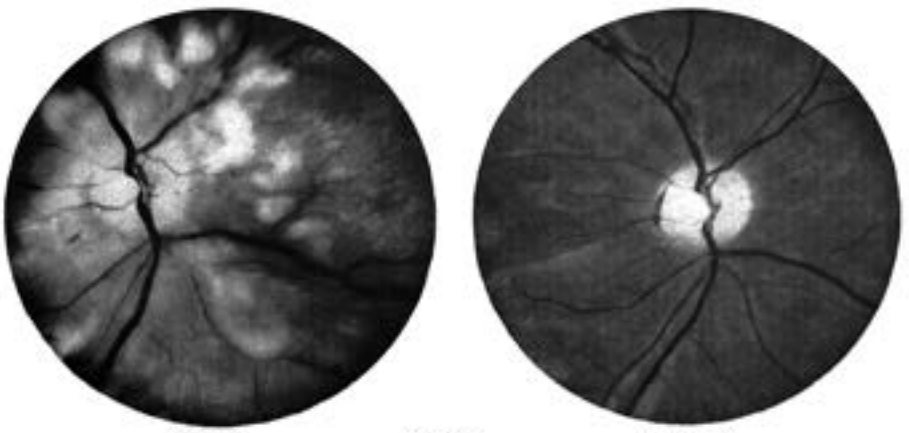

8-26-48 RIGHT 10--24-49

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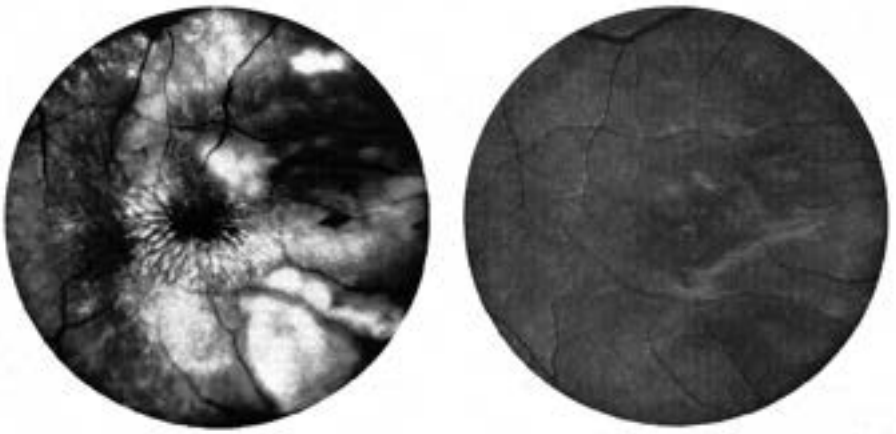

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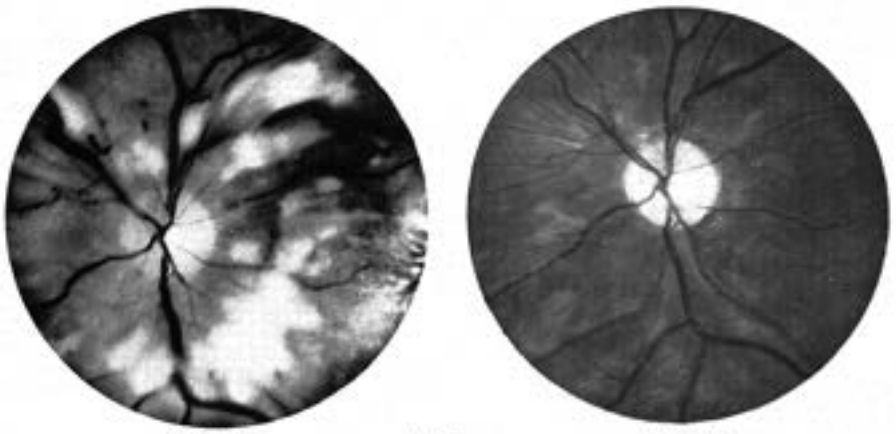

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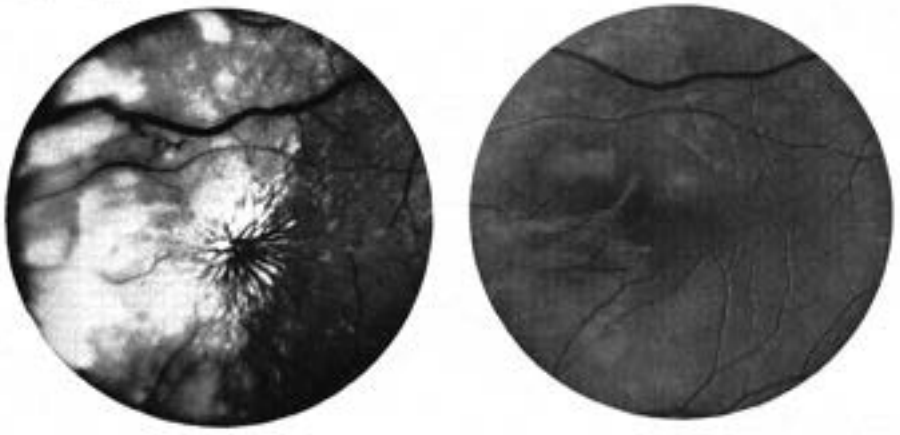

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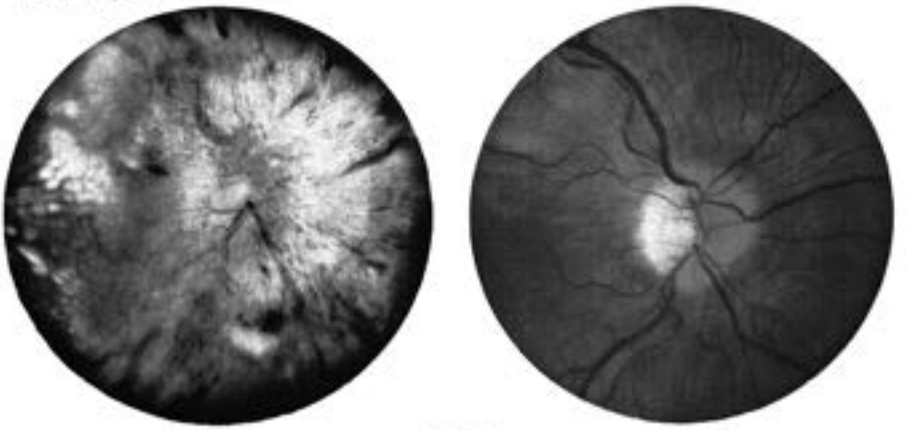

11-6-44 RIGHT 11-10-49

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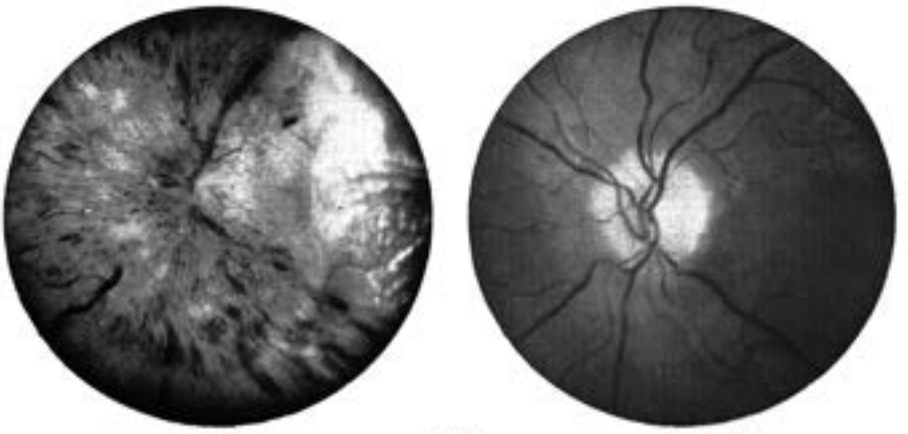

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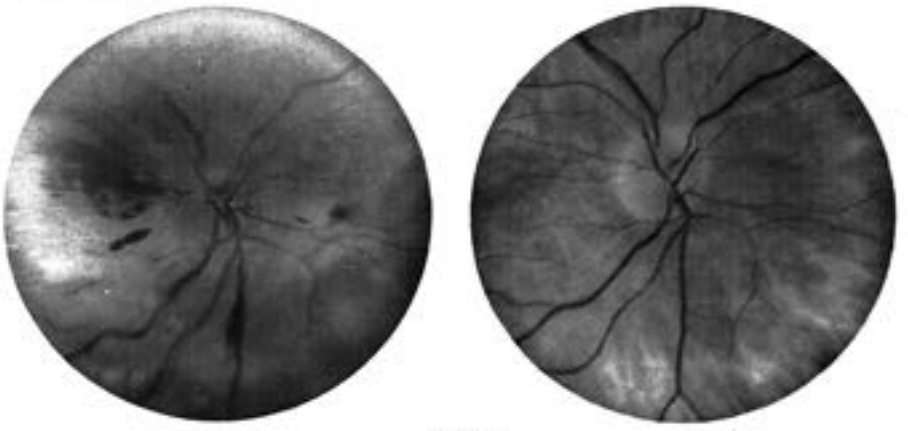

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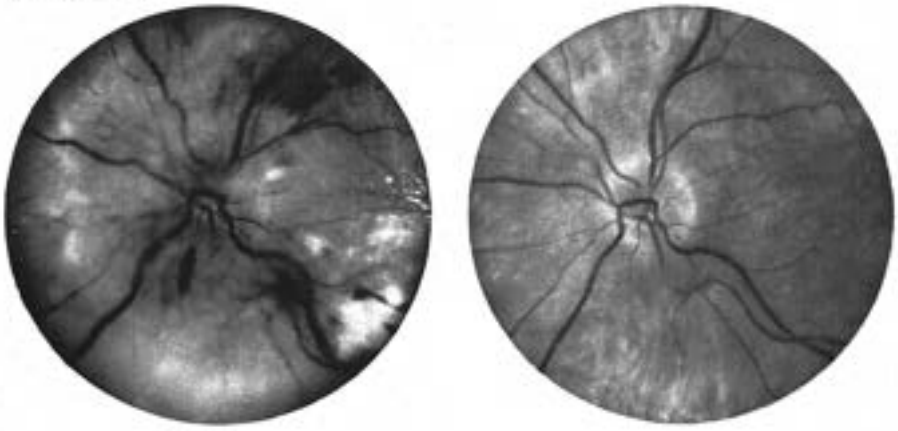

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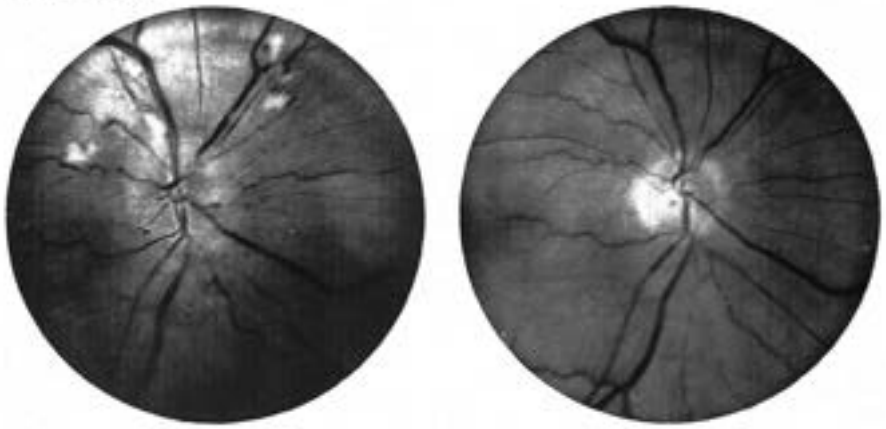

2-12-49 RIGHT 11-1-49

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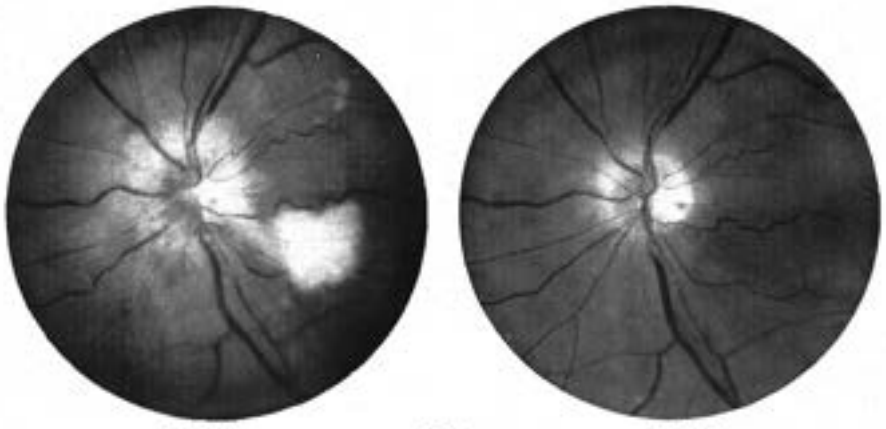

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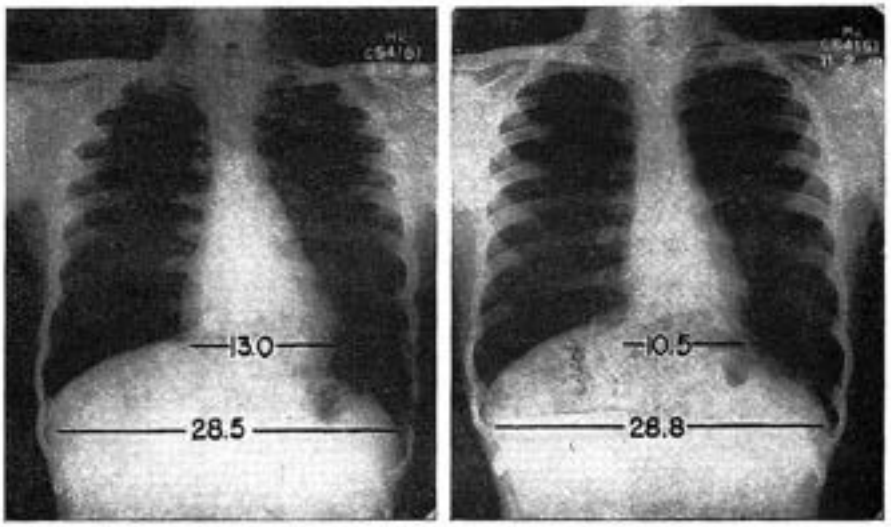

2-11-49 D. G.V.6.5 11-2-49 D. GV. 54

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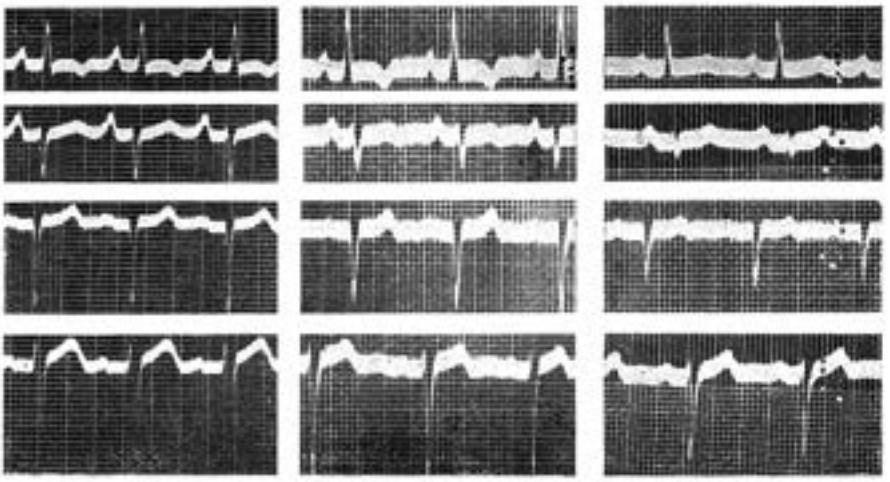
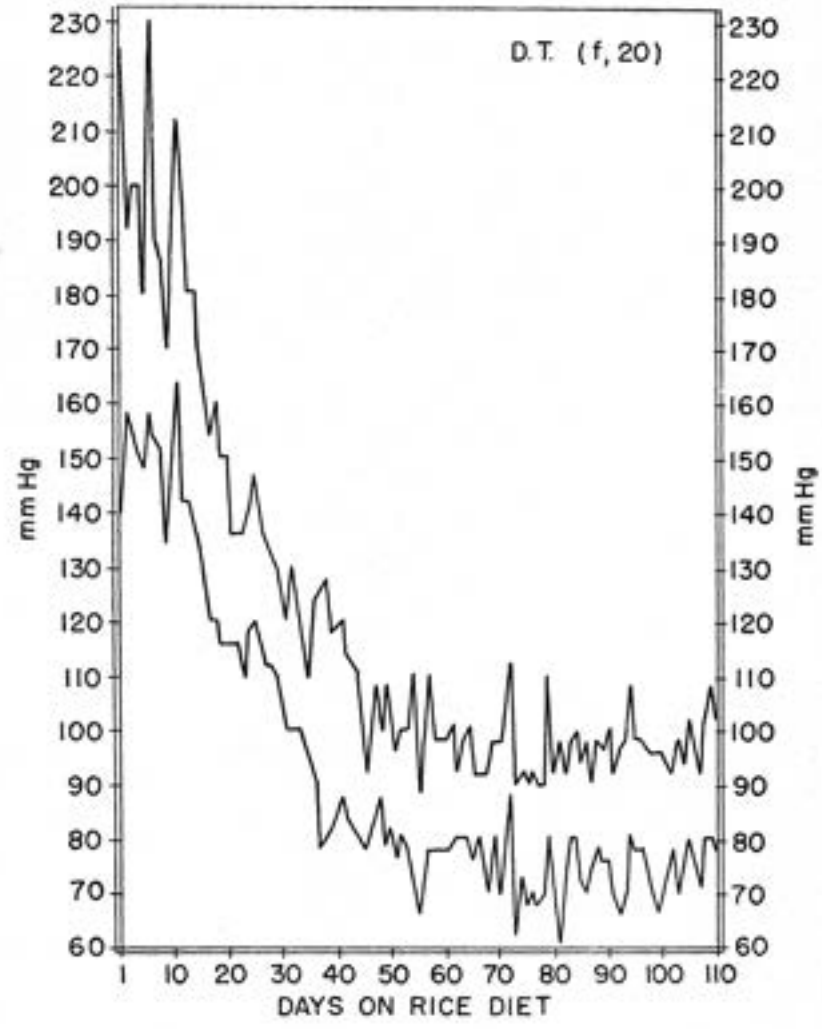
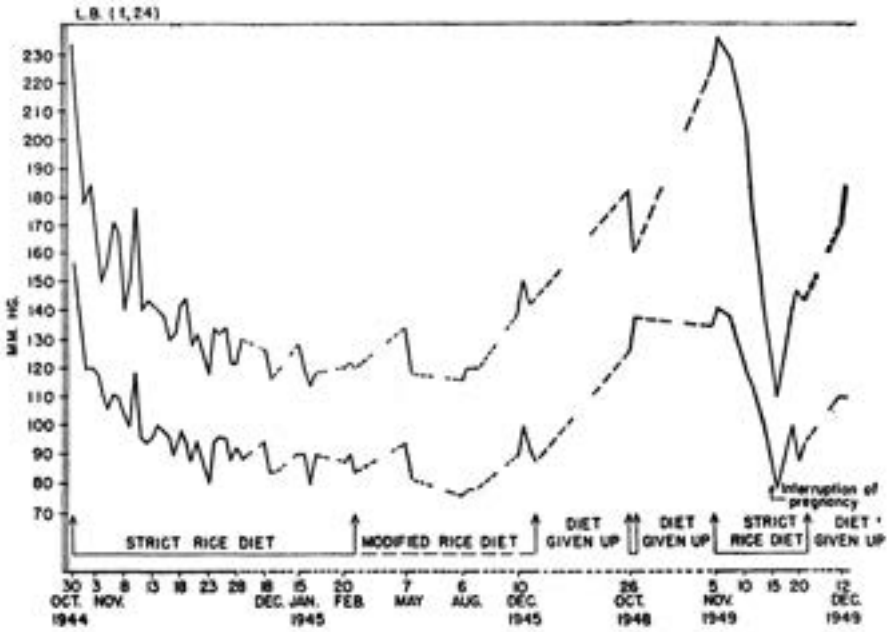


7-24-44 9-17-48 2-2-50


D.T. (f, 20)
mm Hg
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
1 10 20 30 40 50 60 70 80 90 100 110
DAYS ON RICE DIET


L.B. (1,24)
MM. HG.
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
STRICT RICE DIET
MODIFIED RICE DIET
DIET GIVEN UP
DIET GIVEN UP
STRICT RICE DIET
DIET GIVEN UP
Interruption of pregnancy
30 OCT. 1944
3 NOV.
8
13
18
23
28
18 DEC.
15 JAN. 1945
20 FEB.
7 MAY
6 AUG.
10 DEC. 1945
26 OCT. 1948
5 NOV. 1949
10
15
20
12 DEC. 1949

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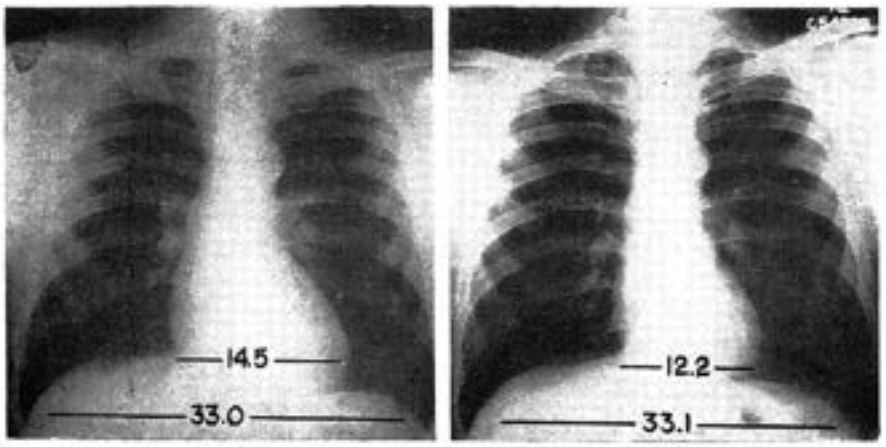

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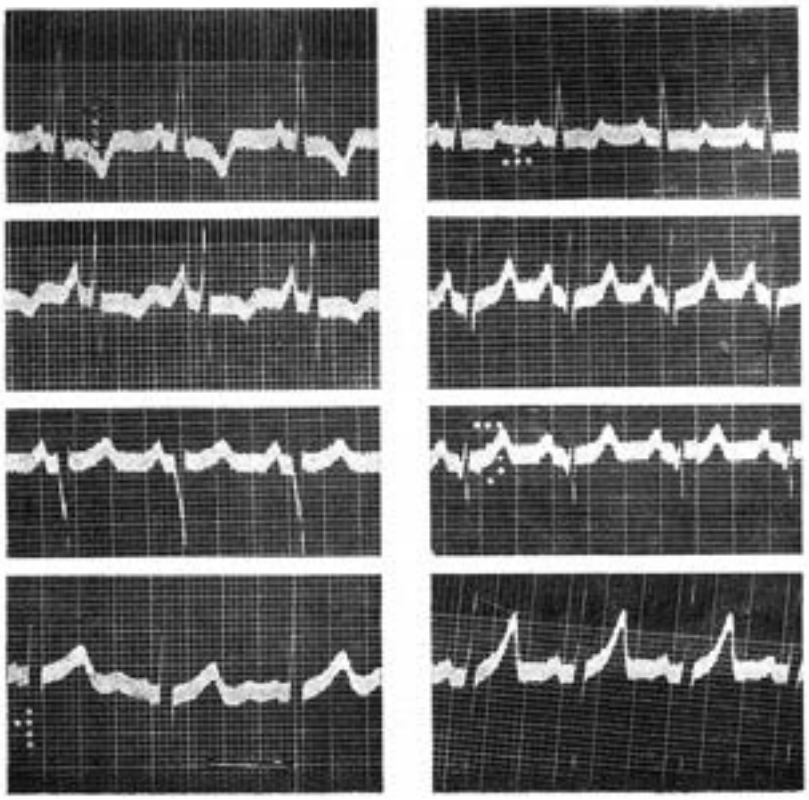

2-14-49 11-1-49

Potassium Deficiency as Cause of the So-Called Rheumatic Heart Lesions of the Adaptation Syndrome

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pp. 399-407

POTASSIUM DEFICIENCY AS CAUSE OF THE SO-CALLED RHEUMATIC HEART LESIONS OF THE ADAPTATION SYNDROME*

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From the Departments of Medicine and Pathology, Duke University, School of Medicine, Durham, North Carolina

IN THE course of experiments designed to study the relationship of diet and hypertension, various techniques of inducing hypertension in rats were used including Selye's method which he describes in his communication on pathogenetical correlations between periarteritis nodosa, renal hypertension and rheumatic lesions (Selye and Pentz, 1943). This method consists of overdosage with desoxycorticosterone acetate (DCA) with or without high sodium chloride intake in unilaterally nephrectomized rats. Selye found that severe overdosage with DCA reproduces in the rat morphological lesions similar to those seen in periarteritis nodosa, malignant hypertension and rheumatic fever. He concludes that these diseases are, at least partly caused by an abnormal adaptive response of the adrenal cortex and represent diseases of adaptation.

In the first series of our experiments when rats with an average weight of 168 grams were treated with DCA overdosage following unilateral nephrectomy, hypertension was only rarely produced, and periarteritis nodosa was not seen. (In further experiments using younger rats of 80 to 124 grams as in Selye's original work, hypertension did consistently develop and periarteritis nodosa was occasionally found; cardiac lesions occurred only in some animals, corresponding with the observations reported in this paper.)

Despite the failure to produce hypertension in the earlier experiment, cardiac lesions were noted which were identical with those reported by Selye and Pentz (1943) as resembling rheumatic heart disease in man. However, the experimental set-up and our past experience (Smith, Black-Schaffer and Lasater, 1950) enabled us to show that these lesions are not related to rheumatic fever, etiologically or pathogenetically, but are the consequence of potassium deficiency.

METHODS

Female albinos of the Osborne-Mendel strain weighing between 112 and 219 grams, average 168 grams, were used. As indicated in Table 1, 39 rats were divided into eight groups of 4 to 5 animals each. The weight distribution among the groups was approximately equal.

Each group was placed on a diet consisting of one well defined food stuff (such as beef, fat cheese, rice, potatoes, etc.) supplemented by vitamins. The vitamin supple-

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ments per rat and per day were: thiamine 40 γ; riboflavin 100 γ; niacin 500 γ; pyridoxine 40 γ; calcium pantothenate 150 γ; choline 7 mg.; ascorbic acid 2.5 mg.; β-carotene 200 γ; vitamin D 5 USP units; α-tocopherol 500 γ. Control animals, not treated with nephrectomy or DCA and placed on rice without additional sodium chloride, were killed after 25, 50, 100, 200, 400 and 600 days respectively. The microscopic examinations did not reveal pathological changes in any organ. This indicated that the vitamin supplements were sufficient.

The daily food intake of the individual animal was measured by comparing the weight of the food container when filled and ready to be put into the cage, and when taken out after 24 hours. Detectable spilling of food did not occur. Raised wire mesh bottoms in the

TABLE 1. EFFECT OF DIETS WITH DIFFERENT POTASSIUM CONTENT ON SURVIVAL TIME OF DCA-TREATED, UNILATERALLY NEPHRECTOMIZED RATS

Diet		Fat cheese	Rice	Bread	Eggs	Beef	Dog chow	Peas	Potatoes
Mg. potassium in 24 hr. diet		7	12	22	31	59	160	167	188
Survival time (days)	Tap water	35	**	45	*	**	*	*	*
		40	**	*	*	**	*	*	*
	1% NaCl solution	14	19	30	A.	33	*	*	*
		18	20	31	33	44	*	*	*
		24	21	A.	A.	**		*	*

* Killed after 75 days. ** Killed after 425 days. A. Died accidentally

cages prevented access to excreta. Average food intakes for each diet group were calculated from the food consumptions of the individual rats.

Tap water was the drinking fluid for two animals in each group while the remainder received a 1% sodium chloride tap water solution.

DCA (in aqueous suspension, 20 and 30 mg. per cc. respectively) was injected twice daily for 40 days as follows: 8.0 mg. per diem, subcutaneously, for the first 10 days and 12.0 mg. per diem, for the following 30 days. The injections were started ten days after the special diets were begun. The diets with or without saline were continued without change after the DCA was discontinued. All survival times were calculated from the beginning of DCA administration.

RESULTS

Only one animal developed persistent hypertension which varied between 150 and 178 mm. Hg (systolic). This animal was on beef diet with additional high sodium chloride intake. Occasional blood pressure readings of 138 to 168 mm. Hg were obtained in four others—one from the bread group, two from the potato group, and another one from the beef group, all on additional high sodium chloride intake.

Fourteen animals died between the 14th and the 46th day. Three additional rats died accidentally: one was suffocated on the seventh day, the two others died during cardiac puncture on the 45th day. Seventeen of the 22 survivors were killed on the 75th and the remaining 5 on the 425th day after the start of the experiment.

All the rats who died before the 46th experimental day (with the exception of 2 of the 3 who died accidentally) developed to a greater or lesser degree some or all of the following symptoms suggesting cardiac failure: dyspnea, cyanosis, peripheral edema, ascites, pleural effusions. There was no indication of infections of the respiratory system, but the microscopic examination showed passive congestion of lungs, liver and spleen in all the 14 rats who died spontaneously, and in one who died accidentally on the 45th day.

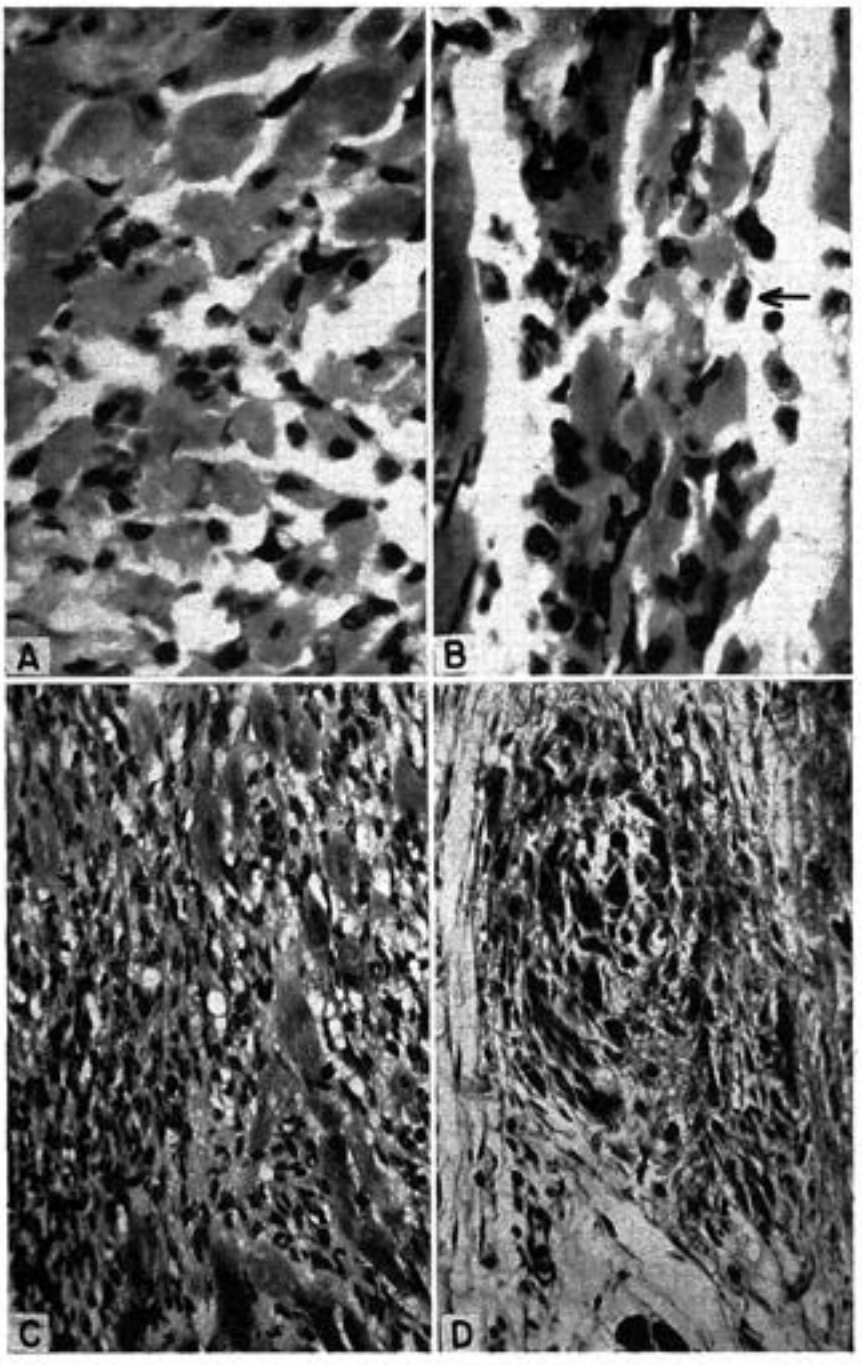
The myocardium of several of these animals showed greyish foci measuring up to about 3 mm. in greatest diameter.

The hearts of all the rats (with the exception of 2 of the 3 who died accidentally) who died before the 46th day of the experiment showed, histologically, a qualitatively uniform lesion—myocardial necrosis and an accompanying cellular reaction. The development of these lesions could be studied by comparing the microscopic appearance in different animals representing different stages of cardiac damage. The process is first visible in the fibers subjacent to the endocardium of the four chambers. The left ventricular wall is most frequently and extensively involved followed in diminishing order by the right ventricular myocardium and that of the auricles. The myocyte striations lose their distinctness and the sarcoplasm assumes a homogenous hyaline appearance (Figure 1A). The changed sarcoplasm then breaks up into smaller and larger eosinophilic particles with ultimate fragmentation of the entire myocyte (Figure 1B). The nucleus meanwhile becomes pyknotic or swells and disappears. Individual fibers separated by seemingly normal myocytes undergo this change particularly in the inner third of the left ventricular myocardium. The Masson trichrome stain (Mallory, 1938) is very helpful in demonstrating the eclectic nature of the necrosis since in its earliest manifestations there is no cellular exudate or connective tissue reaction to focus attention. Nowhere may damaged vessels or thrombosis be seen.

The fibrocytes and capillary endothelial cells respond to the necrosis by proliferation (Figure 1B). Among the fibroblasts are many characteristic Anitschkow cells, a small number of polymorphonuclear leucocytes and some monocytes. These last manifest their phagocytic property and enlarge to typical macrophages.

As the process advances large areas in the inner third of the left ventricle, and to a lesser extent elsewhere, show complete replacement by fibroblasts and Anitschkow cells (Figure 1C). Multiplication of these elements is rapid, and numerous mitotic figures are readily found.

The oldest lesions, usually in the papillary muscles and the trabeculae carneae show a very slight increase in reticulin fibers: an early indication of eventual scarring.


A
B
C
D

In no instance was a valvulitis seen.

No trace of any myocardial lesion resembling that described above was found in the hearts of the rats killed after 75 days and 425 days respectively.

To one acquainted with the lesions of severe hypopotassemia in the rat it is at once apparent that the cardiac changes produced in this experiment are identical with those easily produced in the same species by means of a low potassium diet (Schrader, Prickett and Salmon, 1937; Thomas, Mylon and Winternitz, 1940; Follis, Orent-Keiles and McCollum, 1942; Kornberg and Endicott, 1946). Furthermore, it is just as apparent that both, in all respects, are similar to those depicted and described by Selye and Pentz (1943) as analogues of rheumatic myocarditis in man.

To test the conclusions arrived at from a consideration of the pathologic anatomy of the hearts, the potassium contents of the various diets were estimated according to the tables of McCance and Widdowson (1947). Table 1 lists the average amount of potassium actually consumed for each category. Correlating survival time and number of survivors with the average daily consumption of potassium reveals that rats receiving diets with low amounts of potassium died in larger numbers and sooner than those on a higher potassium intake.

The serum potassium level of 10 normal control rats, determined gravimetrically, was found to be 5.17 ± 0.29 m.eq./l. (average, with standard deviation). On the 75th day, i.e. 35 days after DCA was stopped, four of the tap water survivors—2 from the egg group, 1 from the pea group and the fourth from the potato group (all relatively high potassium diets)—showed serum potassium levels of 4.30, 4.71, 3.84 and 4.43, average 4.32 ± 0.36 m. eq./l. In contrast 3 rats with high sodium intake (saline drinking water and potato diet) had serum potassium concentrations of 3.94, 2.56 and 3.99, average 3.50 ± 0.81 m. eq/l. Statistical analysis shows both these averages to be significant decreases from the normal, P being less than 0.01. It is apparent therefore that continuing the high sodium chloride intake even after the DCA has been discontinued maintains the decreased

FIG. 1. A. The upper half illustrates early necrosis of the myocytes indicated by loss of striations, homogenization of the sarcoplasm and disappearance of the nuclei. The lower portion shows the earliest manifest connective tissue cell and monocyte response to the myocardial necrosis. B. Progressive necrosis of the myocardium is indicated by complete fragmentation of myocytes and the further proliferation of fixed tissue cells, many of them Anitschkow cells (arrow), and monocytes. C. The disappearance of dead myocardium is apparent as well as its replacement by rapidly proliferating fibroblasts and Anitschkow cells. D. In contrast to the above, photograph D presents an Aschoff nodule in the heart of a child. Note the interstitial location, the relatively well defined appearance of the nodule and the characteristic fibrinoid change of the connective tissue; all absent in A, B and C above.

potassium concentration in the serum. However, on these diets, the hypopotassemia caused by these factors alone is not severe enough to produce death of the animals or myocardial lesions.

As an additional control, we placed twelve rats each weighing between 86 and 112 grams (average 98 grams) on a diet identical to that of group 2 (rice). All twelve received as drinking water a 1% sodium chloride solution. To this, for six of the animals, potassium chloride to make up a 1.27% solution was added. Desoxycorticosterone acetate (in aqueous suspension, concentration 15 mg. per cc., dose 6.0 mg. per day) was injected twice daily subcutaneously into all twelve rats.

Of the six animals without potassium chloride supplement, four died spontaneously, three on the 23rd day after the start of the experiment, the fourth on the 27th day. The remaining two were killed on the 28th day. Two of the rats dying on the 23rd day did not show any recognizable cardiac lesions, the other four revealed characteristic lesions as described above.

All six rats receiving potassium chloride supplement were killed on the 28th experimental day; none showed cardiac necrosis.

The serum potassium concentrations of three of these control rats without potassium chloride supplement were found at the time of death to be 1.71, 2.81 and 2.16, average 2.23 ± 0.55 m. eq./l. The serum potassium concentrations of four rats with potassium chloride supplement were 4.13, 4.51, 3.20 and 5.12, average 4.24 ± 0.80 m.eq./l. Both these averages represent statistically significant decreases from the normal. Ten normal rats showed an average serum potassium level of 5.17 ± 0.29 m.eq./l.

DISCUSSION

It has been found that the addition of large amounts of sodium to a diet poor in potassium results in a more rapid loss of potassium (Gamble, 1947; Burnett, Burrows and Commons, 1949; Howard and Carey, 1949). It is further known that DCA increases potassium excretion (Regan, Ferrebee, Phyfe, Atchley and Loeb, 1940; Ferrebee, Parker, Carnes, Gerity, Atchley and Loeb, 1941; Loeb, 1942; Darrow and Miller, 1942). Both factors, DCA plus sodium overdosage, therefore act synergistically toward depleting the body of its potassium. In this respect the first five dietary groups are characteristic. While 11 out of 12 high sodium intake animals (3 accidental deaths not included) died, all showing the typical cardiac lesions of severe hypopotassemia, only 3 out of 10 tap water animals died, likewise showing the cardiac changes of potassium deficiency. Of these three, 2 were in the fat cheese group with the lowest potassium intake.

Fifty-nine mg. of potassium daily are apparently insufficient to prevent the anatomic manifestations of potassium deficiency under the conditions

of this experiment. Diets with a higher potassium content (Table 1, groups 6, 7, 8) are adequate to maintain the animals in equilibrium. Kornberg and Endicott (1946) in their low potassium diet experiments determined the minimum daily potassium intake necessary to prevent myocardial lesions. They found it to be 12.6 mg. per rat. It is obvious that this amount is too small as indicated above for the conditions of "stress" imposed by the DCA and sodium overdosage of the present experiment.

The cardiac lesion of severe hypopotassemia is well known. Selye (Selye and Hall, 1943; Selye and Dosne, 1940) tried to rule out this etiologic factor by giving potassium chloride additions to dogs and rats which had been treated with overdosage of DCA and sodium chloride and showed the toxic manifestations characteristic of their species. It has been demonstrated (Smith, Black-Schaffer and Lasater, 1950) that dogs in severe hypopotassemia brought about by special depletion diets develop a flaccid paralysis of the skeletal muscle but never myocardial necrosis. The rat in contrast develops myocardial necrosis but never recognizable skeletal muscle changes. The canine paralysis is completely reversible when adequate amounts of potassium are administered (Ruegamer, Elvehjem and Hart, 1946; Smith, Black-Schaffer and Lasater, 1950). Selye (Selye and Hall, 1943) gave the two dogs with the typical paralysis, produced by DCA overdosage and high sodium intake, 20 cc. of a 2% solution of potassium chloride. This corresponds to 154 mg. potassium chloride per kg. of body weight. Since this was without any noticeable effect, he concluded that the paralysis which is analogous to the myocardial necrosis of the rat, was not due to potassium deficiency. Smith (1946) has found that dogs with potassium deficiency following potassium restriction in the diet could always be cured of paralysis, and death prevented by a dose of 200 mg. potassium chloride per kg. of body weight, but never by 100 mg. per kg. Selye's dose lies between these two figures and is probably inadequate under the conditions of "stress" of his experiment. Also in the case of rats, Selye (Selye, Mintzberg and Rowley, 1945) did not reach the conclusion that the damaging effect of DCA upon cardiac structure might be secondary to its blood potassium depressing effect. He states that the administration of potassium chloride is ineffective to antagonize the actions of DCA in the rat, and that the decrease in the potassium content of the serum caused by DCA cannot be made responsible for the morphologic manifestations of DCA overdosage. But comparing, in his table, the group which received sodium chloride alone, with the group which received potassium chloride in addition, one notices a reduction in the incidence of cardiac lesions from 100% in the former to 17% in the latter, and a reduction in the intensity of the lesions found from 55% to 8%.

The same interpretation of the heart lesions occurring in DCA-treated

animals is contained in Selye's recent book "Stress" (1950). The lesions are again considered as resembling those of rheumatic fever, and rheumatic fever is therefore considered to be a manifestation of the adaptation syndrome. Selye emphasizes again that the changes caused by DCA are not prevented by the feeding of excess potassium.

Since the question of the etiology of rheumatic fever was raised by Selye and his coworkers, it is necessary to point out that the Aschoff nodule of rheumatic fever is a lesion appearing in the interstices of the heart (Figure 1D), centering about a fibrinoid change of the collagen. The myocardial fibers are little if at all involved by this lesion in its early manifestations. The nodule is fairly well circumscribed and composed of Anitschkow cells as well as giant cells (Aschoff cells) whose nuclei retain the characteristic chromatin distribution of the Anitschkow cell. Since the Anitschkow cell is not pathognomonic (Zak, 1947), the abundant presence of these cells alone in the necrotic heart of DCA overdosed rats is no proof of the presence of rheumatic fever.

SUMMARY

Myocardial necrosis was found in rats in which potassium depletion had been caused by low potassium diets together with DCA overdosage with or without high sodium intake.

Both the rapidity with which death occurred, and the number of deaths were inversely proportional to the potassium consumption.

Myocardial lesions and death did not occur if sufficient amounts of potassium had been added.

These findings do not support the view that the heart lesions found in DCA overdosed rats have any connection with rheumatic fever or the adaptation syndrome. The pathologic anatomic studies showed that the myocardial lesion is different from that of rheumatic fever and identical with that produced by potassium exclusion diets.

Acknowledgment

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Tratamiento de Enfermedades Cardíacas y Renales, Retinopatías y Enfermedades Vasculares Arterioscleróticas e Hipertensivas con la Dieta de Arroz

This paper summarizes information on the Rice Diet contained in other (English-language) papers in this volume. It presents no new data.

Tratamiento de Enfermedades Cardíacas y Renales, Retinopatías y Enfermedades Vasculares Arterioscleróticas e Hipertensivas con la Dieta de Arroz

REIMPRESO DE
Archivos Médicos de Cuba
MARZO DE 1952

ESTUDIOS CLINICOS

◆ **LOS RESULTADOS** de la dieta de arroz de Kempner descritos por su propio autor.

Tratamiento de Enfermedades Cardíacas y Renales, Retinopatías y Enfermedades Vasculares Arterioscleróticas e Hipertensivas con la Dieta de Arroz

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Durham, N. C., E. U. A.

COMPOSICION DE LA DIETA

La dieta de arroz, tal como se ha usado en más de 1,800 pacientes con enfermedades del corazón y del riñón, retinopatía y enfermedades vasculares arterioscleróticas e hipertensivas, consiste exclusivamente de arroz, azúcar, frutas y jugos de frutas. Contiene en cada 2,400 calorías, menos de 150 mgms. de sodio, 200 mgms. de cloruro, 5 gms. de grasa (ningún colesterol) y aproximadamente 25 gms. de proteína derivada del arroz y de las frutas. Los únicos suplementos añadidos son vitaminas A, B y C para tener la seguridad de satisfacer los requerimientos diarios. El número de calorías ingeridas se varía según la necesidad del paciente de ganar o de perder en peso. En muchos pacientes con enfermedades vasculares está indicado restringir las calorías para obtener pérdida de peso, pero en pacientes cuyo peso es demasiado bajo, se aumentan las calorías hasta conseguir el peso deseado.

PROCEDIMIENTO

La dieta de arroz tiene que seguirse estrictamente y tiene que ser administrada bajo condiciones rígidamente controladas.

Si después de un examen completo, incluyendo análisis químico de la sangre y de la orina, electrocardiograma, radiografía, fotografía del fondo del ojo y otros exámenes especiales según el caso, se decide que la enfermedad es lo bastante grave para justificar el uso de la dieta de arroz, el procedimiento es generalmente, tener al paciente aquí bajo observación diaria de tres a cuatro meses. A ser posible, los pacientes no permanecen acostados, sinó levantados y ambulantes. Se alojan en casas privadas o hoteles en la vecindad del hospital, recibiendo la dieta en casas especiales, donde es preparada bajo minuciosa vigilancia. Unicamente pacientes en estado crítico son hospitalizados. Los que no pueden comer se alimentan por medio de un tubo gástrico por el cual 100 c.c. (100 calorías) de arroz, azúcar, frutas y jugos de frutas hemogenizadas en un "Waring blender" son introducidos una vez por hora de día y de noche. (Una paciente, después de un ataque de apoplejía, tuvo que alimentarse de este modo durante 14 meses).

Transcurridos estos primeros tres o cuatro meses, es posible formarse una idea, de hasta que punto el paciente puede ser beneficiado por la dieta. La más rápida baja de tensión arterial ocurió a los cuatro días después de iniciarse el régimen; en otros casos puede ser una cuestión de años, siendo aproximadamente 4 meses el término medio. El promedio de duración hasta disminuir el tamaño del corazón es de 3 a 4 meses, y de 6 a 12 meses hasta aliviarse la retinopatía. Cambios favorables en el electrocardiograma tardan un promedio de 10 a 12 meses en manifestarse.

Al final del período pasado aquí, es también posible decidir si el paciente debe de continuar la dieta básica o si está permitido (o aún indicado), añadir ciertas modificaciones, y cuáles. El paciente vuelve entonces a su casa y a los cuidados de su médico de cabecera, siendo deseable que éste vea al enfermo con frecuencia, observando su progreso y alentándolo a seguir el régimen prescrito sin desviaciones

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Dieta de Arroz — *Kempner*

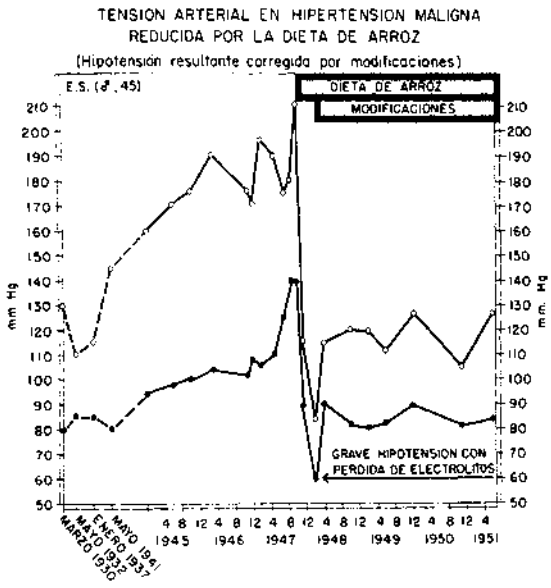
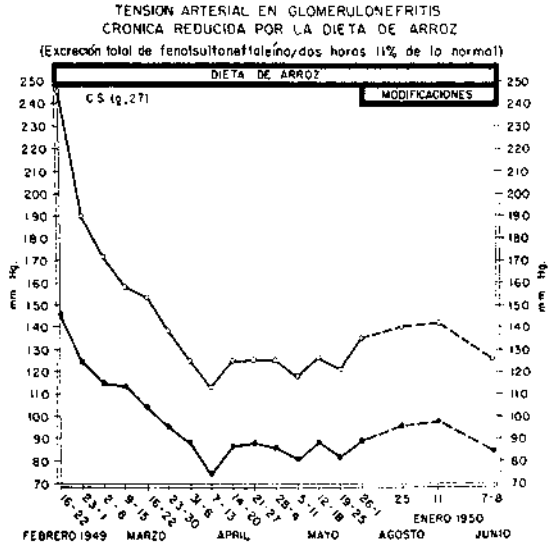


Fig. 1

ni desfallecimientos. Dos o tres meses más tarde el paciente debiera de volver aquí para ser de nuevo observado durante unos días o semanas a fín de determinar si se puede considerar seguir amplificando la dieta o si hay que revocar las modificaciones anteriores; y de ahí en adelante, reexaminaciones periódicas a intérvalos de dos meses a un año, según el caso, son aconsejadas.

Dada la importancia de seguir la dieta con la mayor fidelidad sin desvío alguno para resultar ésta eficaz, conviene cerciorarse a menudo si el paciente se adhiere rigurosamente al régimen o no. El análisis repetido de la excreción de nitrógeno, sodio y cloruro en la orina es una manera sencilla de averiguarlo. (Incluso a los pacientes que han regresado a sus casas, se les exije que manden orina para este análisis una o dos veces al mes, o más amenudo, en los intérvalos entre reexaminaciones). El promedio de la excreción urinaria total en 24 horas debe ser de 2,6 gms. de nitrógeno, 100 mgms. de cloruro y 10 mgms. de sodio, después de adaptación completa a la dieta. Esta adaptación no se consigue hasta dentro de 1 a 4 meses, aún en pacientes cuyos riñones son capaces de regulación normal.

Fig. 2



PELIGROS

Modificaciones no autorizadas, por mínimas que sean, pueden comprometer seriamente, o echar a perder del todo el efecto terapéutico de la dieta. Por otra parte, en pacientes con propensión a pérdida de electrolitos, varias formas, a veces graves, de desequilibrio electrolíticos pueden ocurrir a cualquier momento del tratamiento. (Figura 1). Exámenes continuos de la química sanguínea y urinaria son precisos para descubrir cualquier desequilibrio químico que pudiera sobrevenir en el curso de un régimen tan riguroso (natropenia, hipocloruremia, hiperpotasemia, alcalosis, etc.). Si resulta necesario, la dieta se modifica adecuadamente para remediar estos trastornos. (El peligro de desequilibrio químico podría aun ser intensificado por el uso de diuréticos mercuriales, resinas sodio-absorbentes y otros tratamientos que tienden a alterar la normalidad electrolítica. Mas conste, que el régimen de arroz propiamente dicho prescinde de tales medidas terapéuticas, como prescinde en absoluto del uso de drogas. Los resultados publicados aquí se han obtenido exclusivamente por la dieta, aún en pacientes que antes dependían de digital, mercuriales, nitroglicerina, barbituratos, etc.).

INDICACIONES Y RESULTADOS CLINICOS

En vista de que la glomérulonefritis aguda a menudo se complica con insuficiencia cardíaca o renal y siempre hay la posibilidad de que se convierta en glomérulonefritis crónica, acostumbro rutinariamente administrar la dieta de arroz en todos los casos graves de glomérulonefritis aguda. En una enfermedad con tan alto porcentaje de curaciones espontáneas sería difícil probar por datos estadísticos el mérito de un régimen especial cualquiera que sea. Sin embargo, estoy convencido por experiencia que la dieta de arroz está tan indicada en las glomérulonefritis agudas, aún no pudiendo fácilmente probar su efecto favorable, como lo

Dieta de Arroz — *Kempner*

CUADRO 1

CAMBIOS CLINICOS Y QUIMICOS EFECTUADOS POR LA DIETA DE ARROZ EN UN PACIENTE CON NEFROSIS (↑ 4)

	Mayo 46	Diciembre 46	Agosto 47	Agosto 48	Noviembre 50	Agosto 51
Tensión arterial (mm. Hg).	98/68	110/68	110/70	90/60	110/70	104/60
Hemoglobina (% de 15.5 gms).	96	79	84	84	90	97
Nitrógeno no proteico (mgms/100 cc. de sangre)	41	22	24	30	35	34
Colesterol (mgms/100 cc. de suero)	920	380	175	160	150	160
Proteínas totales del plasma (mgs/100 cc. de plasma)	4.1	4.0	5.9	6.9	6.7	7.0
Albúmina	0.74	0.74	3.8	4.2	3.5	4.7
Globulina	3.36	3.3	2.1	2.7	3.2	2.3
Relación Albúmina/Globulina	0.22	0.22	1.8	1.5	1.1	2.0
Albuminuria	3 +	3 +	0	0	0	0
Excreción de Fenolsulfoneftaleína en 2 horas (% de normal)	— —	40	60	80	80	76
Edema	++++	0	0	0	0	0

está en la mayoría de los casos de glomerulonefritis crónica, en que los efectos favorables son evidentes y demonstrables con facilidad. (Figura 2).

En un gran número de pacientes con nefrosis, la dieta de arroz, no obstante la rígida restricción de proteína, restablece el nivel normal de las proteínas del plasma. La ascitis y los edemas periféricos desaparecen, la proteinuria disminuye y la tasa anormalmente alta del colesterol sérico se reduce a valores normales. En algunos pacientes la enfermedad desaparece por completo, sin dejar rastro. (Cuadro 1).

La dieta de arroz está también indicada en aquellos casos de insuficiencia cardíaca que no reciben beneficio de las terapias natroprivas habituales o de medicación, ya sea la insuficiencia del miocardio secundario a lesiones valvulares, ya primaria a base de arteriosclerosis, enfermedad vascular hipertensiva, fiebre reumática, lupus eritematoso diseminado, enfermedades del riñón, etc.

Asimismo, pacientes con grave angina de pecho y pacientes con infartos del miocardio son tratados con la dieta de arroz. En estos pacientes el tratamiento debe dirigirse hacia un doble objetivo: contrarrestar la disminución de la irrigación coronaria y reducir las necesidades energéticas del músculo cardíaco.

Las figuras 3-5 demuestran la reducción de la cardiomegalia en pacientes con estenosis e insuficiencia aórtica, estenosis mitral, e hipertensión maligna. (Véase también Figura 6).

La dieta de arroz ha sido hallada eficaz en enfermedades vasculares arterioscleróticas e hipertensivas. Un gran número de pacientes con hipertensión llamada benigna, con o sin complicaciones críticas, han derivado notable beneficio del tratamiento; pero no sólo éstos, sino también muchas cuya hipertensión era del tipo maligno con avanzadas lesiones cardíacas y renales, y con neurorretinopatía hemorrágica y exudativa —signo éste último que solía ser considerado infausto e indicativo de la fase terminal de una enfermedad irreparable. Mi experiencia ha demostrado que la hipertensión maligna, aun con neurorretinopatía avanzada, puede por efecto de la dieta, transformarse en hipertensión benigna o hasta desaparecer completamente.

Como ejemplo se presenta el caso de un paciente de 47 años de edad, enviado aquí por su médico con el diagnóstico de enfermedad cardiovascular hipertensiva en fase maligna. Había tenido hipertensión desde dos años y medio. Sufría, sobretodo, de dolores de cabeza fuertísimos e incapacitantes. El tratamiento había consistido en una dieta pobre en calorías y sedativos. Recientemente la tensión arterial había alcanzado un promedio de 257/173 mm. Hg. (7 observaciones). Su médico inició la dieta de arroz y la tensión bajó un poco, pero al examinar al paciente aquí se le halló aún una tensión de 233/161 mm. Hg. El corazón media 13.8 cm. en su diámetro transverso. La onda TV 6 del electrocardiograma estaba allanada. Los fondos de ojo mostraban cambios vasculares muy acentuados, edemas de papila bilateral, hemorragias y exudados algodonosos. Durante las primeras dos semanas de dieta de arroz en Durham, el promedio de la tensión continuaba siendo alto: 196/122 mm. Hg. Después de 110 días de dieta, el promedio de 10 días era 124/89 mm. Hg. El diámetro transverso del corazón había disminuído a 12.4 cm. La onda TV 6 era normal. El edema pa-

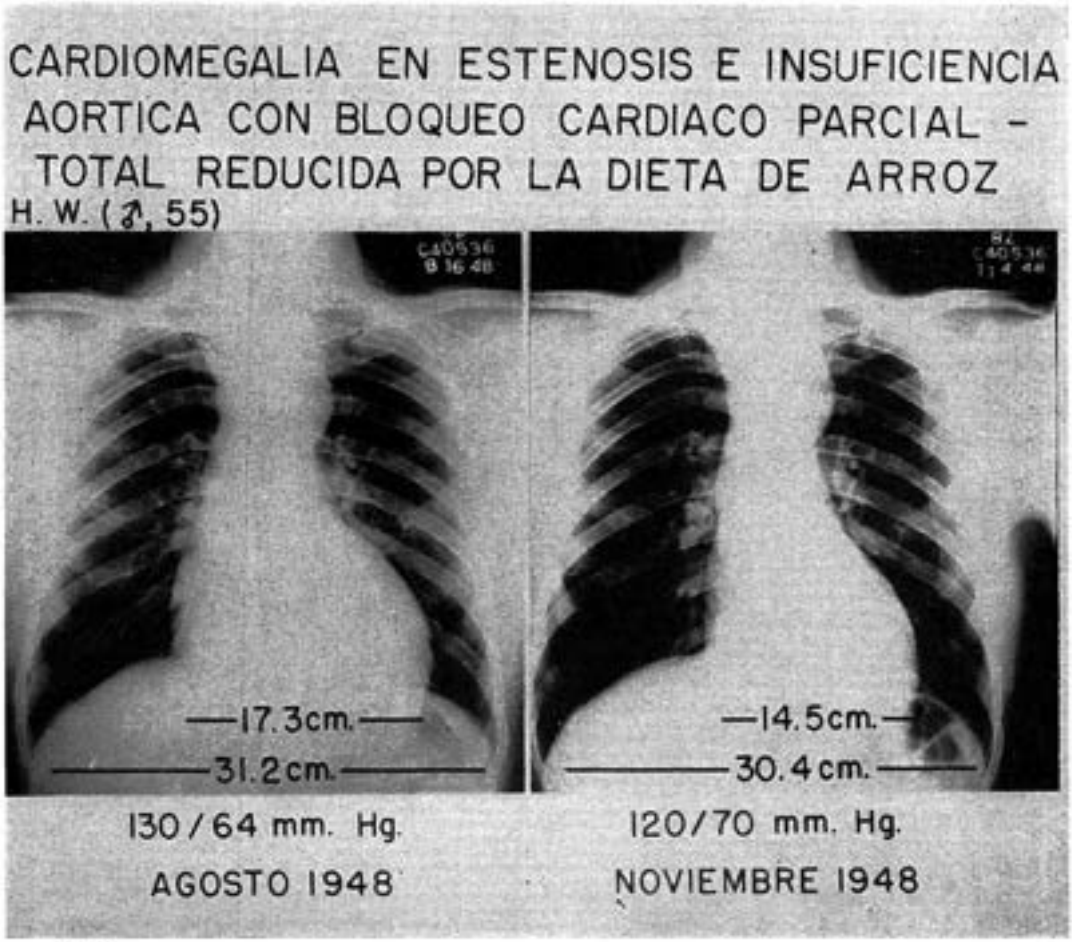
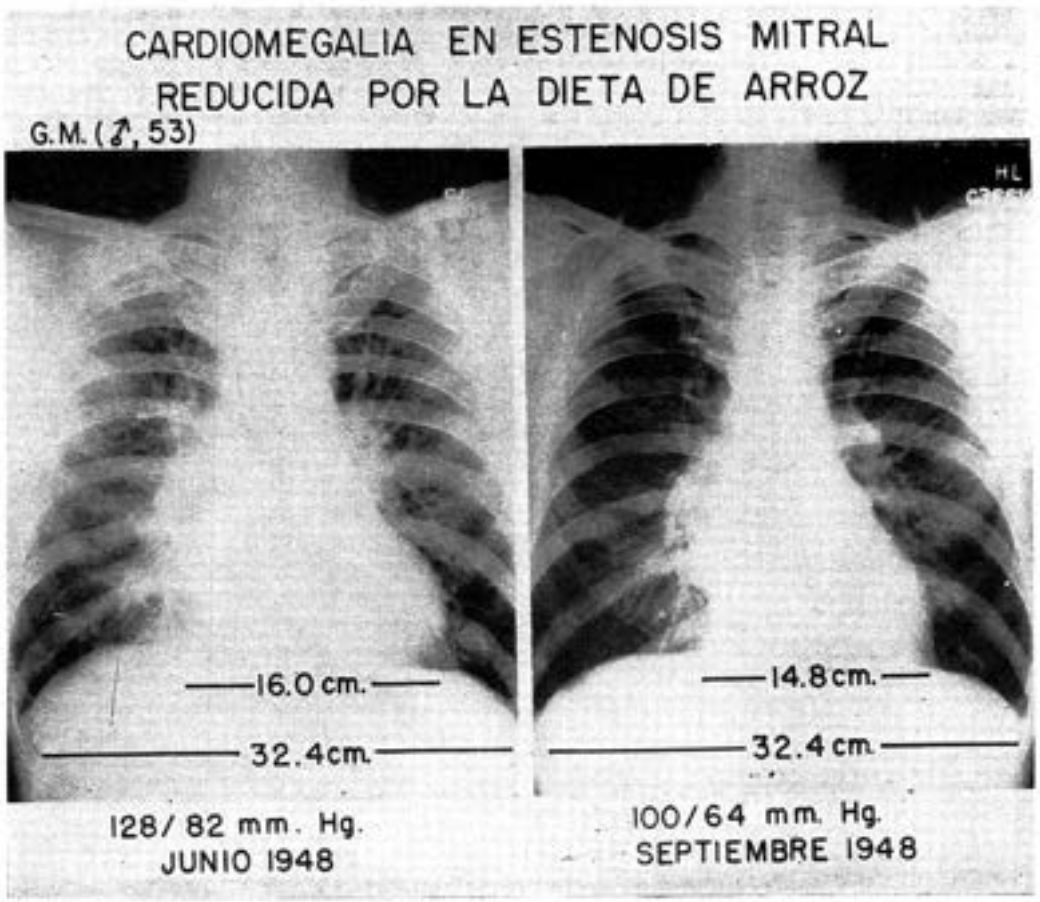

CARDIOMEGALIA EN ESTENOSIS E INSUFICIENCIA AORTICA CON BLOQUEO CARDIACO PARCIAL - TOTAL REDUCIDA POR LA DIETA DE ARROZ
H. W. (♂, 55)
—17.3cm.—
—31.2cm.—
130/64 mm. Hg.
AGOSTO 1948
—14.5cm.—
—30.4cm.—
120/70 mm. Hg.
NOVIEMBRE 1948

Fig. 3

Fig. 4


CARDIOMEGALIA EN ESTENOSIS MITRAL REDUCIDA POR LA DIETA DE ARROZ
G.M. (♂, 53)
—16.0 cm.—
—32.4cm.—
128/82 mm. Hg.
JUNIO 1948
—14.8cm.—
—32.4 cm.—
100/64 mm. Hg.
SEPTIEMBRE 1948

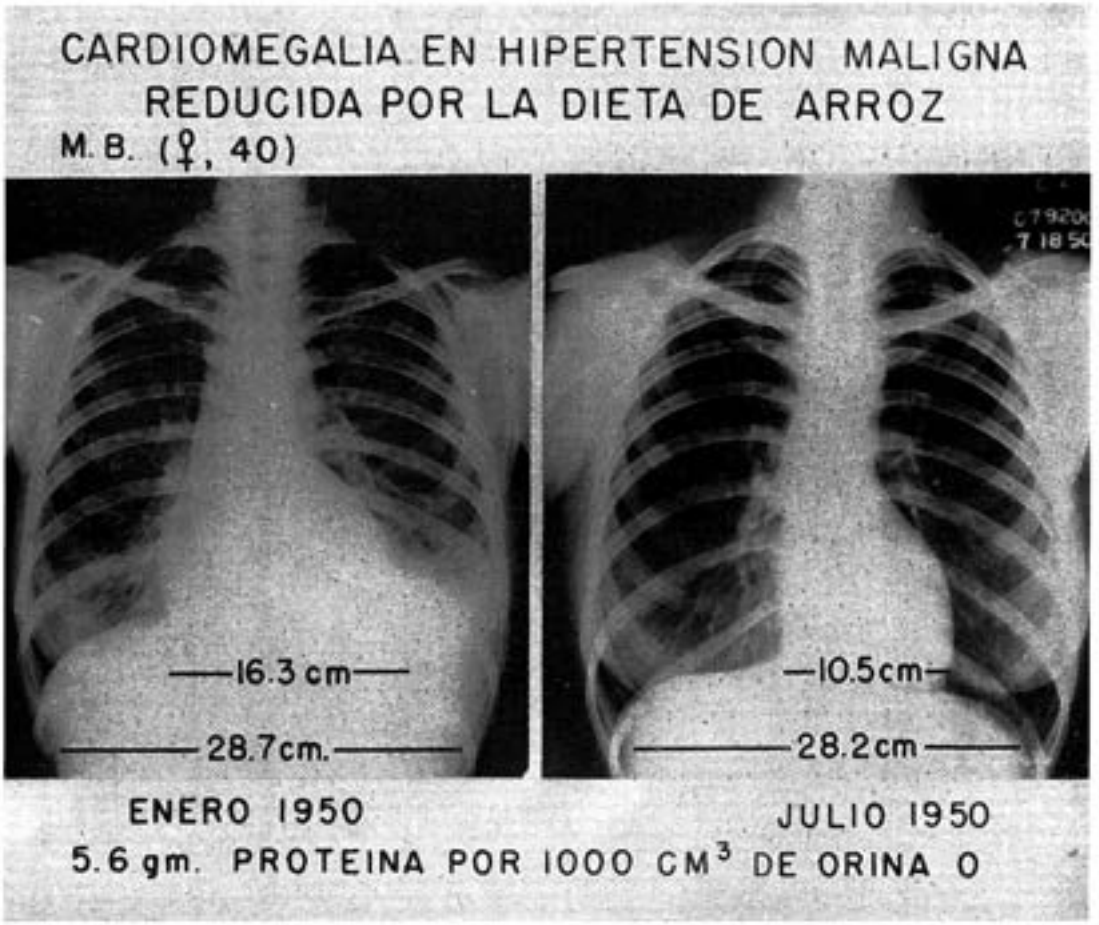
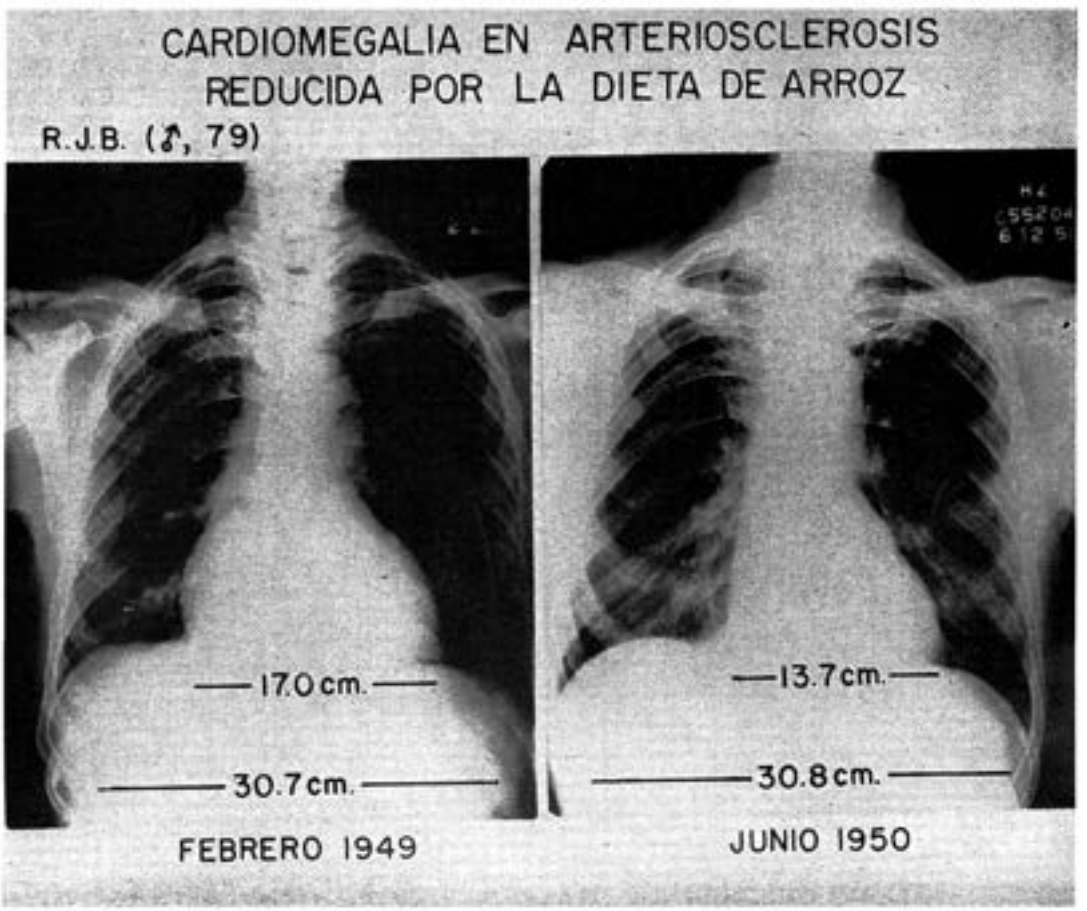

CARDIOMEGALIA EN HIPERTENSION MALIGNA
REDUCIDA POR LA DIETA DE ARROZ
M. B. (♀, 40)
16.3 cm
28.7cm.
10.5cm
28.2cm
ENERO 1950
JULIO 1950
5.6 gm. PROTEINA POR 1000 CM³ DE ORINA 0

Fig. 5

Fig. 6


CARDIOMEGALIA EN ARTERIOSCLEROSIS
REDUCIDA POR LA DIETA DE ARROZ
R.J.B. (♂, 79)
17.0 cm.
30.7cm.
13.7cm.
30.8cm.
FEBRERO 1949
JUNIO 1950

Dieta de Arroz — *Kempner*

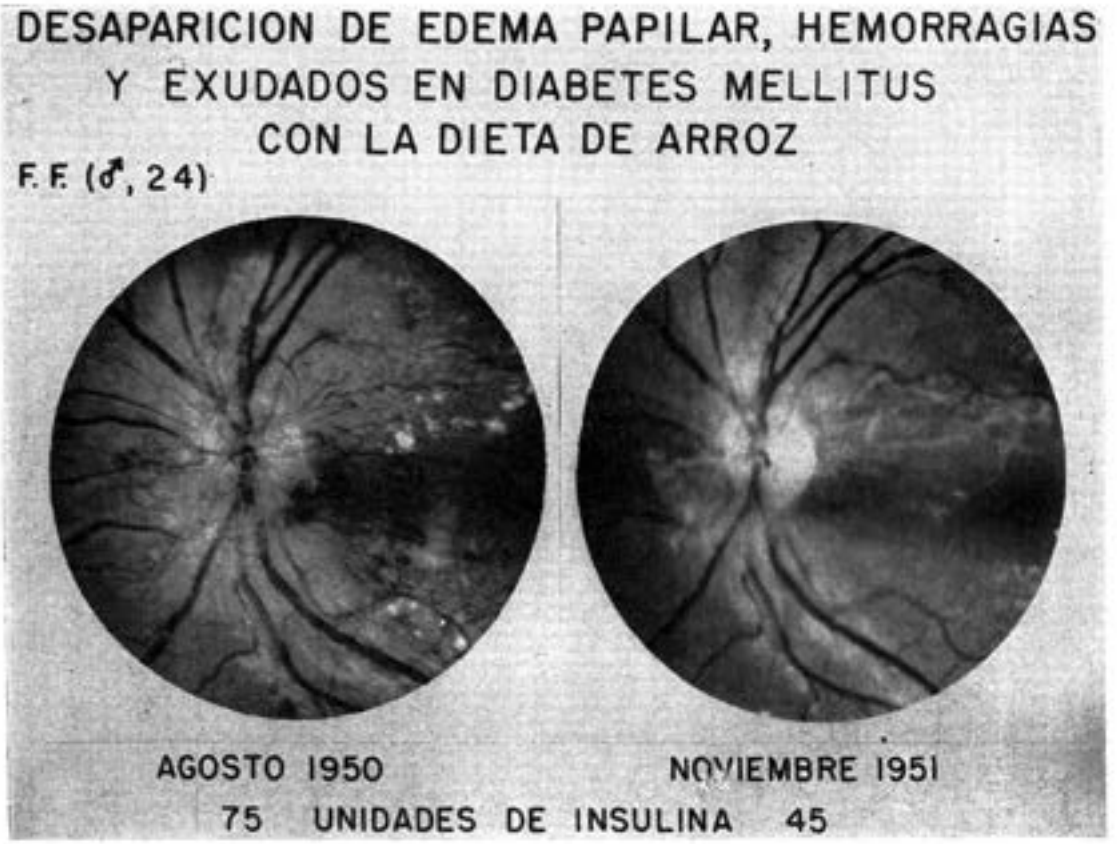
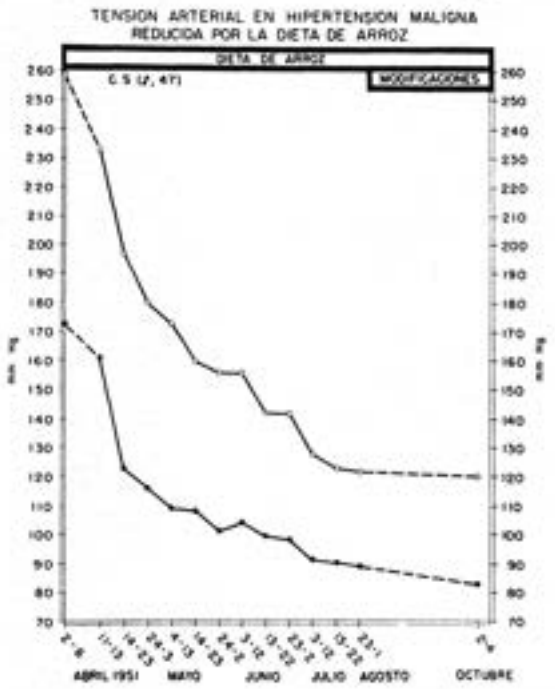


Fig. 7

Fig. 8



pilar, las hemorragias y la mayoría de los exudados habían desaparecido. También habían cesado los dolores de cabeza. El paciente volvió a su casa con una dieta algo amplificada. Se sentía perfectamente bien y asumió su trabajo como director de una empresa comercial. Dos meses más tarde fué reexaminado. El promedio de la tensión arterial de 3 días era 120/83 mm. Hg. (Figura 8). El diámetro transverso del corazón media 12.4 cm. En los fondos de ojo no quedaba ya señal de la retinopatía de hipertensión maligna.

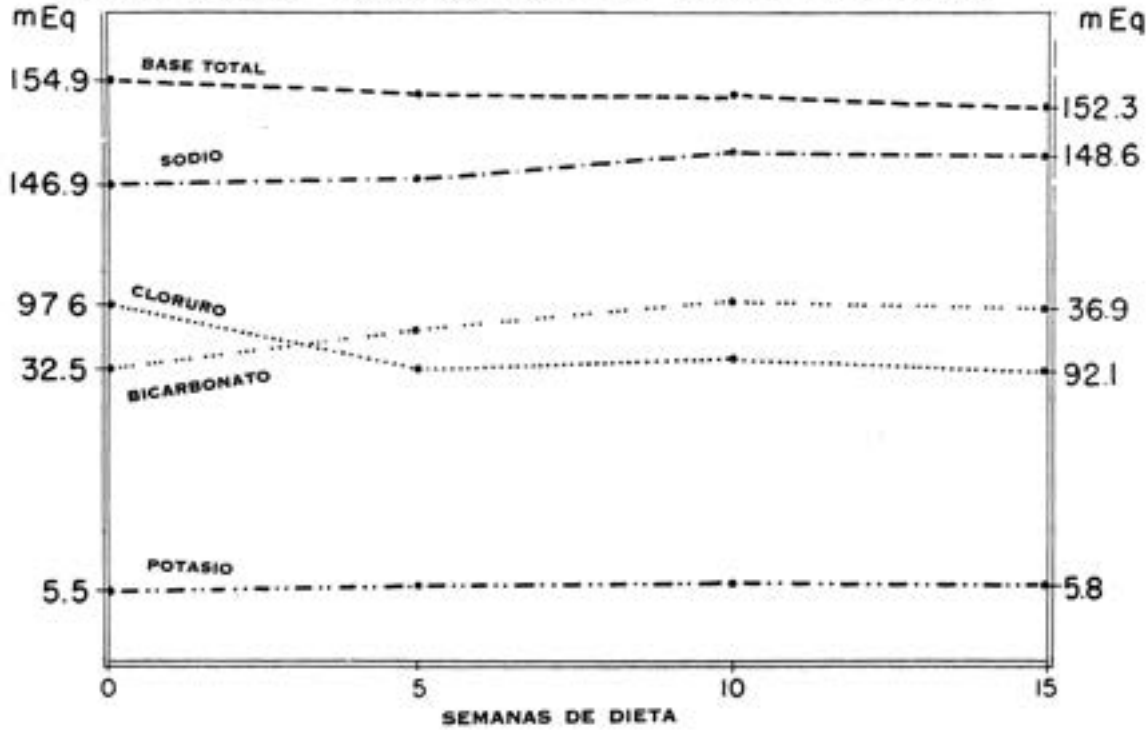
La vejez suele ser considerada por muchos como una especie de bancarrota ocasionada por las deudas vasculares, cardíacas o renales. Conforme a este concepto, los procesos arterioscleróticos y vasculares hipertensivos son aceptados como enfermedades degenerativas, acompañamiento inevitable y casi fisiológico de la edad avanzada. La reversibilidad de estos procesos en muchos de mis pacientes ancianos prueba, no obstante, que esta actitud de resignación hoy día ya no es necesaria.

Servirá de ejemplo la radiografía en Figura 6 que demuestra el efecto de la dieta de arroz sobre el corazón de un paciente de 79 años de edad. Este paciente, un médico, vino a la

Dieta de Arroz — *Kempner*

Figura 9

ELECTROLITOS SERICOS CON LA DIETA DE ARROZ



Valores promedios de 12 pacientes con enfermedad vascular hipertensiva (sin evidencia de participación renal)

Tomada de Annals of Internal Medicine, Vol. 31, No. 5

Clínica Médica de Duke Hospital en 1949. Hacía tres años que sabía que tenía hipertensión sistólica de 180 a 240 mm. Hg. y diastólica de 100 mm. Hg. Había sido tratado con fenobarbital, vasodilatadores y reposo. Intermitentemente había usado digital. Se le halló una tensión arterial de 210/114 mm. Hg. El diámetro transverso del corazón, según la radiografía medía 17.0 cm. Había soplo aórtico sistólico y diastólico. Había también fibrilación auricular. Los vasos periféricos estaban esclerosados. No había edema de la periferia. Los pulmones estaban claros. El hígado descendía un dedo bajo el margen costillar al inspirar profundamente. La prueba de función renal reveló una excreción total de fenolsulfoneftaleína de 43% de lo normal en 2 horas. En los fondos de ojo se descubrieron moderados cambios arterioscleróticos. Después de 3 meses de dieta de arroz, la tensión había bajado de un promedio (10 días) de 221/118 mm. Hg. a un promedio de 148/87 mm. Hg. El tamaño del corazón había disminuído considerablemente, siendo de 17 por ciento el cambio en la medida del diámetro transverso. 16 meses después de iniciarse la dieta de arroz, el diámetro transverso medía 13.7 cm. El paciente que ahora tiene 81 años ha vuelto al ejercicio de su profesión y ha reanudado sus actividades habituales, completamente libre de síntomas cardíacos.

Pacientes con diabetes mellitus no sólo toleran bien la dieta de arroz, sino que en un número considerable de ellos tanto la glicemia como los requerimientos de insulina disminuyen. Además, en algunos la dieta puede ser de un valor especial dado el papel peligroso de la hipercolesterolemia en esta enfermedad.

Cuarenta y ocho pacientes con diabetes complicada por enfermedad renal o vascular han sido tratados con la dieta de arroz. El período de observación ha sido de 8 semanas a 5 años y 10 meses, o sea un promedio de 59 semanas. En 17 de los 48 se registró un cambio de más de 30 mgms. en la glicemia de ayunas: en 3 la glicemia de ayunas aumentó, en 14 dis-

Dieta de Arroz — *Kempner*

minuyó. En los demás el nivel glicémico, o mostraba gran inestabilidad, o no se modificó más que insignificantemente.

En 29 de los 48 pacientes no hubo cambio en los requerimientos de insulina. Diez y nueve presentaron cambios notables, 4 necesitando más insulina (de 20 unidades promedio cuando empezaron a 41 unidades promedio siendo la mayor diferencia un aumento de 0 a 30 unidades) y 15 menos (de 45 unidades promedio a 22 unidades promedio, siendo la mayor diferencia una baja de 90 a 30 unidades).

La reacción favorable de estos pacientes, junto a la experiencia de que un alto porcentaje de diabéticos mueren o por lo menos son incapacitados por enfermedad vascular, sugiere el uso de la dieta de arroz en cada caso de diabetes mellitus que empieza a mostrar síntomas de enfermedad cardíaca, renal, retinal o perifero-vascular.

Figura 7 demuestra el efecto de la dieta de arroz sobre la retinopatía de un paciente con diabetes mellitus.

RESULTADOS QUIMICOS

Para evaluar comprehensivamente los efectos de la dieta de arroz tienen que estudiarse, además de los resultados clínicos, los cambios químicos que produce.[1-14] Los más importantes serán brevemente resumidos.

Estudios del balance nitrogenado indican que el equilibrio se restablece y mantiene después de aproximadamente 13 semanas de dieta de arroz. El cuadro 2 da un resumen de 12 estudios de balance nitrogenado en 11 pacientes con enfermedad vascular hipertensiva. Las observaciones fueron hechas después de estar sometidos los pacientes a la dieta durante 13 semanas y después de habérseles estabilizado el peso. Estos resultados químicos, como por otra parte la experiencia clínica de que no sobreviene anemia y que las proteínas del plasma se mantienen normales, prueban que la cantidad de proteínas es suficiente en la dieta.

CUADRO 2

BALANCE NITROGENADO

En 11 Pacientes con Enfermedad Vascular Hipertensiva Después de 13 Semanas de Dieta de Arroz

Nitrógeno Total (gms. N en 24 horas) Promedio de 4 días consecutivos

Ingestión	Excreción		Balance
	Heces	Orina	
	1.55	2.57	
4.37	4.12		+ 0.25

No obstante las restricciones alimenticias hay notable diferencia entre el efecto sobre el metabolismo de la dieta de arroz y el de la estarvación. En la estarvación, la hemoglobina, el calcio sérico, las proteínas del plasma, la glicemia, la tolerancia carbohídrica y el poder combinativo de CO_2 disminuyen; la dieta de arroz o bien no los afecta, o los aumenta. El nitrógeno no proteico y la urea de la sangre y la creatina, amoníaco, y ácidos orgánicos de la orina aumentan en la estarvación; la dieta de arroz los disminuye. El volumen de la sangre y del flúido intersticial no cambian en la estarvación, pero disminuyen con la dieta de arroz.

CUADRO 3

PROMEDIOS DE NITROGENO NO PROTEICO Y UREICO DE 766 PACIENTES CON ENFERMEDAD VASCULAR HIPERTENSIVA

(Nitrógeno no proteico inicial: 20 a 45 mgms. por 100 cc. de sangre)

	Antes	Después de 105 días (promedio) de DIETA DE ARROZ
Nitrógeno no proteico (mgms/100 cc. de sangre)	34	29
Nitrógeno ureico (mgms/100 cc. de sangre)	14	9

El cuadro 3 sumariza el efecto de la dieta de arroz sobre los valores de nitrógeno no proteico y uréico en la sangre de 766 pacientes con enfermedad vascular hipertensiva sin uremia. La disminución es de un promedio de 34 mgms. por 100 cc. a un promedio de 29 mgms. por 100 cc., siendo casi enteramente en la fracción de nitrógeno uréico.

En pacientes cuya regulación renal es normal, el cloruro del suero disminuye ostensiblemente con la dieta de arroz; el bicarbonato del suero aumenta; el sodio, el potasio y las bases totales se mantienen relativamente constantes. (Figura 9).

Una concentración elevada del colesterol en el suero es un hallazgo frecuente en pacientes con arteriosclerosis, enfermedad de las arterias coronarias, enfermedad vascular hipertensiva, retinopatía vascular exudativa, enfermedades del cristalino y del cuerpo vítreo, en diabetes mellitus no regulado y en la fase nefrótica de las nefritis.

El cuadro 4 muestra el efecto de la dieta de arroz sobre el colesterol sérico de 826 pacientes con enfermedad vascular hipertensiva. En 237 pacientes (29%) cuya tasa de colesterol

Dieta de Arroz — *Kempner*

era normal al iniciarse el tratamiento (por debajo de 220 mgms. por 100 cc. de suero), el promedio de la diferencia entre la concentración inicial y la concentración después de un promedio de 116 días de dieta era de 14 mgms. por 100 cc. de suero. En 589 pacientes (71%) que habían tenido hipercolesterolemia antes de empezar a tomar la dieta, la diferencia después de un promedio de 109 días era de 73 mgms/100 cc. de suero, siendo el promedio de la concentración 207 mgms/100 cc.

La reducción del colesterol total es debida a la disminución tanto del colesterol libre como del colesterol esterificado.

La relación entre el colesterol libre y el colesterol total fué estudiada en 100 pacientes antes y después de períodos más o menos largos de dieta de arroz. El promedio de la relación fosfolípidos-colesterol libre $\left(\frac{\text{mEq./litro fósforo lípido}}{\text{mEq./litro colesterol libre}}\right)$ antes de la dieta era 1.61, después de un promedio de 72 días de dieta, 1.79. El promedio de la relación fosfolípidos-colesterol total $\left(\frac{\text{mEq./litro fósforo lípido}}{\text{mEq./litro colesterol total}}\right)$ era 0.45 antes y 0.55 después de un promedio de 72 días de dieta.

CUADRO 4

COLESTEROL TOTAL DEL SUERO DE 826 PACIENTES CON ENFERMEDAD VASCULAR HIPERTENSIVA

	Antes de la Dieta de Arroz	Después de la Dieta de Arroz	Días de Dieta de Arroz (promedio)
237 pacientes con concentración inicial por debajo de 220 mgms. por 100 cc. de suero	187	173	116
589 pacientes con concentración inicial de más de 219 mgms. por 100 cc. de suero	280	207	109

La dieta de arroz, pues, no sólo efectúa una reducción de colesterol libre y colesterol total del suero, sino también un aumento de la relación fosfolípidos-colesterol.

DATOS ESTADISTICOS

Para obtener un cuadro objetivo de los resultados de la dieta de arroz, se han hecho estudios comparativos en grupos extensos de

CUADRO 5

EFECTO DE PERIODOS CORTOS Y LARGOS DE DIETA DE ARROZ SOBRE LA TENSION ARTERIAL DE PACIENTES CON ENFERMEDAD VASCULAR HIPERTENSIVA

	Número de Pacientes	Porciento del Total	Tensión Arterial Antes de la Dieta de Arroz	Tensión Arterial Después de la Dieta de Arroz	Promedio de días de Dieta de Arroz
		4 a 1595 días			
Total	1150				
Tensión arterial no mejorada	304*	26	195/115	179/109	84
Tensión arterial mejorada	846	74	195/115	148/ 93	118
		4 a 30 días			
Total	162				
Tensión arterial no mejorada	82**	51	197/115	180/111	18
Tensión arterial mejorada	80	49	195/116	151/ 97	22
		31 a 89 días			
Total	340				
Tensión arterial no mejorada	105***	31	191/113	174/107	55
Tensión arterial mejorada	234	69	197/115	149/ 94	58
		90 a 1595 días			
Total	648				
Tensión arterial no mejorada	116****	18	197/116	182/110	144
Tensión arterial mejorada	532	82	196/115	146/ 91	158

* Incluyendo 51 pacientes que murieron cuya tensión no está incluída en los promedios.
** Incluyendo 14 pacientes que murieron cuya tensión no está incluída en los promedios.
*** Incluyendo 30 pacientes que murieron cuya tensión no está incluída en los promedios.
**** Incluyendo 7 pacientes que murieron cuya tensión no está incluída en los promedios.

Dieta de Arroz — *Kempner*

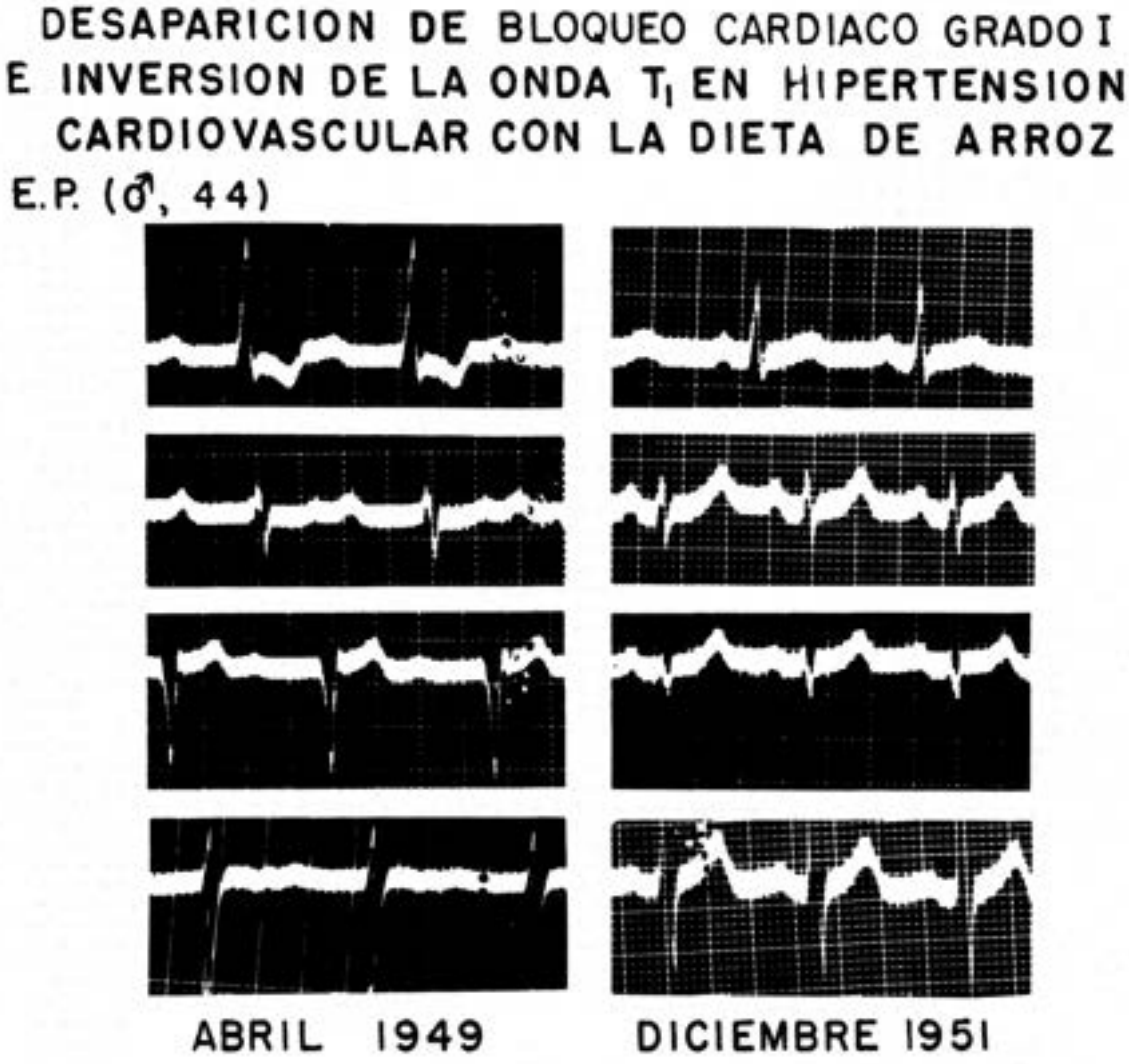


Fig. 10

pacientes, comparando el estado "antes" y "después" de la tensión arterial, el tamaño del corazón, el electrocardiograma y el fondo del ojo (además de la química de la sangre y orina referida anteriormente). En el curso de estos estudios se ha destacado la importancia del factor tiempo. El cuadro 5 demuestra el efecto de períodos cortos y largos de dieta sobre la tensión arterial de 1150 pacientes con enfermedad vascular hipertensiva. La tensión mejoró (es decir, hubo una baja de tensión sistólica y diastólica combinadas de 40 mm. Hg. o más) solamente en 49 por ciento de los 162 pacientes tratados de 4 a 30 días; 51 por ciento no mejoraron (bajo este criterio). De los 340 pacientes tratados con la dieta de 31 a 89 días, la tensión mejoró en 69 por ciento, no mejoró en 31 por ciento. De los 648 pacientes tratados 90 días o más, la tensión mejoró en 82 por ciento. La reducción de la tensión en todo el grupo de 846 pacientes que mejoraron fué de un promedio de 195/115 mm. Hg. a un promedio de 148/93 mm. Hg. después de un promedio de 118 días de dieta de arroz. De los 648 pacientes sometidos a la dieta 90 días o más, la tensión bajó a un nivel normal (esto es, a 140/90 o menos) en 212 (30.6%). En estos 212 pacientes el promedio de tensión antes de la dieta de arroz era 180/106, después de un promedio de 156 días de dieta 127/81 mm. Hg.

En una serie de 186 pacientes con enfermedad vascular hipertensiva sometidos a la dieta de arroz durante un promedio de 123 días, el tamaño del corazón aumentó en 15, siendo de un promedio de 2.6 por ciento el aumento de la medida del diámetro transverso. En 271 de los 286 pacientes el tamaño del corazón disminuyó, siendo el promedio de reducción de

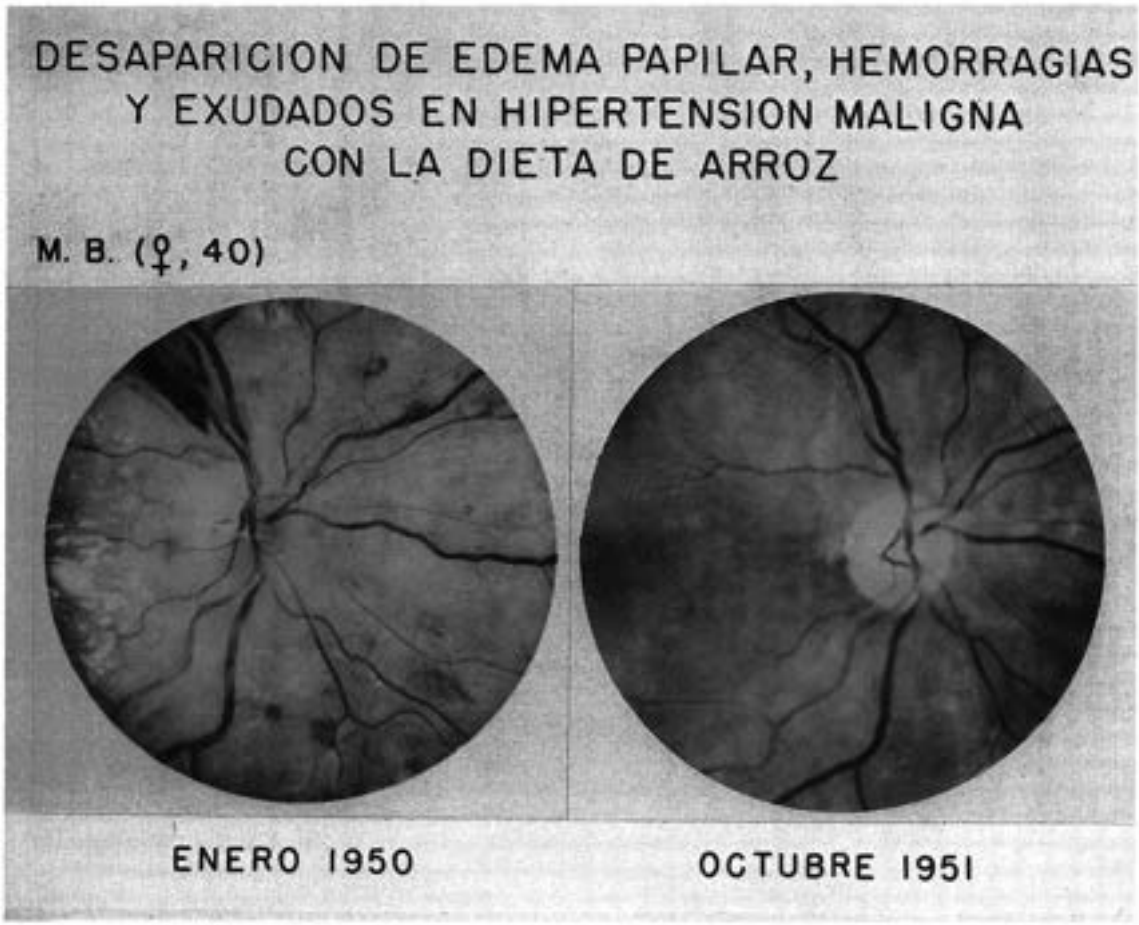
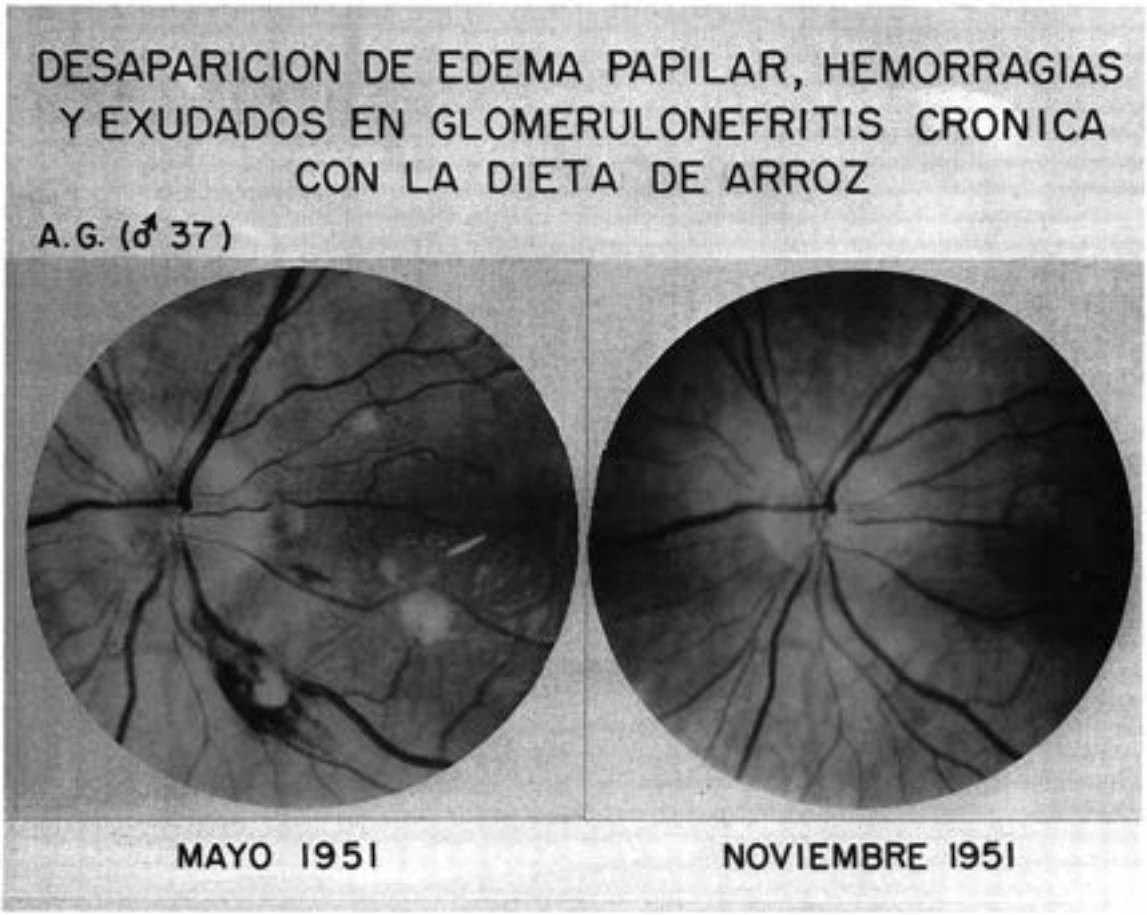

DESAPARICION DE EDEMA PAPILAR, HEMORRAGIAS
Y EXUDADOS EN HIPERTENSION MALIGNA
CON LA DIETA DE ARROZ
M. B. (♀, 40)
ENERO 1950
OCTUBRE 1951

Fig. 11

Fig. 12


DESAPARICION DE EDEMA PAPILAR, HEMORRAGIAS
Y EXUDADOS EN GLOMERULONEFRITIS CRONICA
CON LA DIETA DE ARROZ
A.G. (♂ 37)
MAYO 1951
NOVIEMBRE 1951

Dieta de Arroz — *Kempner*

la medida del diámetro transverso de 6,2 por ciento en 146, de 14.2 por ciento en 106 y de 24,4 por ciento en 19. La reducción de la cardiomegalia no depende ni de la baja de la tensión arterial ni de la pérdida de peso.

En una serie de 120 pacientes la onda T1 del electrocardiograma era negativa al iniciarse la dieta de arroz. En 68 pacientes quedó negativa (después de un promedio de 7 meses); en 52 cambió de negativa a positiva (después de un promedio de 10 meses). (Figura 10). En una serie de 291 pacientes la onda T1 era positiva al iniciarse la dieta. En ninguno de estos pacientes cambió de positiva a negativa (durante un promedio de 11 meses de dieta).

Fotografías del fondo de ojo fueron hechas en una serie de 225 pacientes con retinopatía vascular avanzada (edema papilar, hemorragias o exudados) antes y después de 1 a 90 meses de dieta de arroz. (Figuras 11 y 12). Cuarenta y dos de los 225 pacientes tenían nefritis crónica, 183 enfermedad vascular hipertensiva. Cincuenta y cuatro de los 225 tenían edema papilar al iniciarse la dieta de arroz. En uno de estos pacientes no hubo cambio; en 6 el edema papilar desapareció en parte, en 47 por completo. 173 pacientes tenían hemorragias. En uno aumentaron; en 9 no hubo cambio. (En un paciente que tenía hemorragias pero no exudados al empezar, un exudado apareció durante el período de tratamiento). 180 pacientes tenían exudados al iniciarse la dieta. En 3 aumentaron; en 13 no hubo cambio; en 61 los exudados desaparecieron en parte, en 103 completamente.

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Electrolyte Metabolism during Rice Diet, I.

Serum Electrolytes in Hypertensive Patients without Evidence of Advanced Renal Involvement

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ELECTROLYTE METABOLISM DURING RICE DIET

I. Serum Electrolytes in Hypertensive Patients Without Evidence of Advanced Renal Involvement

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AND
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DURHAM, N. C.

A DRASTIC change of the mineral supply represents one of the main characteristics of the rice diet.[1] The sodium and chloride intake is extremely restricted, about 4.3 mEq. of sodium and 5.6 mEq. of chloride in 24 hours, the potassium intake is unchanged or moderately increased, between 75 and 100 mEq., varying according to the amount and kind of fruits and fruit juices consumed. There is no doubt that a major part of the beneficial results achieved by the rice diet is due to the change in mineral metabolism.

On the other hand, one of the objections to the rice diet is that this drastic change in the electrolyte supply might endanger the maintenance of the concentrations of the individual electrolytes, as well as of the total osmolar concentration, of the body fluids.

Irrespective of the possible benefits or dangers of the treatment, the patient who follows the regimen strictly gives an opportunity for study of the extent and limits of the adjustability of the physiological regulation of body fluid electrolytes in response to a drastic change in the electrolyte supply. For many weeks, the patient is kept under well-defined conditions of intake without major alterations from day to day. The long-continued, radical restriction of the sodium and chloride intake deviates to an extreme degree from the normal if one defines "normal" as the habits of nutrition developed over the centuries. Several publications already contain contributions to this question.[2]

From the Department of Medicine, Duke University School of Medicine.

This work was aided by grants from the Anna H. Hanes Memorial Fund and the National Heart Institute of the National Institutes of Health, Public Health, Public Health Service.

1. Kempner, W.: (*a*) Compensation of Renal Metabolic Dysfunction: Treatment of Kidney Disease and Hypertensive Vascular Disease with Rice Diet, North Carolina M. J. **6**:61 (Feb.) 1945; (*b*) Treatment of Hypertensive Vascular Disease with Rice Diet, Am. J. Med. **4**:545 (April) 1948; (*c*) Treatment of Heart and Kidney Disease and of Hypertensive and Arteriosclerotic Vascular Disease with the Rice Diet, Ann. Int. Med. **31**:821 (Nov.) 1949.

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2

The present communication is concerned with serum electrolyte changes during rice-diet treatment in hypertensive patients without evidence of advanced renal involvement.[3]

MATERIAL AND METHODS

In order to study the "average" response of the serum electrolyte pattern to the conditions of the rice diet, patients were taken at random from those who were scheduled to start the rice-diet treatment. The only point of selection for this series was that the clinical diagnosis in each case was the same, i. e., hypertensive vascular disease without heart failure and without gross evidence of advanced renal involvement. Absence of gross evidence of advanced renal involvement was defined relatively generously, in that patients showing a slight albuminuria before the treatment or a total phenolsulfonphthalein excretion in two hours of not less than 40% were not excluded from this series.

Strict observance of the diet can easily be checked by determining the urinary excretion of sodium and chloride, which drops to a very low level. Any additions to the diet are reflected quickly in increased excretion of these electrolytes. Those patients who, on the basis of the urinary electrolyte excretion, were suspected to have deviated from the strict regimen were excluded from the series. This is an infrequent occurrence under the conditions prevailing in Durham: Only two patients who had been included originally had to be eliminated.

Except for these 2, who were replaced by 2 others, the series consisted of 80 consecutive patients.

The age of the patients ranged from 19 to 67, average 51 years. There were 44 men and 36 women. They were all ambulatory, stayed in hotels or private homes, but took their meals at places where the rice diet is prepared under supervision.

Thirty-nine of the 80 patients had albuminuria when they started the rice-diet treatment. Twenty-eight of the 80 patients had a total phenolsulfonphthalein excretion in two hours of between 40 and 50%; in the others the phenolsulfonphthalein excretion was above 50%.

The serum electrolytes measured were sodium, potassium, total base, chloride, and bicarbonate. In a number of the patients, the pH of the blood was also determined. All the determinations were done on blood samples drawn in the morning in the postabsorptive state of the patient one day before the start of the dietary treatment and after 5, 10, and 15 weeks on the diet. Venous blood was used, and no attempt was made to arterialize it. The arteriovenous differences with regard to carbon dioxide content and pH can be assumed to be relatively constant, venous blood being approximately 2 mEq. per liter higher in carbon dioxide and 0.03 lower in pH. These differences can be disregarded here, since the main interest lies in comparing the values before and during the treatment.

Sodium and potassium were determined with the flame photometer (Perkin-Elmer, Models 52A and 52C), using the lithium internal standard procedure.[4] Care was taken to avoid hemolysis. Total base was determined with the microelectrodialysis method described by Consolazio and Talbot,[5] serum chlorides with the Van Slyke method,[6] and bicarbonate with

3. Further communications are in preparation on serum electrolytes during rice-diet treatment in hypertensive patients with evidence of major renal involvement; on serum electrolytes in hypertensive rats treated with rice diet, and on the correlation between electrolyte concentration and volume of extracellular body fluids in hypertensive patients on rice diet.

4. Berry, J. W.; Chappell, D. G., and Barnes, R. B.: Improved Method of Flame Photometry, Indust. & Engin. Chem. (Anal. Ed.) **18**:19 (Jan.) 1946. Hald, P. M.: The Flame Photometer for the Measurement of Sodium and Potassium in Biological Materials, J. Biol. Chem. **167**:499 (Feb.) 1947.

5. Consolazio, W. V., and Talbot, J. H.: The Determination of Total Base in Biological Materials by Electrodialysis, J. Biol. Chem. **132**:753 (Feb.) 1940.

6. Van Slyke, D. D.: The Determination of Chlorides in Blood and Tissues, J. Biol. Chem. **58**:523 (Dec.) 1923.

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Warburg manometers, applying the principles of the Van Slyke procedure [7] to the Warburg apparatus.[8]

RESULTS

The table combines the results of the determinations of the serum electrolytes before and after 5, 10, and 15 weeks on the rice diet. In some cases the sodium values were relatively high, both initially and later (150 to 155 mEq. per liter). No correlation was noticeable between the higher serum sodium values and the clinical picture of the respective patients. On the other hand, some single sodium values after 10 to 15 weeks on the diet were relatively low; these will be discussed later.

The determinations of total base substances, in addition to the separate determinations of sodium and potassium, were included because total base gives a measure of the total osmotic concentration; for the osmotic value of the extracellular fluid—at least under the conditions pertaining to this series of patients—is almost entirely accounted for by its ionic components; nonelectrolytes contribute very little. The total ionic concentration is given by the duplicated amount of either cations or anions since, with the approximately neutral pH of the blood, no appre-

*Serum Electrolytes During Rice Diet**

	Weeks on Diet			
	0	5	10	15
Sodium	145.0 ± 4.1	142.9 ± 3.5	142.3 ± 4.8	143.0 ± 5.4
Potassium	4.9 ± 0.5	5.2 ± 0.5	5.4 ± 0.6	5.5 ± 0.8
Total base	157.6 ± 4.1	155.0 ± 3.7	154.0 ± 4.6	153.8 ± 5.6
Chloride	100.7 ± 3.0	94.1 ± 4.9	94.3 ± 4.9	95.0 ± 5.8
Bicarbonate	31.2 ± 1.8	34.2 ± 2.2	34.5 ± 2.4	34.4 ± 2.5

* Average values, with standard deviations, for 80 patients with hypertensive vascular disease, in milliequivalents per liter.

ciable quantities of free acid or base can exist and the sum of the cations must equal that of the anions. Total base is more important than total acid from the physiological point of view. Loss of anion in the extracellular fluid can easily be made up by increase in bicarbonate, as Gamble [9] has shown and as will be evident again later on. But loss of cation cannot be replaced; it must even reduce the total ionic concentration by double its amount, since it is connected with an equivalent loss of anion.[9b] Loss of cation means, practically, loss of sodium, since more than 90% of the total concentration of cations is sodium.

The average of the initial serum bicarbonate levels is relatively high, even for venous blood. Almost all these patients had been treated previously elsewhere, and many had been placed on diets (though patients who had previously been treated with the rice diet itself were not included in this series). The dietary measures,

7. Van Slyke, D. D., and Cullen, G. E.: Studies of Acidosis: I. The Bicarbonate Concentration of the Blood Plasma; Its Significance, and Its Determination as a Measure of Acidosis, J. Biol. Chem. **30**:289 (June) 1917.

8. Warburg, O.: Ueber den Stoffwechsel der Tumoren, Berlin, J. Springer, 1926, p. 160. (English edition: The Metabolism of Tumours, London, Constable & Co., Ltd., 1930, p. 172.)

9. (*a*) Gamble, J. L., and Ross, S. G.: The Factors in the Dehydration Following Pyloric Obstruction, J. Clin. Invest. **1**:403 (June) 1925. (*b*) Gamble, J. L.: Chemical Anatomy, Physiology and Pathology of Extracellular Fluid, Cambridge, Mass., Harvard University Press, 1947.

for the most part, included some sodium chloride restriction, usually very moderate compared with that of the rice diet. But it induced to a certain degree the electrolyte changes which are apparent in this survey. (The same consideration applies to a slight reduction in the average of the initial serum chloride levels.)

Statistical analysis shows that all changes of the means, with reference to the initial values, are highly significant, P being less than 0.01 in each instance. Estimation of the significance of the differences of the means for each five-week period reveals that the significant changes take place during the first five weeks. P is less than 0.01 for the mean differences of the 0 to 5-week periods and greater than 0.05 for the mean differences of the 5 to 10- and 10 to 15-week periods for each of the electrolytes examined.

COMMENT

Sodium, potassium, and total base concentrations remained practically the same during the observation period of 15 weeks. (Total amounts of extracellular sodium and total base decrease because of the changes in extracellular fluid volume, as described by Murphy.[10]) The slight drop in the concentration of sodium and total base and the slight increase in potassium, though statistically significant, are without clinical importance. Occasional determinations of the serum electrolytes after additional intervals of 3 to 36 months have proved that no patient whose serum electrolytes showed the "average" pattern, as described above, during the first period of strict dietary treatment and close observation deviated from that pattern in the period thereafter. The satisfactory regulation of serum sodium, potassium, and total base decides whether the strict, unmodified diet can safely be used.

Hyperpotassemia in the strict sense, as defined by a serum potassium concentration exceeding 5.5 mEq. per liter, is not an infrequent finding in patients on rice diet. As the Table shows, there is an increase throughout the period of strict rice-diet treatment, though very moderate on the average. But even in those instances in which the hyperpotassemia was somewhat more pronounced, there was never any indication of potassium intoxication.

Whereas remarkable changes in the sodium, potassium, or total ionic concentrations of the serum would clinically be of great importance, the not inconsiderable drop in serum chloride and the rise in serum bicarbonate, both usually observed in the rice-diet patient, do not represent any clinical dangers as long as they remain within the range found in the patients of this series.

The urinary concentration of chloride, though greatly diminished, remains slightly higher than that of sodium (Fig. 1); the reverse is true for the fecal excretion of these electrolytes.

Increase in bicarbonate and drop in chloride, though correlated, were not of equivalent magnitude in the subjects of this series, the latter exceeding the former by about 3 mEq. per liter—approximately the amount of decrease in sodium.

Measurements of blood pH in a number of patients showed that on the average there was no change of statistical significance. In 45 patients on the rice diet for 1 to 6 weeks, the pH of the venous blood averaged 7.38, with a standard deviation of 0.04; in 60 patients on the diet for 7 to 15 weeks, the pH averaged 7.41 $\pm$ 0.05; 17 persons on a normal mixed diet had a blood pH of 7.37 $\pm$ 0.03. But if one

10. Murphy, R. J. F.: The Effect of "Rice Diet" on Plasma Volume and Extracellular Fluid Space in Hypertensive Subjects, J. Clin. Invest. **29**:912 (July) 1950.

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considers the relation between blood pH and serum bicarbonate (Fig. 2), one finds a slight deviation of the pH toward the alkaline side of 7.4 in the patients with more pronounced bicarbonate increase. This is to be expected in the case of the

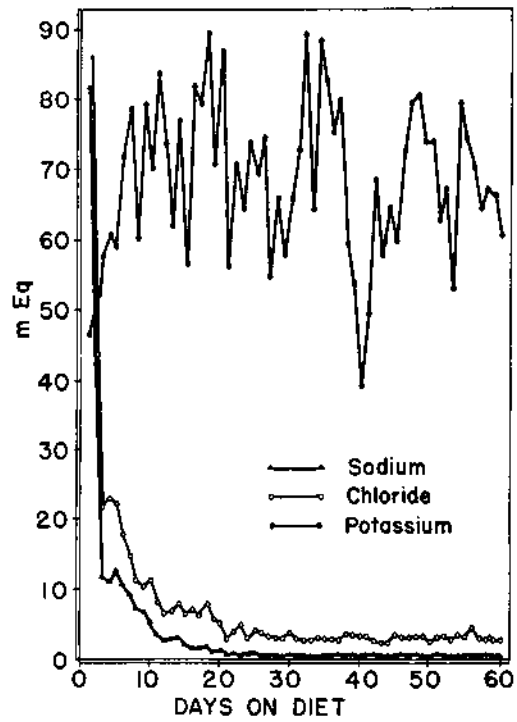

Fig. 1.—Urinary electrolyte excretion of a patient on rice diet. Electrolytes are measured in milliequivalents per 24 hours.

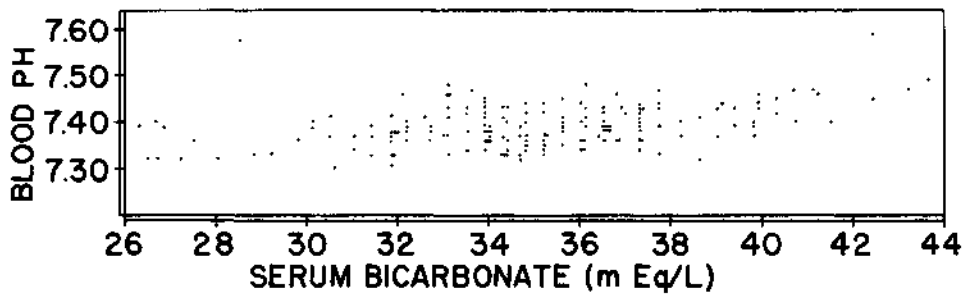

Fig. 2.—Relation of venous blood pH to serum bicarbonate in patients with hypertensive vascular disease on rice diet.

so-called compensated metabolic alkalosis, since the adjusting defense mechanism does not usually prevent departure of pH completely.

The changes found in the electrolyte pattern of the rice-diet patient take place mostly in the first five weeks of the dietary treatment. Then an equilibrium is reached, which shows that complete adjustment to the change in mineral intake can be achieved and is achieved in the patient with intact renal electrolyte regulation.

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Though this is true for the vast majority of patients without gross evidence of advanced renal involvement, it cannot be completely relied upon in each individual instance. Four patients in this series had severe serum electrolyte disturbances as hyponatremia, hyperpotassemia, and hypochloremia. The 5% incidence of the low-sodium syndrome is similar to that observed in several hundreds of additional patients without major renal disease who were studied less systematically. The maximal deviations found in those four patients were 117.4 mEq. per liter of sodium, 74.9 mEq. per liter of chloride, and 7.4 mEq. per liter of potassium; these were easily corrected by small additions of sodium chloride as such or in form of toast or vegetables. (The serum electrolyte values which were found after the additions were given are not included in the calculation of averages.) These four patients did not, to begin with, present a clinical picture different from that of the other patients included in this study: the urinary findings were normal or minimally abnormal, and the phenolsulfonphthalein excretions in two hours were 49, 74, 46, and 71%, respectively.

Patients in heart failure were not included in this series because they are under different conditions of "intake," owing to the additional supply of electrolytes from the edema fluid after diuresis has begun. No patient with cardiac decompensation was seen who displayed an electrolyte imbalance on the strict rice diet. It is to be emphasized that these patients received neither ammonium chloride nor mercurial diuretics.

It is concluded that satisfactory renal electrolyte regulation under the conditions of the strict rice diet can be expected in 95% of the patients without advanced renal involvement.

SUMMARY AND CONCLUSIONS

A survey is given of the serum electrolyte pattern of patients on strict rice diet. Sodium, potassium, total base, chloride, and bicarbonate were determined in 80 consecutive patients with hypertensive vascular disease without gross evidence of advanced renal involvement. The determinations were made one day before the patient started the diet and after 5, 10, and 15 weeks.

A moderate drop in chloride and, correspondingly, an increase in bicarbonate occur, both developing during the first weeks of the treatment. Sodium, potassium, and total ionic concentrations are essentially maintained.

The metabolic state with regard to serum electrolytes of the "average" hypertensive patient on rice diet, that is, a patient with relatively undisturbed renal regulatory function, is that of a compensated metabolic alkalosis.

The strict rice diet can be given without danger of serum electrolyte disturbance to all patients with cardiac decompensation and to 95% of those with good renal regulation. Difficulties have to be expected in patients with severe primary or secondary renal impairment (to be discussed in a later paper) and might arise in 5% of those in whom urinary findings and results of renal-function tests seem to indicate an undisturbed renal regulatory function.

The procedures were greatly assisted by the able technical work of Mr. Cecil Appleberry, Mrs. Evelyn Cohn, Mrs. Ruth Georgiade, Miss Margaret Nelson, and Miss Fides Ruestow.

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Electrolyte Metabolism during Rice Diet, II.

Serum Electrolytes in Patients with Severe Primary or Secondary Renal Disease

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ELECTROLYTE METABOLISM DURING RICE DIET

II. Serum Electrolytes in Patients with Severe Primary or Secondary Renal Disease

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DURHAM, N. C.

IN A PREVIOUS paper,[1] a survey was given of the serum electrolyte pattern of patients on strict rice diet who had hypertensive vascular disease without advanced renal involvement. It was found that in 95% of these patients, serum electrolyte concentrations were well maintained. One should expect this to be different in patients with advanced kidney disease, and doubts are occasionally expressed whether or not salt restriction is applicable at all in such instances. The purpose of this paper is to report on the tolerance to rigid salt restriction in a series of patients with severe renal disease who were treated with the rice diet.

The presence of renal insufficiency greatly complicates the study and interpretation of chemical changes which take place in the body fluids as a result of dietary measures. Whereas in the previous group of patients a systematic approach was possible, determining the serum electrolytes at equal time intervals and under the influence of diets of identical composition, this procedure is not feasible for patients with definite renal insufficiency. Here modifications of the basic scheme of the diet, especially with regard to electrolyte intake, are frequently unavoidable. The point at which these modifications become necessary can hardly be predicted. Kempner,[2] therefore, considers the rice diet to be contraindicated unless frequent checks of the patient's blood chemistry are possible.

MATERIAL AND METHODS

The present series consisted of 80 patients chosen from those who were scheduled to start the rice diet treatment. The clinical diagnoses are listed in Table 1.

There were 55 males and 25 females. The ages ranged from 4 to 64, averaging 40 years. The patients were either hospitalized or ambulatory, in the latter case taking their meals under

From the Department of Medicine, Duke University School of Medicine, Durham, N. C.

The procedures were greatly assisted by the able technical work of Mrs. Evelyn Cohn, Mrs. Ruth Georgiade, Mrs. Margaret Harvey, and Miss Fides Ruestow.

This work was aided by grants from the Anna H. Hanes Memorial Fund and the National Heart Institute, of the National Institutes of Health, Public Health Service.

1. Peschel, E., and Lohmann-Peschel, R.: Electrolyte Metabolism During Rice Diet. I. Serum Electrolytes in Hypertensive Patients Without Evidence of Advanced Renal Involvement, A. M. A. Arch. Int. Med. **89**:234 (Feb.) 1952.

2. Kempner, W.: Treatment of Hypertensive Vascular Disease with Rice Diet, Am. J. Med. **4**:545 (April) 1948.

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supervision. Adherence to the prescribed form of diet was currently checked by determining the urinary excretion of sodium and chloride, with simultaneous observation of the serum concentrations.

The majority of these patients had previously been treated elsewhere with some sodium chloride restriction, the degree of which could be estimated from the initial urinary electrolyte excretion. According to this criterion, 3 of the 80 patients had been on a rigid salt restriction

TABLE 1.—*Clinical Diagnoses*

Diagnosis		Patients, No.
I. Primary kidney disease		46
a. Chronic glomerulonephritis	33	
1. Nephrotic stage	8	
2. Hypertensive stage	25	
b. Kimmelstiel-Wilson syndrome	5	
c. Chronic pyelonephritis	4	
d. Polycystic kidney disease	4	
II. Secondary kidney disease		34
a. Arteriolonephrosclerosis	24	
b. Malignant hypertension	10	

TABLE 2.—*Initial Blood Nonprotein Nitrogen Values*

Patients, No.	Nonprotein Nitrogen	
	Range	Average
13	40 or below	33
27	41-60	48
17	61-80	74
5	81-100	88
15	101-200	135
3	Above 200	232

TABLE 3.—*Results of Phenolsulfonphthalein Tests*

Patients, No.	Total Excretion in 2 Hours, %	
	Range	Average
10	Above 40	52
16	30-39	34
17	20-29	24
13	10-19	15
6	5-9	7
18	Below 5	1

corresponding to that of the rice diet; 11 on a fairly marked restriction; 32 on moderate restriction, and 34 on a normal salt intake. For the purpose of this paper, all the 80 patients are considered as previously untreated, in order to apply the most rigid measure in regard to tolerance to the change in electrolyte intake.

Tables 2 and 3 indicate the degree of impairment of kidney function in the patients of this series. (In all instances in which the total phenolsulfonphthalein excretion in two hours was above 40%, there was an established history of chronic nephritis.) The average of the initial nonprotein nitrogen values of the 80 patients was 77 mg. per 100 cubic centimeters of blood; the average phenolsulfonphthalein excretion (total excretion in two hours) was 22%. Proteinuria was initially present in all 80 patients.

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All patients were started on the strict rice diet without any modifications. This was continued for three months, or until the serum electrolyte determinations indicated major deviations from the values found to be average for patients with unimpaired renal regulatory function.[1] The electrolytes measured were sodium, potassium, chloride, and bicarbonate. Total base was determined in some instances, and in a number of patients the pH of the venous blood was also measured.

TABLE 4.—*Incidence of Serum Electrolyte Disturbance in 80 Patients with Renal Insufficiency on Rice Diet*

Patients with Serum Electrolyte Disturbance	None After 3 Mo.	After				Before Start of (Modified) Rice Diet
		3 Mo.	2 Mo.	1 Mo.	½ Mo.	
No.	36	6	15	14	6	3
%	45	7.5	18.8	17.5	7.5	3.7

TABLE 5.—*Relation of Serum Electrolyte Disturbance to Clinical Diagnosis*

	Serum Electrolyte Disturbance *					
	None After 3 Mo.	After				Before Start of (Modified) Rice Diet
		3 Mo.	2 Mo.	1 Mo.	½ Mo.	
Primary kidney disease	41.5	13	24	15	4.5	2
Secondary kidney disease	50	..	11.5	21	11.6	6
Chronic glomerulonephritis	40	16	26	13	5	..
Nephrotic stage	37	25	25	13	...	..
Kimmelstiel-Wilson syndrome	(40)	..	(60)	..	...	..
Chronic pyelonephritis	(75)	..	..	..	...	(25)
Polycystic kidney disease	(25)	..	(25)	(50)	...	..
Arteriolonephrosclerosis	67	..	8	12.5	12.5	..
Malignant hypertension	10	..	20	40	10	20

* Incidence in per cent of the respective group. The percentage figures have been put in parentheses when the total number of cases was less than eight.

TABLE 6.—*Relation of Serum Electrolyte Disturbance to Initial Blood Nonprotein Nitrogen and Phenolsulfonphthalein*

Serum Electrolyte Disturbance	Patients, No.	Average NPN, Mg./100 Cc.	Average PSP, Total Excretion in 2 Hr.
1. None after 3 mo.	36	61	29
2. After 3 mo.	6	52	28
3. After 2 mo.	15	77	21
4. After 1 mo.	14	121	14
5. After ½ mo.	6	72	14
6. Before start of rice diet	3	117	2

Technical details of the procedures were the same as described in the previous paper,[1] except for the time intervals between the tests, which, in this series, varied from patient to patient, depending on clinical indications and the outcome of previous electrolyte determinations.

RESULTS

In order to arrive at a somewhat quantitative estimation of the tolerance to rigid restriction of sodium chloride intake in patients with impaired renal function, we have grouped the patients of this series according to the length of time they were given the strict rice diet before major disturbances of the serum electrolyte equilibrium occurred (Table 4). One or more of the following criteria were con-

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sidered major disturbances: serum sodium concentration below 130 mEq per liter, potassium concentration above 6.5 mEq per liter, and chloride concentration below 85 mEq per liter. Such a definition of "major disturbance" is necessarily arbitrary, both in a general sense and with regard to the clinical importance in the individual case.

In Table 5, serum electrolyte regulation has been correlated with clinical diagnoses. Table 6 lists the relations of serum electrolyte disturbance to initial blood nonprotein nitrogen and to phenolsulfonphthalein excretion.

Total base determinations showed that the difference between serum total base and sodium concentrations is not altered in cases of low serum sodium; it averaged 11.5 mEq per liter in 15 patients with a low (average 124.8 mEq per liter) serum sodium concentration as compared with 11.7 mEq per liter in 80 patients with a normal (average 142.3 mEq per liter) serum sodium concentration. This shows again that changes in serum sodium concentration indicate corresponding changes in total ionic concentration and tonicity.

Determinations of pH on venous blood and measurements of serum bicarbonate showed the picture to be similar to that in the group of hypertensive patients without major renal involvement,[1] if patients in the last two or three days of terminal renal failure are excluded. Except for those, there was no instance of uncompensated acidosis. Nor did compensated acidosis occur except in the last days of life. Bicarbonate measurements in the present series of patients before starting the rice diet and after 5, 10, and 15 weeks on the rice diet showed averages of 26.6, 31.7, 33.2, and 32.0 mEq per liter respectively.

COMMENT

Of the amount contained in the glomerular filtrate, 99.566% is reabsorbed in a person on a normal mixed diet [3] and 99.997% in a person on rice diet. The figures are similar in regard to chloride. Calculated on this basis, a small change in reabsorption could have far-reaching consequences; if other factors remained unchanged, a 0.1% reduction of reabsorptive capacity would increase the 24-hour urinary sodium excretion of a patient on rice diet from 0.5 mEq to 25.5 mEq. Other factors, such as glomerular filtration rate, will not remain unchanged in the conditions under consideration. But even if the glomerular filtration rate would be decreased by 50%, the 0.1% reduction of reabsorptive capacity would increase the daily urinary sodium loss of the rice diet patient to 13 mEq. That means, in terms of sodium chloride, that the minute reduction in sodium reabsorption of 0.1% would cause a daily loss of 0.75 gm. of sodium chloride, about three times as much as the total daily intake of a patient on rice diet. Considering this, it should be anticipated theoretically that with a severely damaged kidney serum electrolyte concentrations could never be maintained when sodium and chloride intake are extremely restricted over an extended period, whether the insufficient sodium reabsorption is primary, or secondary to diminished ammonia production, and whether it is irreversible or reversible.[4]

3. Gamble, J. L.: Chemical Anatomy, Physiology and Pathology of Extracellular Fluid, Cambridge, Mass., Harvard University Press, 1947.

4. Kempner, W.: Anoxemia of the Kidney as Cause of Uremic Acidosis: Inhibitory Effect of Low Oxygen Tension on the Deamination of Aminoacids in Kidney Tissue, Am. J. Physiol. **123**:117 (July) 1938.

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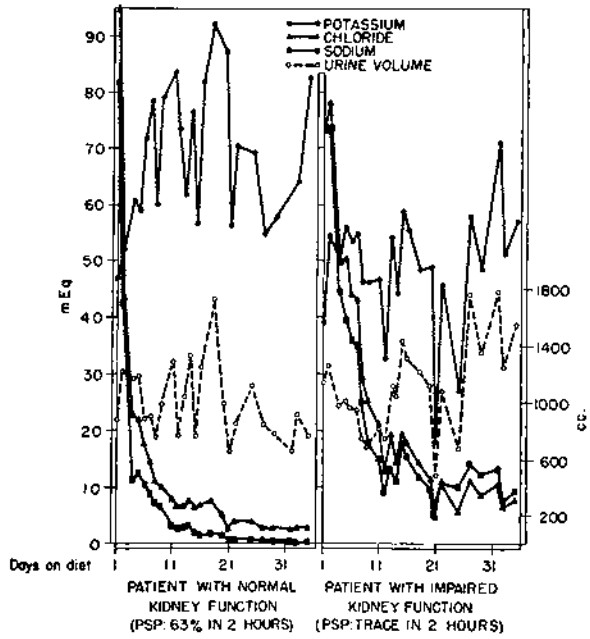

Chart 1.—Urinary electrolyte excretion (mEq. in 24 hours) in first five weeks on rice diet.

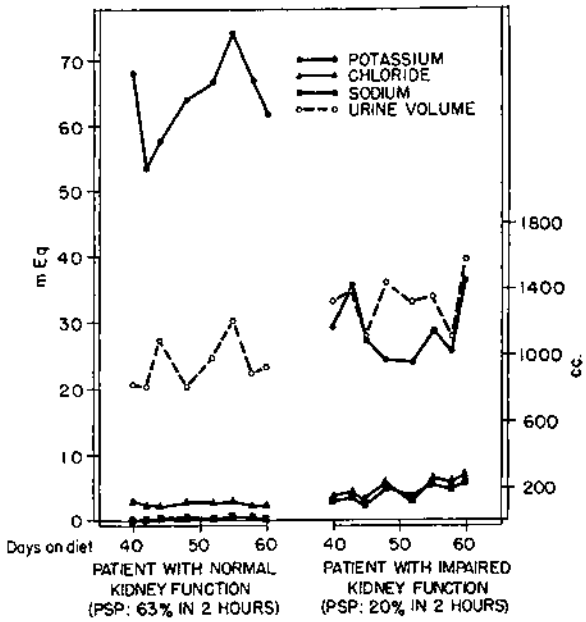

Chart 2.—Urinary electrolyte excretion (mEq. in 24 hours) after 40 days on rice diet.

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Practically, the urinary losses of sodium and chloride are smaller than would be expected from the theoretical considerations set forth above. Charts 1 and 2 illustrate with representative examples the renal electrolyte conservation on strict rice diet in patients with severe kidney disease as compared with that of patients with unimpaired renal regulatory function. With the same intake, patients with severe renal disease excrete more sodium and chloride and less potassium, and it might be noted that, as a consequence of the loss of functional elasticity of the kidney, the fluctuations in the daily excretion of the single electrolytes parallel each other to a certain degree, all being influenced by the 24-hour urine volume (compare the 12th to 15th and 21st to 35th days in Chart 1).

If one agrees that therapeutically the most rigid salt restriction compatible with the individual condition is desirable, then it is of importance to know when, approximately, a severe serum electrolyte disturbance is to be expected, whether there is a criterion for predicting its occurrence, and when and in what amounts modifications should be introduced.

As to the patients studied in this series, it is remarkable that serum electrolyte equilibrium was satisfactorily maintained in 45%. This group of 36 patients could be treated as if they had completely normal renal regulatory capacity, although an average initial nonprotein nitrogen of 61 mg. per 100 cubic centimeters of blood and an average phenolsulfonphthalein excretion of 29% in two hours indicated the severity of impairment of renal function. These patients did not receive any modification of the strict rice diet for three to four months; after that time, slight additions were started in each instance, amounting, in terms of sodium chloride intake, to 2 to 4 mEq. per day. Further serum electrolyte determinations were done after an additional period of two to three months and from then on in varying intervals up to a total observation period of several years. In 12 of the 36 patients a major electrolyte disturbance developed later, after additional periods of 2 to 17 (average 6) months; it was compensated by increased modifications. Twenty-four of the 36 patients went along satisfactorily on the same type and amount of additional food as was given to patients without renal involvement.

Three patients showed a serum electrolyte disturbance at the initial examination prior to the scheduled start of the rice diet treatment. None of them belonged in the group of patients who had been treated previously with a marked or fairly marked restriction of sodium chloride intake. This emphasizes again that the natural course of severe kidney disease itself includes the tendency toward electrolyte derangement, a factor which might be involved in other cases of this series too.

In 55% of the 80 patients of this series, a major serum electrolyte disturbance developed within four months. A classification according to the underlying disease (Table 5) shows that the tolerance to the rigid restriction of sodium chloride intake is not distinctly correlated with the nature of the processes which led to the renal insufficiency. A larger number of observations might confirm a better tolerance in cases of arteriolonephrosclerosis and chronic pyelonephritis. In the nephrotic stage of chronic glomerulonephritis, as in cases with cardiac edema, an additional electrolyte supply can occur when a mobilization of the edema fluid has been achieved and when, of its contents, more water than electrolytes is excreted in the urine.

Table 6 shows that the degree of azotemia is a relatively unreliable guide for predicting the occurrence of serum electrolyte disturbance on strict rice diet. There is a correlation with the result of the phenolsulfonphthalein test which, at first

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glance, seems to be rather close. The lower the phenolsulfonphthalein excretion the earlier one should expect a major disturbance in the electrolyte equilibrium. However, in this series at least, statistical significance can be attributed only to Groups 4 and 6 as compared with Group 1, *P* being less than 0.01 for Group 4 and about 0.02 for Group 6 but above 0.05 for the other Groups.

Clinically, the serum electrolyte disturbance, if sufficiently pronounced, usually manifested more or less the well-known features of the low salt syndrome.[5] Symptoms suggesting electrolyte derangement are occasionally seen with serum sodium or chloride values higher than 130 or 85 mEq per liter, respectively. On the other hand, there are patients who seem to establish a new equilibrium at a sodium level of as low as 120 mEq per liter without directly apparent clinical consequences. In a few of the cases studied, hyperpotassemia with or without the typical electrocardiogram changes was found when there was no simultaneous hyponatremia or hypochloremia of similar degree.

The low salt syndrome progressed only rarely to the critical picture of peripheral vascular collapse and renal shutdown with oliguria or anuria; in most instances, it was possible to correct it in time by modification of the diet, consisting of sodium chloride administration. In terminal phases, it was sometimes impossible to repair the electrolyte derangement. Usually, even in patients with extremely low kidney function, one can compensate the deficiency in renal electrolyte conservation by astonishingly small additions if they are given early enough. These additions, still keeping the diet well within the range of a very low sodium diet, might consist of vegetables, for example, celery (100 gm. of raw celery contains about 0.3 gm. of sodium chloride) or of regular bread (one slice contains approximately 0.2 gm. of sodium chloride), or, if the deficit is severer, sodium chloride may be given parenterally, preferably in hypertonic solution, since the disturbance is usually that of a hypotonic dehydration. It seems preferable for this type of patient to give the amount of salt which is considered necessary to repair the electrolyte equilibrium in small and repeated portions rather than in massive doses, in order to forestall pulmonary edema. Additions containing sodium chloride should be supplied as soon as a major electrolyte disturbance arises because only early replacement of the salt deficit maintains or restores efficient cardiovascular function and prevents the vicious circle: renal disease → serum electrolyte disturbance → peripheral circulatory insufficiency → prolonged renal vasoconstriction → additional kidney damage.

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SUMMARY AND CONCLUSIONS

A study was made on 80 patients with severe primary or secondary kidney disease in regard to the tolerance to a rigid restriction of sodium chloride intake, as in the rice diet. The degree of impairment of kidney function was characterized by an average initial blood nonprotein nitrogen of 77 mg. per 100 cubic centimeters and an average phenolsulfonphthalein excretion (total in two hours) of 22%. The serum electrolytes sodium, potassium, chloride, and bicarbonate and, in some instances, total base or blood pH were determined at monthly or shorter intervals. All patients were maintained on the strict rice diet until the serum electrolyte determinations indicated major deviations. The period of time on strict rice diet until such major electrolyte disturbances developed was used as a criterion for the tolerance to the rigid restriction of sodium chloride intake.

Contrary to what would be expected on the basis of theoretical considerations, advanced renal disease allows maintenance of serum electrolyte concentrations in a considerable number of patients when their sodium and chloride intake are extremely restricted over an extended period. It was found that in this series of patients 45% did not show a major electrolyte disturbance after three months on strict diet, 7.5% showed it after three months, 18.8% after two months, 17.5% after one month, and 7.5% after half a month; 3.7% were in major electrolyte imbalance before the diet (in modified form) was started.

There was no distinct correlation of these findings with the nature of the processes which led to the renal insufficiency. The degree of azotemia was a relatively unreliable guide for predicting the occurrence of serum electrolyte disturbance, whereas there was a correlation with the result of the phenolsulfonphthalein test.

The deficiency in renal electrolyte conservation could be compensated by astonishingly small additions of sodium chloride if these were given early enough so that even with the modifications the diet could be kept well within the range of a very low sodium diet.

Acidosis did not occur (except during the last days of life, in some instances), although the general clinical state of many of these patients would have led one to expect its presence. The composition of the rice diet helps to reduce the production of acid radicals and favors the formation of bicarbonate reserve.

The strict rice diet can be given to patients with the most severely impaired kidney function, but checks of the serum electrolytes have to be done at at least biweekly intervals, more frequently, of course, if a disturbance has been found or if clinical indications suggest it. The lower the result of the phenolsulfonphthalein test, the earlier one must expect a major disturbance in the electrolyte equilibrium.

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Radical Dietary Treatment of Hypertensive and Arteriosclerotic Vascular Disease, Heart and Kidney Disease, and Vascular Retinopathy

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Radical Dietary Treatment of Hypertensive and Arteriosclerotic Vascular Disease, Heart and Kidney Disease, and Vascular Retinopathy

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THE death rate in this country from hypertensive vascular disease, arteriosclerosis, and kidney disease leading to heart failure, coronary thrombosis, stroke, or uremia is greater than that of any other group of diseases. According to the latest statistics available, these diseases kill three times as many people as cancer, seven times as many as accidents, and twenty times as many as tuberculosis. In addition to causing more deaths than cancer, tuberculosis, and accidents together, they also make many more chronic invalids: the heart cripples incapacitated by shortness of breath, anginal pain, and dropsy; the kidney cripples with uremia; those blind from vascular retinopathy; and the paralytics unable to talk, to swallow, or to use their limbs.

The time has passed when this problem could be brushed aside with the argument that these diseases must run the inevitable course of progressive degeneration. Just as it is unjustifiable to delay treatment in cases of cancer or tuberculosis, it may before long be considered malpractice for a physician to treat patients with hypertensive vascular disease or chronic heart and kidney disease with sympathetic generalities such as "take it easy," or "don't worry," or "forget about it."

When between April and July, 1944, the first three reports on the rice diet appeared, the results were received with a good deal of skepticism. These reports showed the effects of the rice diet on 150 patients treated between 1939 and 1944. The main findings were: in a large percentage there was a marked decrease in blood pressure, the enlarged heart became normal in size, the inverted T_1 in the electrocardiogram became upright, hemorrhagic exudative neuroretinopathy disappeared, and the elevated blood nonprotein nitrogen and serum cholesterol decreased to normal.

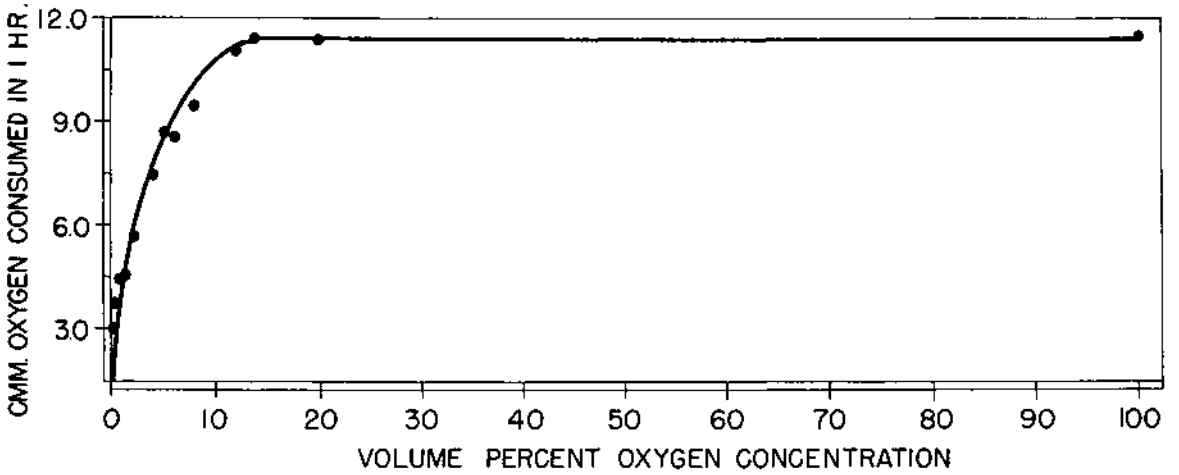
The years between 1944 and 1954 have helped us not only to confirm and extend, with more than 2,000 cases, the results originally reported in 150 cases but have also produced a complete change in the attitude of those who, a few years ago, flatly stated that diet has no place in the treatment of hypertensive vascular disease and arteriosclerosis.

A brief summary of the facts which gradually brought about this change will be given, not because of academic or historical interest, but because a knowledge of the scientific basis of this treatment has a direct bearing on the practical therapeutic success with the individual patient. Without this knowledge the physician will not be able to enforce the diet and to supervise the patient intelligently. Furthermore, no dietary treatment which involves such drastic restriction and daily sacrifice is conceivable without a great deal of self-discipline and will power on the part of the patient, and no physician will be able to convince the patient of the necessity for this unless he is himself convinced by the scientific facts.

Salt Restriction

Salt restriction of varying degrees was in common use at the beginning of the century in the treatment of heart and kidney disease and hypertension, and was again advocated in the twenties by Allen in this country and by Volhard in Europe.

In 1922 Allen published a report on 180 patients



American Review of Tuberculosis, 1939

Figure 1. Effect of various oxygen concentrations on rate of respiration (1 mg. tubercule bacteria, 38° C.).

with hypertension. Their diet was regarded as "salt free" when the chloride content of the urine (expressed as sodium chloride) was not more than 500 mg. a day. In 125 patients a decrease in blood pressure was found.

The response to Allen's paper was discouraging. The *Journal of the American Medical Association* made the following comment in an editorial: "Lately, therapeutic success has been made to correspond with restriction in salt intake. What the next *fashion in dietary proscription* will be remains to be learned." Other authorities argued that it is hard to believe that a reduction in salt intake from 2 Gm. to 0.5 Gm. would prove so much more effective than the restriction from 10 Gm. to 2 Gm., as had been tried frequently.

This argument shows clearly the chief difficulty which many physicians and most patients have in understanding the meaning of the word "restriction," although there are numerous biologic processes where an analogy might be found. For example, a reduction of the oxygen concentration from 100 to 10 vol. per cent merely lowers the oxygen saturation of the hemoglobin from 100 to 90 per cent. In order to produce a significant lowering of the oxygen saturation, the oxygen concentration must be reduced still further. The dependence of cellular respiration on variations of the oxygen concentration is another phenomenon of this kind. Here too one fails to find any effect unless the oxygen concentrations are reduced to minimal values (*Figure 1*).

Physicians who are familiar with the treatment of various allergies could give examples of a similar kind, and any patient who has suffered from poison ivy knows that it might not help him enough if instead of touching 100 poison ivy leaves he touches only 10 or 20.

With this in mind it should be possible to understand that, in certain diseases, an increase from 10 Gm. to 20 Gm. of salt per day or a decrease from 10 Gm. to 2 Gm. may be virtually ineffective, and that nevertheless significant changes might occur if the daily salt intake were decreased from 2 Gm. to 0.3 Gm. or below.

The Rice Diet

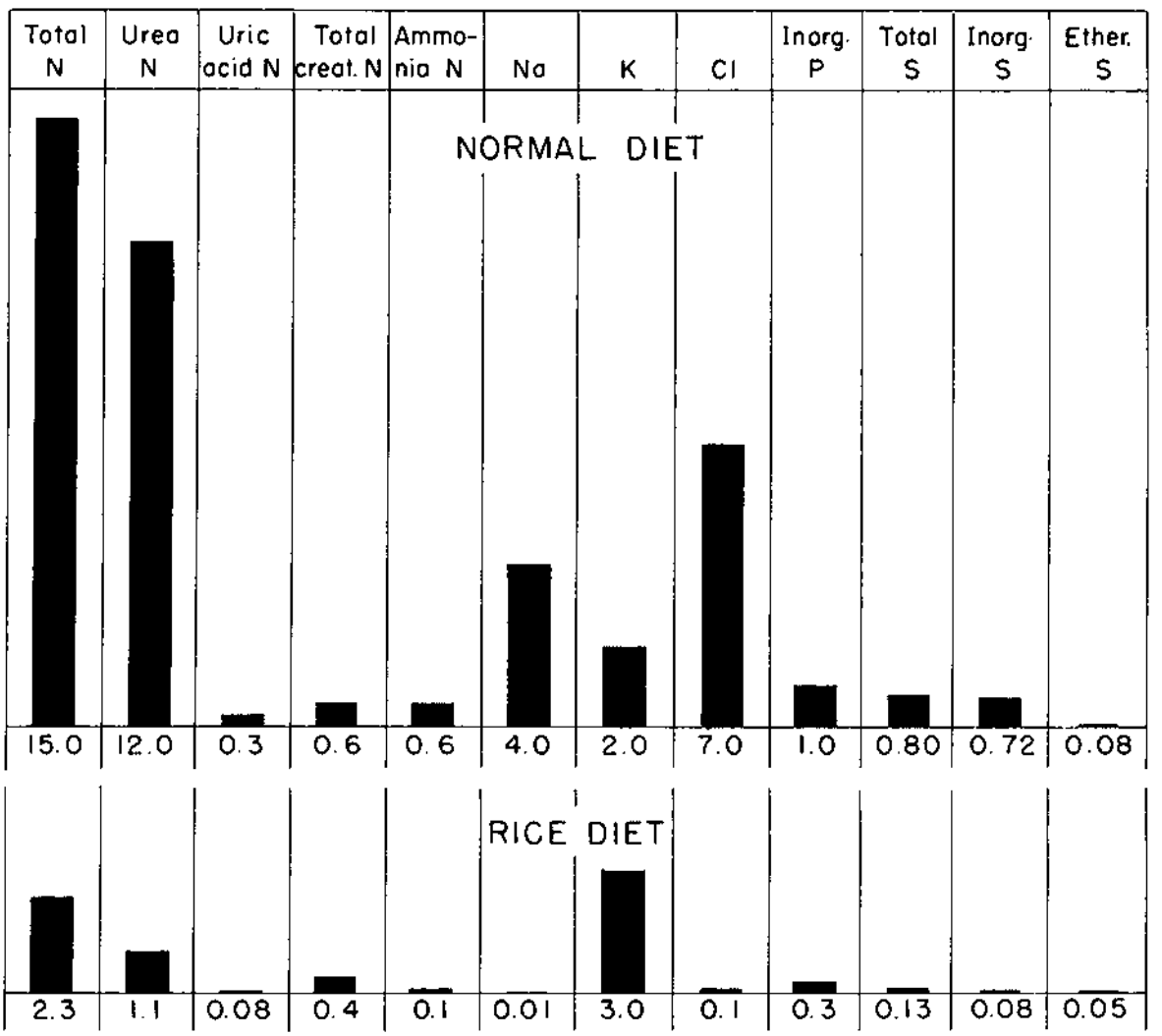
The salt restriction in the rice diet is more rigid than in any other diet used in the treatment of acute and chronic kidney disease, hypertensive vascular disease, arteriosclerosis, heart disease, and vascular retinopathy. It contains, in 2,400 calories, 70 mg. to 120 mg. of sodium and 140 mg. to 240 mg. of chloride. This can be further reduced by eliminating all fruit and fruit juices and allowing only white rice, tea, and white sugar. Such a diet contains, in 2,400 calories, 20 mg. Na and 70 mg. Cl. In a number of cases we have also used exchange resins in addition, to remove sodium from the gastrointestinal tract. However, this paper will not include the results of the "sub-basic" diet nor of the additional use of resins but will be confined, unless specifically stated, to the effects of the ordinary *basic* rice diet—without any medication except additional vitamins A, B, C, D. The rice diet is monotonous, but it has

the practical advantage of simplicity. No elaborate directions are necessary, and it is easy to prepare.

The urinary excretion of chloride after one to two months on the basic rice diet (*Figure 2*) is between 2 and 10 mg. per 100 cc. of urine (expressed as NaCl: about 100 mg. per day). The urinary sodium excretion is between 0.3 and 2 mg. per 100 cc. Figures higher than these, except in patients who are losing edema or who are chronic or acute "salt losers," show that either intentionally or inadvertently errors have been made in the diet.

The chief danger of rigid dietary restriction of NaCl is "salt-losing," with resulting hypochloremia and/or hyponatremia, which may frequently be combined with hyperkalemia, alkalosis, or azotemia.

In nineteen out of twenty patients who show no signs of advanced renal impairment, the extreme restriction of NaCl in the rice diet is well tolerated because a normal undisturbed renal regulatory function achieves a maximum conservation of sodium and chloride and the serum equilibrium is maintained. A moderate drop in serum chloride and a corresponding increase in bicarbonate occur. Sodium, potassium, and total ionic concentrations remain essentially unchanged. However, in one case out of twenty, electrolyte disturbances may develop on the rice diet in spite of the fact that urinary findings as well as kidney function tests seem to



Annals of Internal Medicine, 1949

Figure 2. Urinary excretion (Gm. in twenty-four hours) on "normal" diet and rice diet (for two months or more).

indicate an undisturbed renal function.

In most patients with severe primary or secondary renal impairment, difficulties may be expected because the regulatory mechanism of the kidney is upset. The loss of sodium and chloride in the urine is greater than the intake in the diet, and this may lead to hypochloremia and hyponatremia, accompanied by one or several of the following clinical manifestations: apprehension, psychotic behavior, drowsiness, weakness, headache, anorexia, nausea, diarrhea, muscular cramps, twitching, tachycardia, peripheral circulatory collapse, uremia (*Figures 3 and 4*). A dangerous increase in serum potassium may also occur, resulting in paralysis of the peripheral muscles (which is particularly serious if the respiratory muscles are involved) and in damage to the heart muscle even to the degree of cardiac arrest.

It should also be kept in mind that salt depletion may be caused by extrarenal factors such as profuse sweating, excessive secretion from the respiratory tract, bile drainage, or suction of the stomach.

If these electrolyte disturbances are not recognized soon enough, the consequences may be serious. Medical writings of the past few years repeatedly stress the dangers of low sodium diets because of the possible fatal outcome of salt deprivation.

It is, therefore, obvious that the rice diet, which has the most drastic form of salt restriction, is a dangerous treatment. This is not an argument against the treatment but only an argument against using this treatment where there are no facilities for constant clinical and chemical control and where the patient is not able or not willing to submit to a rather long test period. Fifteen years ago, we thought a test period of two or three weeks would be sufficient. Later on this was extended to two or three months, and now we keep our patients here under daily supervision for four months. The patients are not hospitalized unless they are critically ill or there is some other special reason. Most of them stay in hotels, or in private homes, or in one of the "rice houses." When there is no specific contraindication, they are instructed to lead nor-

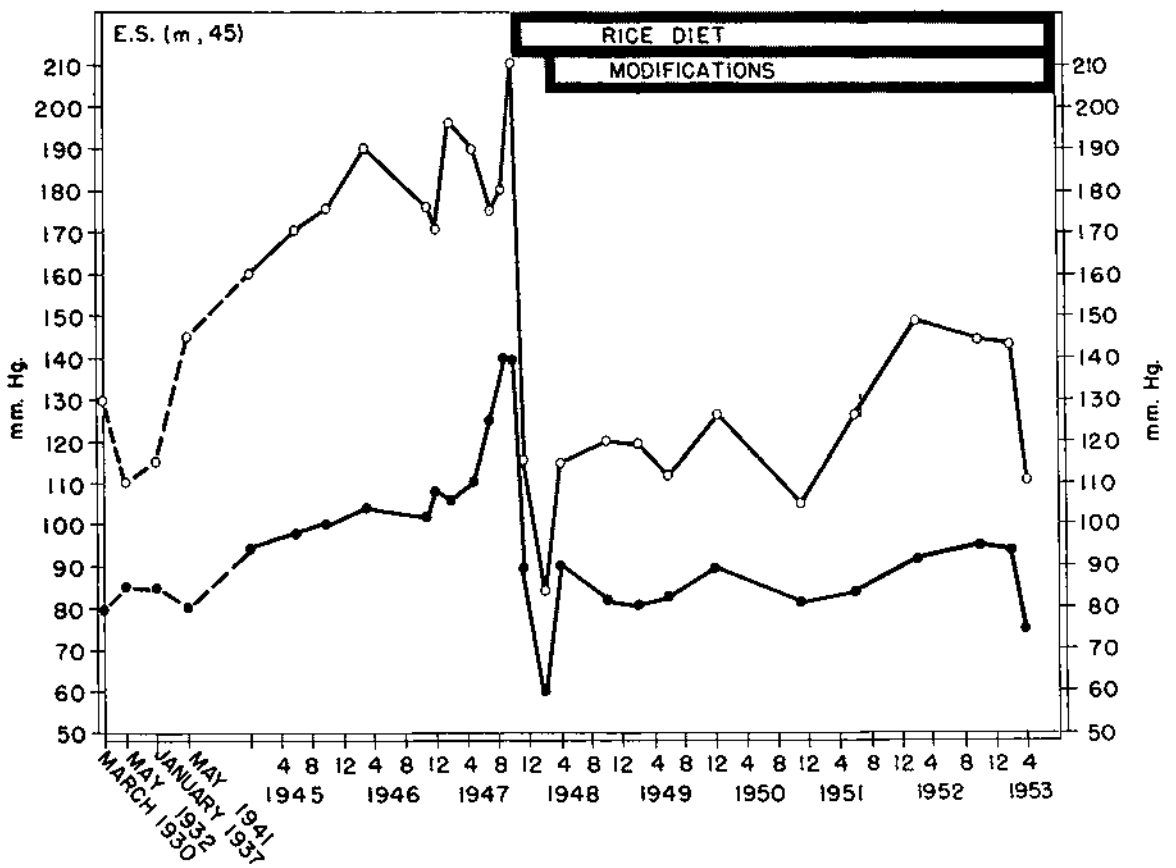


Figure 3. Blood pressure in malignant hypertension reduced by rice diet (dangerous hypotension corrected by additions to diet).

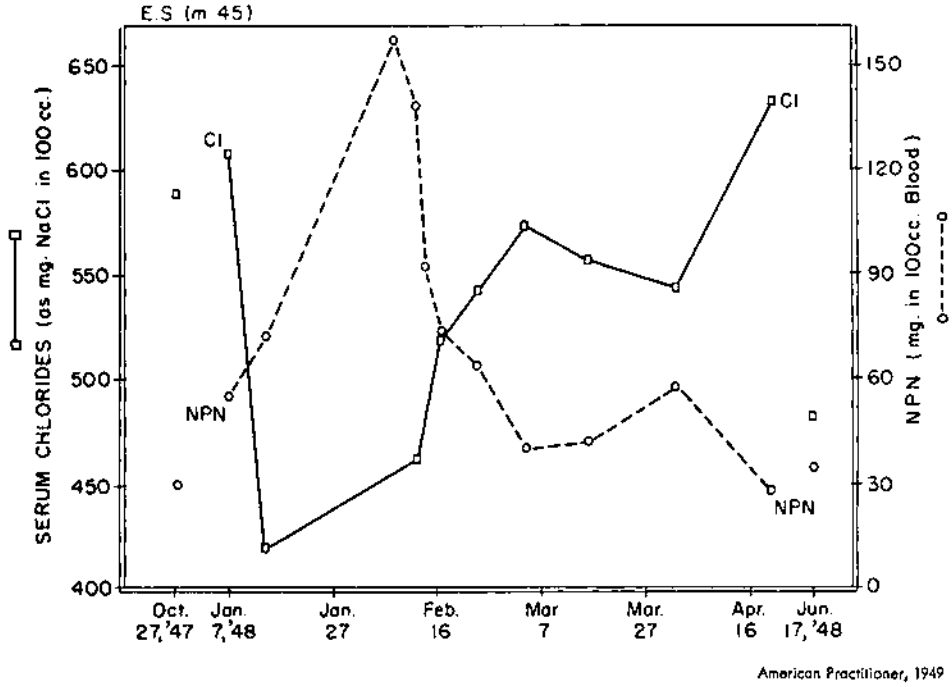


Figure 4. Azotemia following hypochloremia in patient on rice diet (E.S.-m. 45).

mal active lives. After the four months, the patients return home to the care of their family physician who should check them frequently, observe their progress, and encourage them to follow conscientiously the regimen worked out for them. They usually do their work and carry on their ordinary activities. Every two to six months, they should return for two to fourteen days, so that it can be determined whether further modification of the diet is indicated, or whether some of the additions previously given should be discontinued. Urine specimens are sent to our laboratory at least once or twice a month in the intervals between examinations.

Fat and Cholesterol Restriction

Of all the diets used in the treatment of acute and chronic kidney disease, hypertensive vascular disease, arteriosclerosis, heart disease, and vascular retinopathy, the rice diet contains the smallest amount of fat (less than 5 Gm. in 2,400 calories), and it contains no cholesterol.

According to Watt and Merrill, 300 Gm. of white rice (dry weight) contains 0.9 Gm. of fat; 12 oz. of orange juice and 12 oz. of grapefruit juice together contain 1.05 Gm.; 1 lb. of apples, 1 lb. of grapefruit, and 1 lb. of peaches together contain 2.7 Gm.; total daily fat intake thus being 4.65 Gm.

Attempts to replace the rice diet by other food combinations have, as far as salt restriction is concerned, been aimed in the right direction. However, the fat content has not been kept low enough. Even the substitution of one cereal for another may alter this decisively. Thus, 300 Gm. of oatmeal (dry weight) contains 22.2 Gm. of fat, compared to 0.9 Gm. in the same amount of rice. Grollman and Harrison tried to modify the rice diet and make it more palatable by adding meat, butter, eggs, and dialyzed milk. This diet contains only three times as much NaCl as the rice diet, but more than twenty times as much fat.

Even if the salt content of such a diet were lower, the excessive amount of fat would still make it unsuitable in view of the fact that more than 70 per cent of the patients with hypertensive vascular disease who were treated here with the rice diet had a serum cholesterol level of more than 219 mg. per 100 cc. serum (average: 280 mg.) before beginning the diet.

When I showed a chart illustrating that the rice diet lowers the serum cholesterol concentration of patients with kidney disease and hypertensive vascular disease, ten years ago at the Scientific Exhibit of the American Medical Association in Chicago,

Table 1. Total cholesterol concentration in the serum 800 patients with hypercholesterolemia treated by rice diet (average 124 days).

	number of patients	%	*before rice diet (averages)*	*after rice diet (averages)*
Decreased	747	93	283	205
To 220 or above	257	32	301	245
To 219 or below	490	61	273	184
Increased or unchanged	53	7	262	287

two arguments were raised: (1) Hypercholesterolemia is of no importance in vascular disease. (2) The serum cholesterol concentration cannot be reduced by a reduction in the dietary cholesterol intake.

Now everybody talks about the importance of cholesterol in vascular diseases, especially in connection with angina pectoris, coronary heart disease, and myocardial infarction. A journal such as *Circulation* published, in its twelve issues of 1952, seventeen original articles about cholesterol. It is true that it is often not possible to lower the serum cholesterol level by *moderate* fat and cholesterol restriction, but by the rice diet the serum cholesterol has been lowered in 93 per cent of our cases with hypercholesterolemia (*Table 1*). This is true no matter from what fatty or nonfatty substances the cholesterol in the body is derived, or by what mechanism a high serum cholesterol concentration is produced.

Protein Restriction

It is not within the scope of this paper to consider at length the role of protein in the pathogenesis and treatment of the various vascular diseases. Ten years ago, when the first reports on the rice diet were published, it was argued that diet was of no value in hypertensive vascular disease and arteriosclerosis. The restriction of salt, fat, cholesterol, and protein was considered unwarranted. As far as salt, fat, and cholesterol restriction are concerned, this argument has been settled—there being now an almost general agreement as to the importance of the restriction of these dietary components. As far as protein is concerned, the argument is still going on. No matter what the value of the restriction of protein may be, of all the diets used in the treatment of acute and chronic kidney diseases, of hypertensive vascular disease, arteriosclerosis, heart disease, and vascular retinopathy, the rice diet contains the smallest amount of protein (about 25 Gm. in 2,400 calories).

One still finds the statement that the human body requires, as a minimum, an intake of about 50 Gm. of protein a day to prevent protein starvation, resulting in hypoproteinemia, anemia, and edema. The basis for this belief is the fact that in complete fasting the total daily nitrogen excretion in stool and urine is about 8 Gm. Since to replace a nitrogen loss of 8 Gm., 8 x 6.25 = 50 Gm. of protein is necessary, this amount of protein was considered indispensable and was called the daily "wear and tear quota."

However, if in complete "protein-fasting" enough carbohydrate is taken to supply the necessary calories, the total nitrogen excretion may drop from about 8 Gm. to below 2 Gm.

This is known as the "protein-sparing effect of carbohydrates" and is one of the principles used in the rice diet. The total daily nitrogen excretion in stool and urine on a 125 Gm. daily protein intake is 20 Gm., in complete fasting about 8 Gm., after an average of 88 days on the rice diet about 4 Gm. These patients are in nitrogen equilibrium with a protein intake of 4 x 6.25 = 25 Gm. There is no anemia; on the contrary there is usually a slight increase in the hemoglobin concentration, the plasma protein level is maintained or even increased, and edema not only does not develop but if present almost always disappears.

If, therefore, a lowering of the nitrogen metabolism is desirable, as for instance in many cases of acute and chronic nephritis and nephrosclerosis, then the diet with the smallest total nitrogen excretion should be the most useful. It is evident from the figures above that complete fasting (the treatment recommended by Volhard for acute glomerulonephritis), with a nitrogen excretion of 8 Gm., is preferable to a general diet with an excretion of 20 Gm. But the rice diet, with an excretion of 4 Gm., is still more effective than fasting and, unlike fasting, can be continued for months or years (*Table 2*).

The effect of the rice diet on the blood nonpro-

Table 2. Comparison of blood and urine findings on rice diet and in starvation.

	starvation	*rice diet*
Hemoglobin	Decreased	Unchanged
Serum calcium	Decreased	Unchanged
Plasma total protein; A/G ratio	Decreased	Unchanged or increased
Blood NPN; urea	Increased	Decreased
Blood sugar	Decreased	Unchanged
Carbohydrate tolerance	Decreased	Increased
Plasma alkali reserve	Decreased	Increased
Blood volume; interstitial fluid volume	Unchanged	Decreased
Nitrogen balance	Negative	In equilibrium
Urine creatine, ammonia, organic acids	Increased	Decreased

Table 3. Effect of rice diet on nonprotein nitrogen and urea nitrogen of 950 nonuremic patients (NPN 45 and below) (averages).

	before rice diet	*after 110 days (average) of rice diet*
NPN (mg./100 cc. blood)	34.0	29.0
Urea nitrogen (mg./100 cc. blood)	14.1	8.7

tein nitrogen and urea nitrogen of 950 nonuremic patients with hypertensive vascular disease is shown in *Table 3*. The average NPN is 17 per cent higher on an ordinary diet than on the rice diet, the average blood urea N, 62 per cent.

Even in patients without kidney disease, who have normal nonprotein nitrogen and urea concentrations in the blood to begin with, it is advisable to decrease the protein intake in the diet when the salt intake is drastically restricted since, as is known in cases of profuse sweating, diarrhea, or Addison's disease, a decrease in serum sodium or chloride is often followed by an increase in the blood nonprotein nitrogen and urea.

No one doubts that the protein intake should be restricted to a minimum in patients with advanced kidney insufficiency and uremia no matter whether this impairment is the consequence of parenchymatous or of vascular disease. Usually this restriction is begun only after the total PSP excretion in two hours has decreased to below 10 per cent, and after the nonprotein nitrogen has increased to above 100 mg. In progressive diseases like chronic nephritis and hypertensive and arteriosclerotic renal disease, it might not be unwise to start restriction before the final and fatal consequences are obvious.

Indications

Five years ago, in discussing indications for the rice diet, I wrote:

"The rice diet is indicated in all serious instances of acute and chronic nephritis; in heart failure which does not respond to the customary treatment with salt restriction and drugs; in arteriosclerotic and hypertensive vascular disease with cardiac, cerebral, retinal, or renal involvement.

"The rice diet should be tried in uncomplicated hypertensive vascular disease when a more liberal regimen (fat-poor, salt-poor diets, weight adjustment, restriction of activities, regulation of bowel habits, sedation, etc.) has failed."

These statements were not radical enough. Experience with a great many patients suffering from these diseases has convinced me that treatment should be more aggressive and uncompromising and should be started as soon as the diagnosis is certain. Loss of time is as unjustifiable as it would be in cancer or tuberculosis, and the inconveniences involved are no excuse for delaying optimal dietary treatment until the more unpleasant and often irreversible complications have appeared.

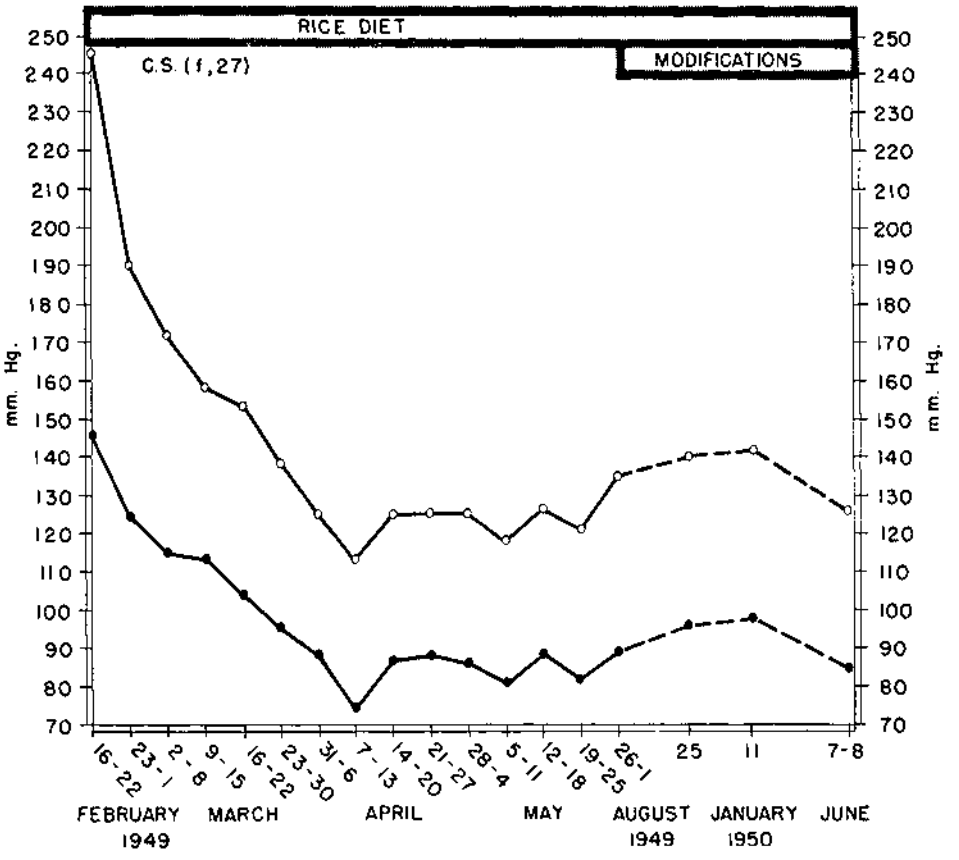
Moreover, just in those cases where the diet is most needed, it sometimes becomes impossible to use it, either because an electrolyte imbalance (hypochloremia, hyponatremia, or hyperpotassemia) has developed, which makes it necessary to give additional salt, or because persistent vomiting makes the patient unable to retain any type of food. Mere difficulties in swallowing, anorexia, and nausea may be overcome by the use of a stomach tube through which 100 cc. (containing 100 calories) of a rice, fruit, fruit juice, and sugar preparation, homogenized in a blender, are given every hour, day and night. (One patient who had had a cerebral vascular accident was fed this way for over a year.)

The rice diet is indicated in *acute nephritis* and in *chronic nephritis*. The high percentage of spontaneous recoveries in acute glomerulonephritis makes a quantitative evaluation difficult. However, in chronic nephritis the beneficial effects of the diet are obvious and easily demonstrable: blood pressure, albuminuria, and azotemia decrease, heart enlargement and retinal hemorrhages, exudates and papilledema disappear (*Figures 5, 6, 7, 8*).

The rice diet is also indicated in *nephrosis*. In many patients with the nephrotic syndrome, there has been a disappearance of ascites, edema, proteinuria, and hypercholesterolemia, and despite the marked protein restriction in the diet, the plasma proteins have returned to normal (*Figure 9*).

The rice diet is indicated in *heart enlargement* and *heart failure*, whether the insufficiency of the heart muscle is secondary to valvular disease or is caused by arteriosclerosis, hypertensive vascular disease, kidney disease, rheumatic fever, disseminated lupus erythematosus, or other disease. *Figures 10, 11, and 12* show decrease in the heart size of patients with valvular disease, coronary artery disease, and malignant hypertension.

Patients with familial and other forms of *hypercholesterolemia* should be treated with the rice diet, as well as patients with *angina pectoris* or *myocardial infarction*. In these, therapy has a double aim: to counteract or to prevent those processes that lead to a decrease in coronary blood flow and to reduce the energy requirements of the myocardium.



Archivos Medicos de Cuba, 1952

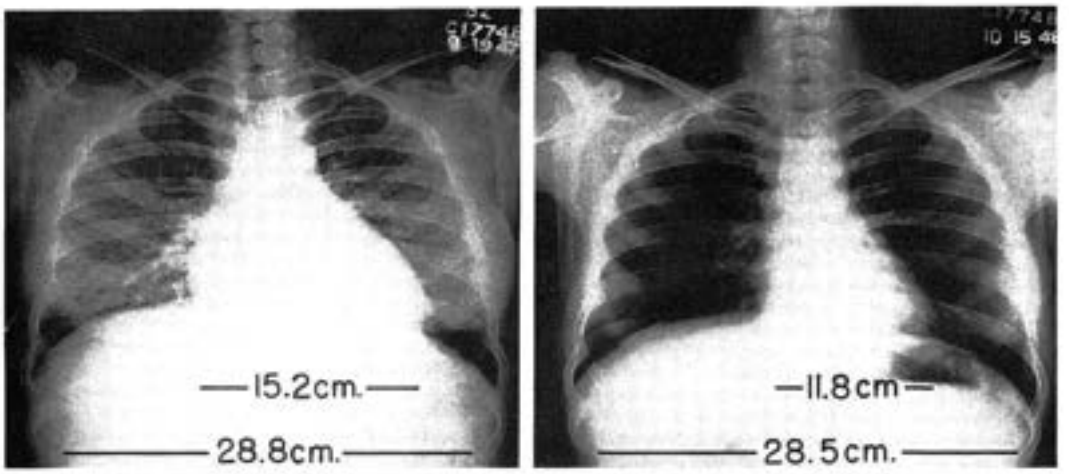
Figure 5. Hypertension in chronic glomerulonephritis reduced by rice diet (total PSP excretion in two hours: 11 per cent).

The rice diet has been found effective in *arteriosclerotic and hypertensive vascular disease.* A great many patients with "benign" hypertension, with and without critical complications, have derived marked benefit from the diet. So have many patients whose hypertension was of the "malignant" type, with severe cardiac, renal, or retinal lesions.

Illustrative Cases

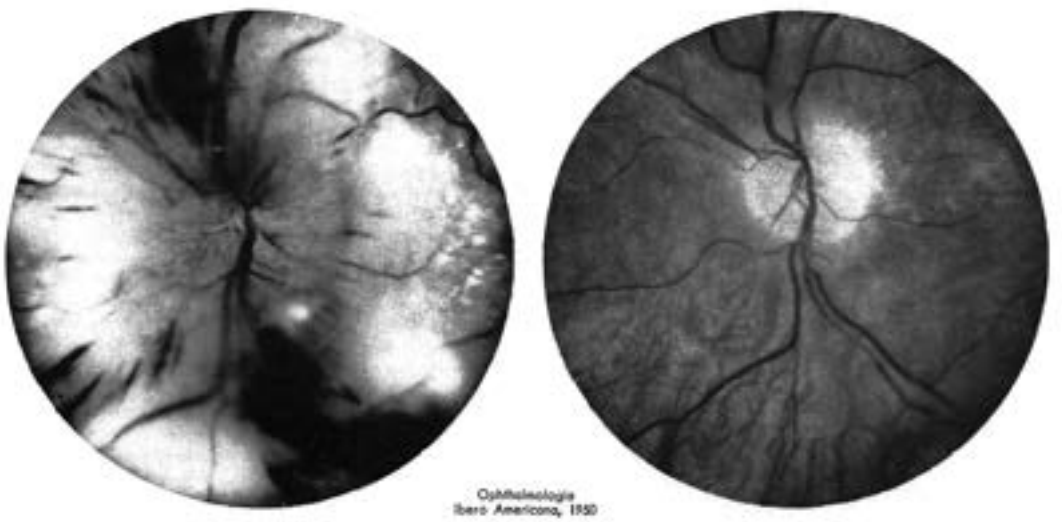
The case of a 47-year-old executive from New York State is given as an example (*Figure 13*). This patient had had hypertension for two and one-half years. He had been treated with a reducing diet and sedatives. Because of severe incapacitating headache, he was sent by his physician to Dr. Raisbeck of the New York Medical College. Dr. Raisbeck found a blood pressure of 257/173 mm. Hg (average of seven readings) and made a diagnosis of hypertensive cardiovascular disease in the malignant phase. He started the patient on the rice diet immediately and advised him to go to Durham as soon as possible. On examination here one week later, the pressure was already slightly lower: 233/161 mm. Hg. The transverse diameter of the heart was 13.8 cm. There were marked vascular changes in the eyegrounds, bilateral papilledema, hemorrhages, and cottony exudates (*Figure 14*).

After 110 days on the rice diet the blood pressure average (ten days) was 124/89 mm. Hg. The transverse diameter of the heart had decreased to 12.4 cm. Papilledema, hemorrhages, and most of the exudates had disappeared, as had also the headaches. The patient returned home on a slightly modified diet. He was feeling perfectly well and resumed his work. Two months later he was reexamined. The blood pressure average during a three days' check-up period was 120/83 mm. Hg. The transverse diameter of the heart was 12.4 cm. The patient was completely asymptomatic. All signs



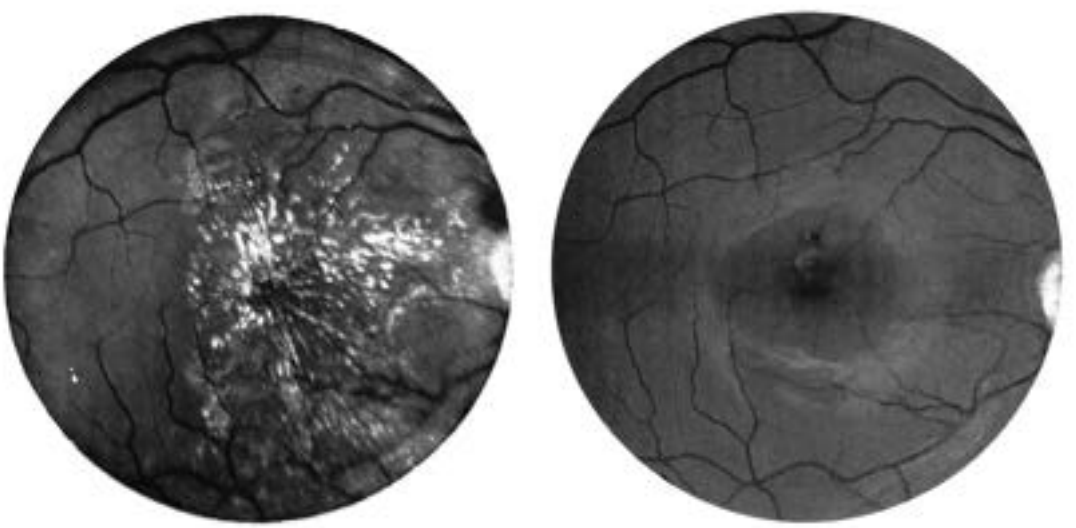
200/98. September, 1947 — 120/80. October, 1948

Figure 6. Heart enlargement in chronic nephritis decreased by rice diet (f. 26).



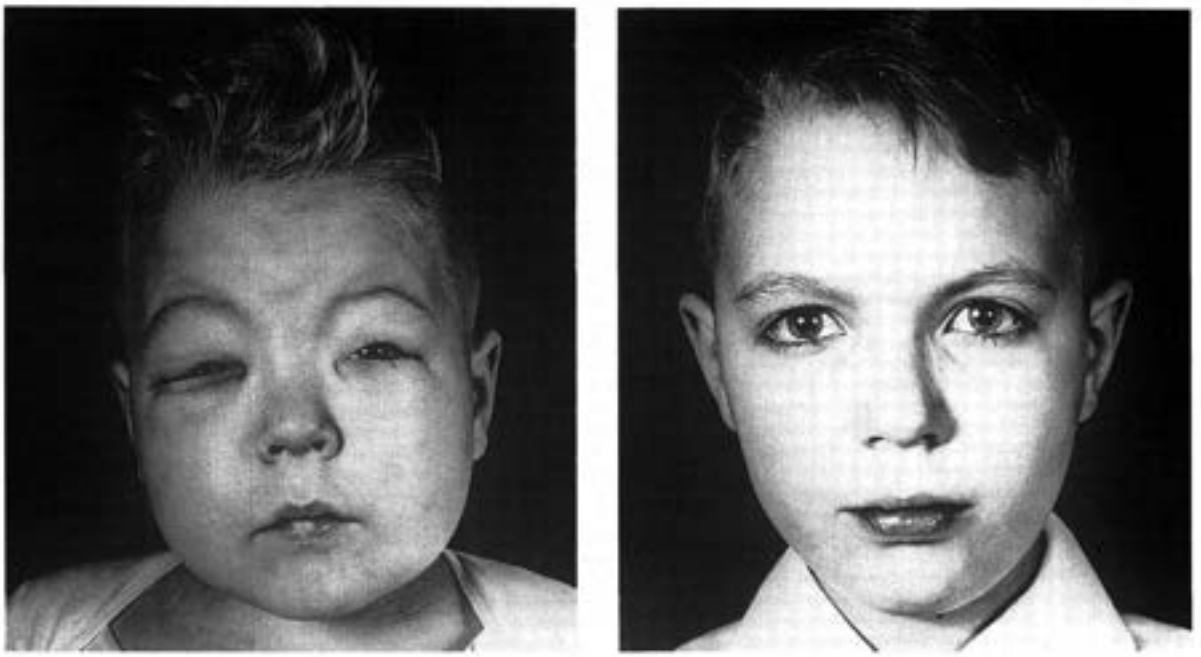
October, 1948 — November, 1949

Figure 7. Disappearance of papilledema, hemorrhages, and exudates in terminal stage of chronic glomerulonephritis treated by rice diet (H. R.-m. 39).



February, 1949 — May, 1952

Figure 8. Disappearance of macular star figure in terminal stage of chronic glomerulonephritis (m. 22).

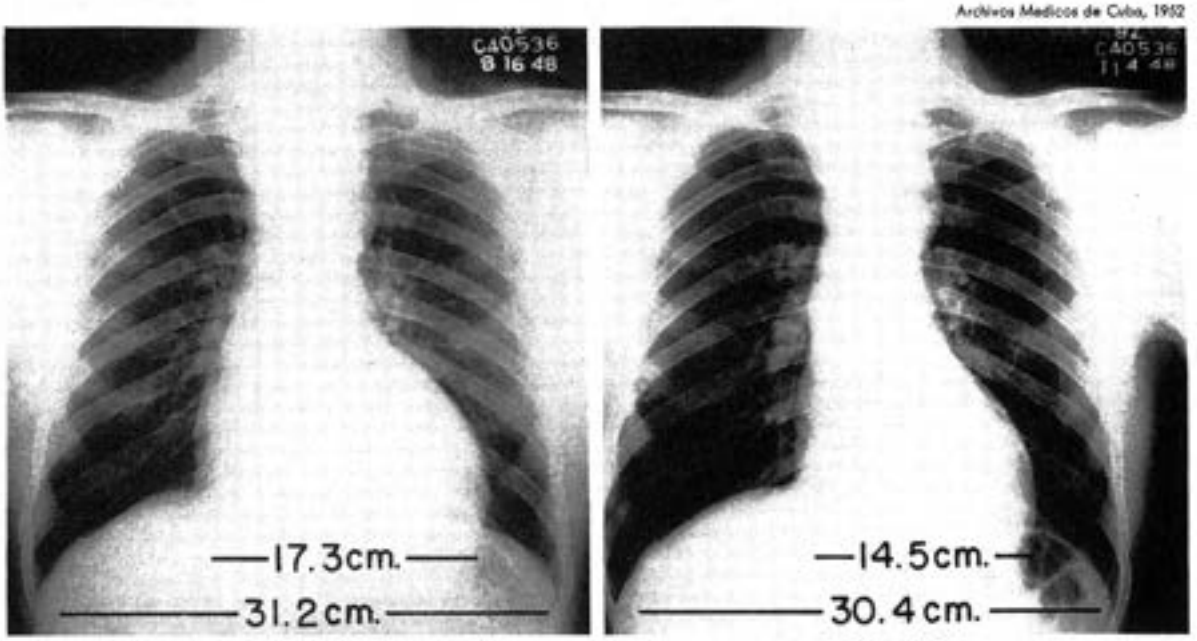


December, 1948 May, 1953

Figure 9. Nephrosis treated with rice diet (D.H.-5 to 10).

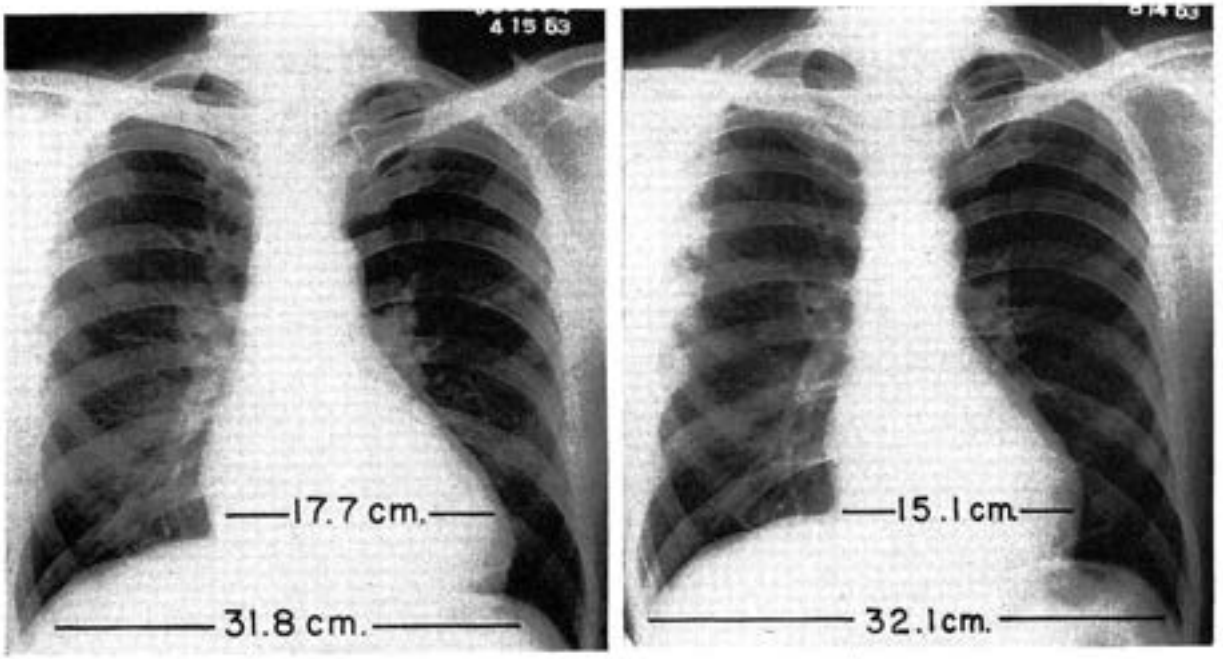
1,100	Cholesteral (mg. per 100 cc. serum)	249
3.9	Total protein (Gm. per 100 cc. plasma)	6.8
42	PSP total excretion in 2 hours (%)	77
4.0	Protein (Gm. per 1,000 cc. urine)	0.2

Archivos Medicos de Cuba, 1952



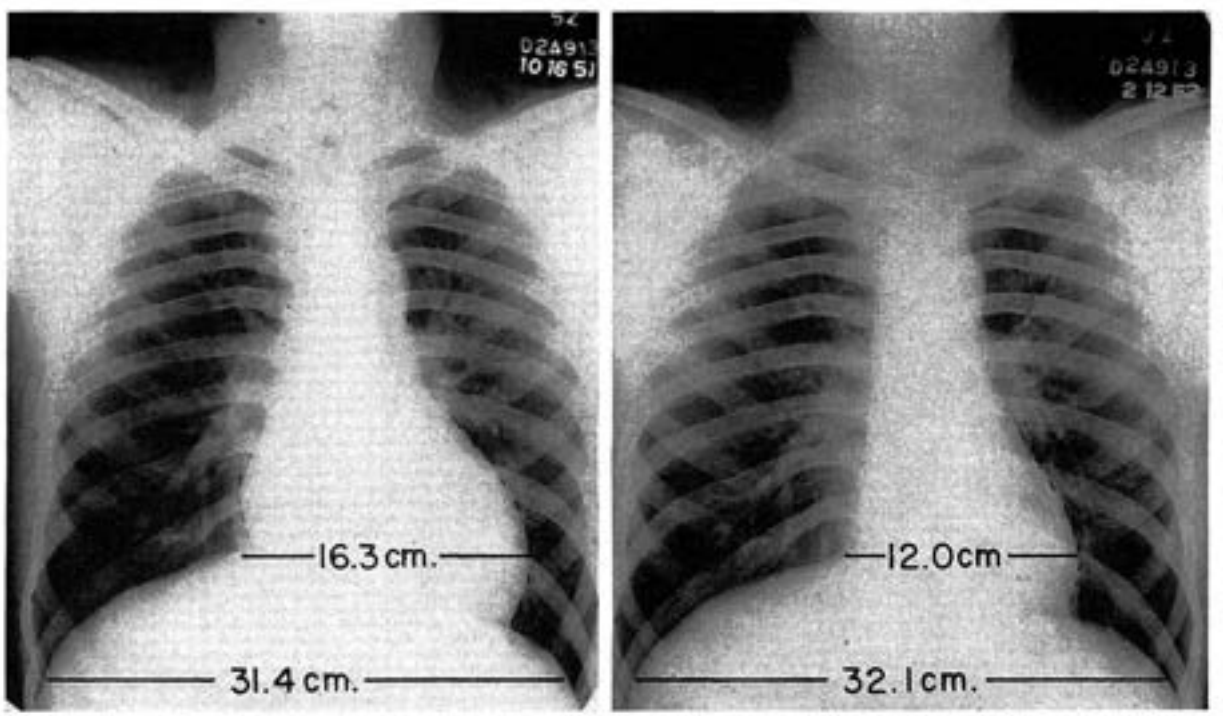
130/64 mm. 8-16-48 120/70 mm. 11-4-48

Figure 10. Heart enlargement in aortic stenosis and insufficiency with partial-complete heart block decreased by rice diet (H.G.W.-m. 55).



120/80. April, 1953 106/77. August, 1953

Figure 11. Decrease in heart size in coronary artery disease treated by rice diet (M.S.-m 47).



October, 1951 February, 1952

Figure 12. Decrease in heart size in malignant hypertension treated with rice diet (S.L.-m. 26).

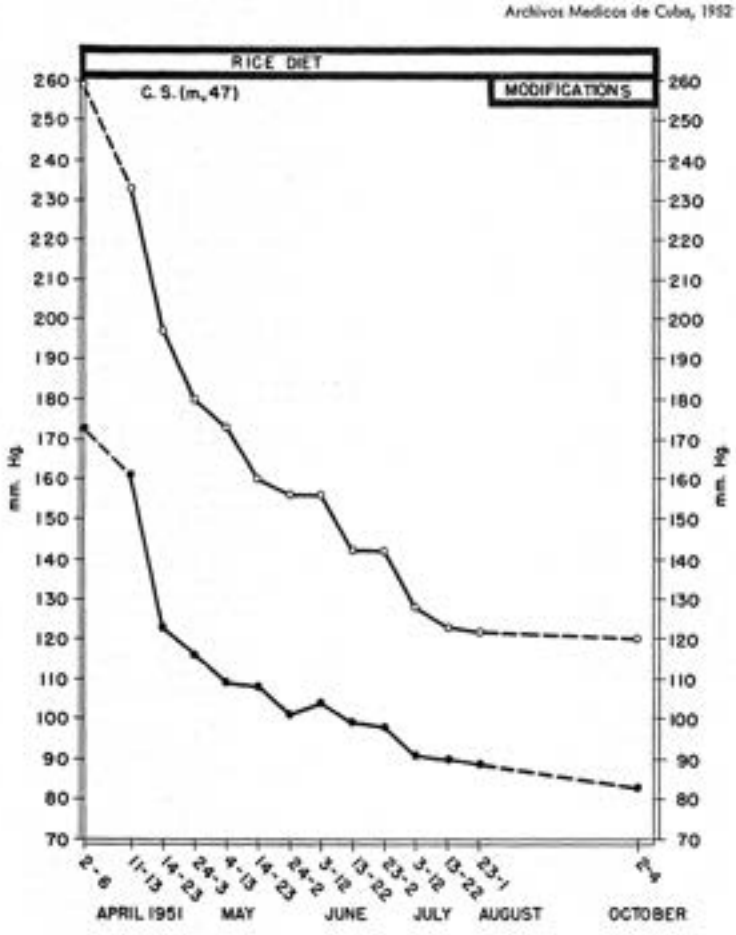


Figure 13. Blood pressure in malignant hypertension reduced by rice diet.

of the advanced retinopathy of malignant hypertension had disappeared.

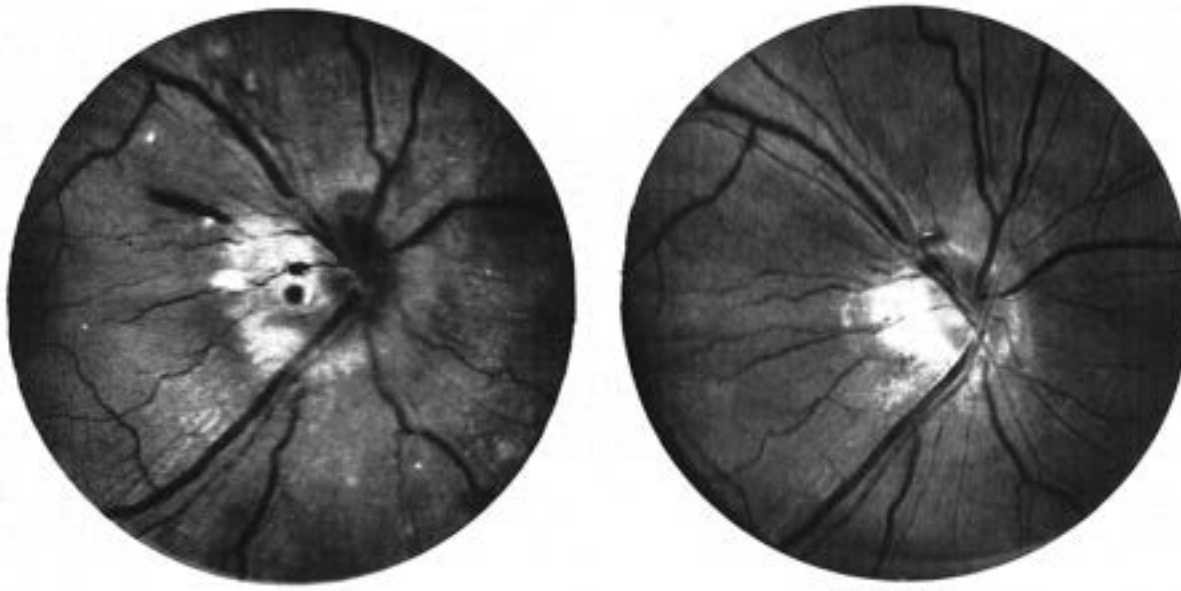
In the case of this patient it took four months for the blood pressure to decrease to normal. *Figure 15* is the blood pressure chart of a woman with so-called "benign" essential hypertension in whom it took four years. Hypertension had been present since 1939. In September, 1943, the blood pressure was 203/109—214/110, and a bilateral lumbodorsal sympathectomy was done by Dr. Smithwick. The blood pressure dropped transiently but within a year had returned to the preoperative level.

By October, 1947, the blood pressure was 245/120. Dr. Irving Wright started her on a modified rice diet, and when after a few months there had been no significant improvement, he advised her to go to Durham.

The patient was then 41 years old. The blood pressure average (February 27 to March 6, 1948) was 222/131 (readings in recumbent position). The only positive finding besides the hypertension was a soft aortic diastolic murmur. The chloride concentration in the urine (as NaCl) was 114 mg./100 cc., as compared with 5 to 15 mg. on the strict rice diet.

The strict rice diet was begun in February, 1948. After 105 days, the blood pressure was 213/122 mm. Hg; after 180 days, it was 212/121. The chloride concentration in the urine (as NaCl) then was still 82 mg.

From that time on, the patient adhered strictly to



April, 1951 — January, 1952

Figure 14. Disappearance of papilledema, hemorrhages, and exudates in malignant hypertension (C.S.-m. 47).

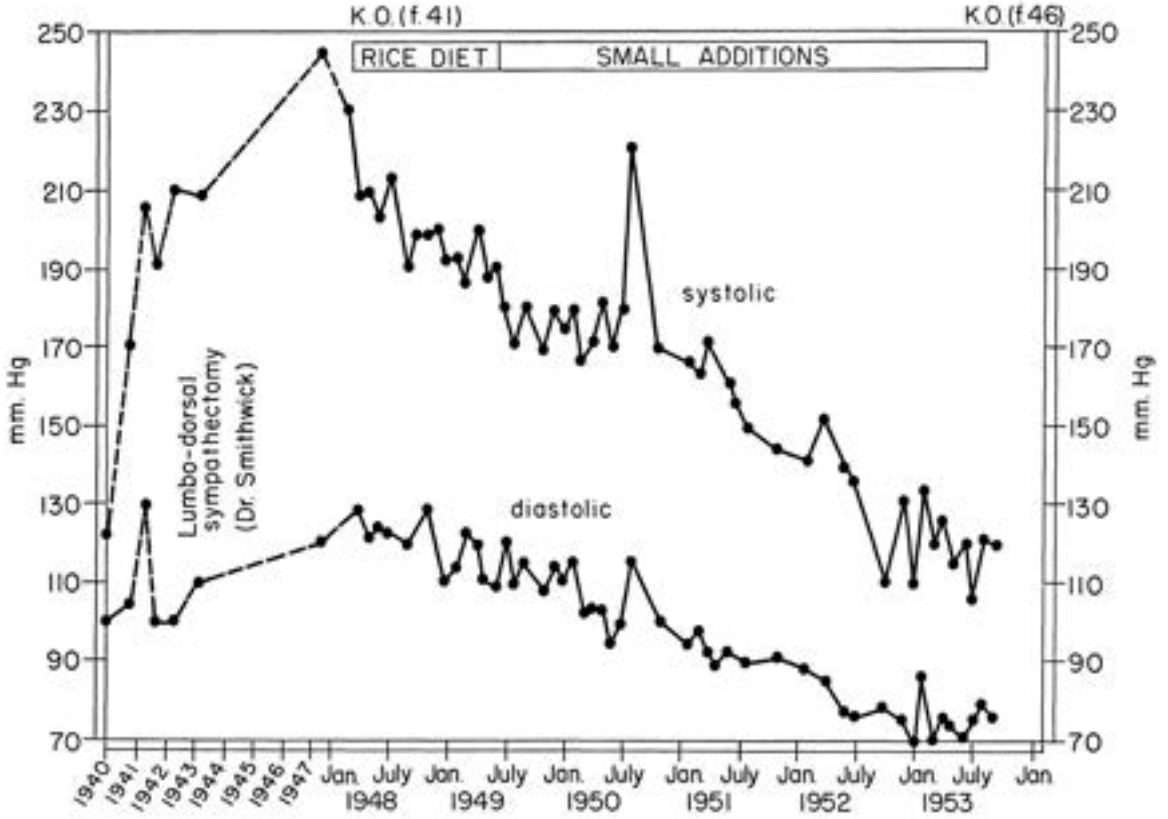


Figure 15. Gradual decrease in blood pressure during five years of treatment with the rice diet.

the rice diet supplemented by minimal additions. The salt concentration in the urine was consistently below 20 mg. However, after one year on the rice diet, the blood pressure was still 192/126, after two years, 167/103. It was not until January, 1952, almost four years after the rice diet had been started here, that the first nearly normal blood pressure reading was obtained: 135/82.

The blood pressure since then has been consistently normal. The average (16 readings) from January to September, 1953, was 120/75 compared to 209/124 (average of 102 readings during the first four months on the rice diet) five years ago. The patient is very active and entirely asymptomatic.

Table 4 shows the effect of the rice diet on the blood pressure in a series of 860 patients with hypertensive vascular disease treated for ninety days or longer (average 146 days). In 709 patients (82.4 per cent) there was a decisive lowering of the blood pressure from an average of 195/114 to an average of 145/91. In 291 patients (34 per cent) the blood pressure decreased to normal: from 180/106 to 127/81 (averages). The percentage of positive results increases with the length of time of treatment.

Rice Diet in Diabetes Mellitus

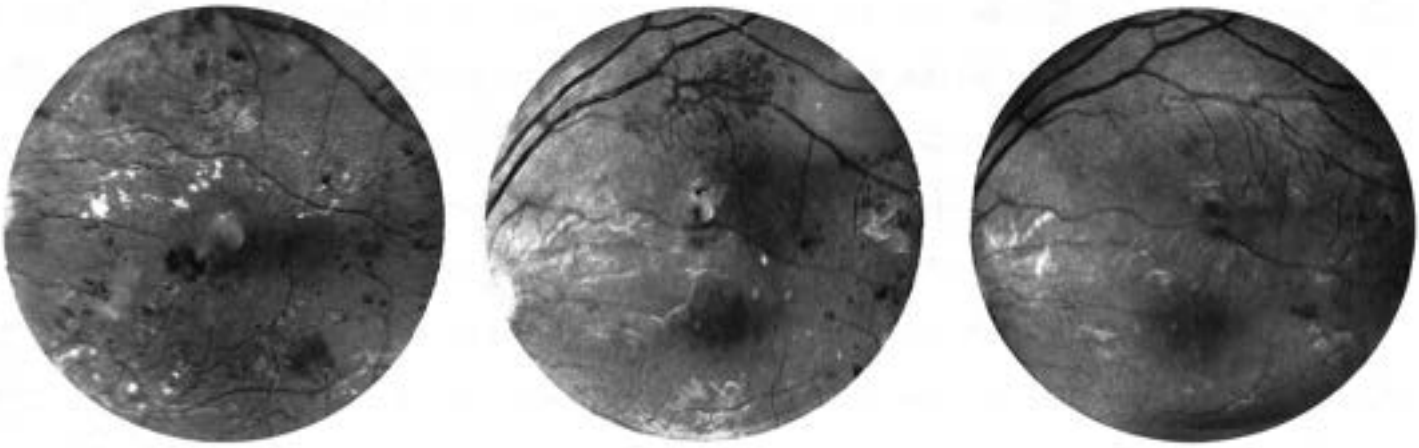
Patients with diabetes mellitus not only tolerate the rice diet well but, in a significant number of patients, the blood sugar level and the insulin requirements are lowered. The diet may also have a special value in the treatment of many patients with diabetes mellitus because of the dangerous role played by hypercholesterolemia in this disease.

Forty-eight patients with diabetes mellitus and complicating renal or vascular disease have been treated with the rice diet. The period of observation was from eight weeks to almost six years (average

Table 4. Effect of rice diet on the blood pressure of 860 patients with hypertensive vascular disease (treated 90 days or longer; average 146 days).

	number of patients	*%*	*blood pressure before rice diet (averages)*	*blood pressure after rice diet (averages)*
Not Improved	151*	17.6	194/114	179/108
Improved	709	82.4	195/114	145/91
Decreased to below 140/90	291	33.8	180/106	127/81

*Including 8 patients who died (blood pressure figures not in the averages).



August, 1950 June, 1951 July, 1953

Figure 16. Disappearance of retinopathy in diabetes mellitus (F.F.-m. 24).

fifty-nine weeks). In seventeen of the forty-eight patients, there was a change of more than 30 mg. in the fasting blood sugar level: in three of them the fasting blood sugar level increased; in fourteen it decreased. The others either had marked fluctuation in blood sugar level or showed only minor changes.

Twenty-nine of the forty-eight patients did not show any change in the insulin requirements. In the other nineteen patients there was a definite change in the insulin requirements: in four patients there was an increase (from an average of 20 units initially to an average of 41 units, the greatest increase being from 0 to 30 units), in 15 a decrease (from an average of 45 units initially to an average of 22 units, the greatest decrease being from 90 to 30 units).

The favorable response of these patients and the fact that a great number of diabetics die of vascular disease or at least are incapacitated by it suggests that the rice diet should be used in the treatment of diabetics who are beginning to show cardiac, retinal, renal, or peripheral vascular disease.

Figure 16 shows the effect of the rice diet on the retinopathy of a 24-year-old patient with diabetes mellitus.

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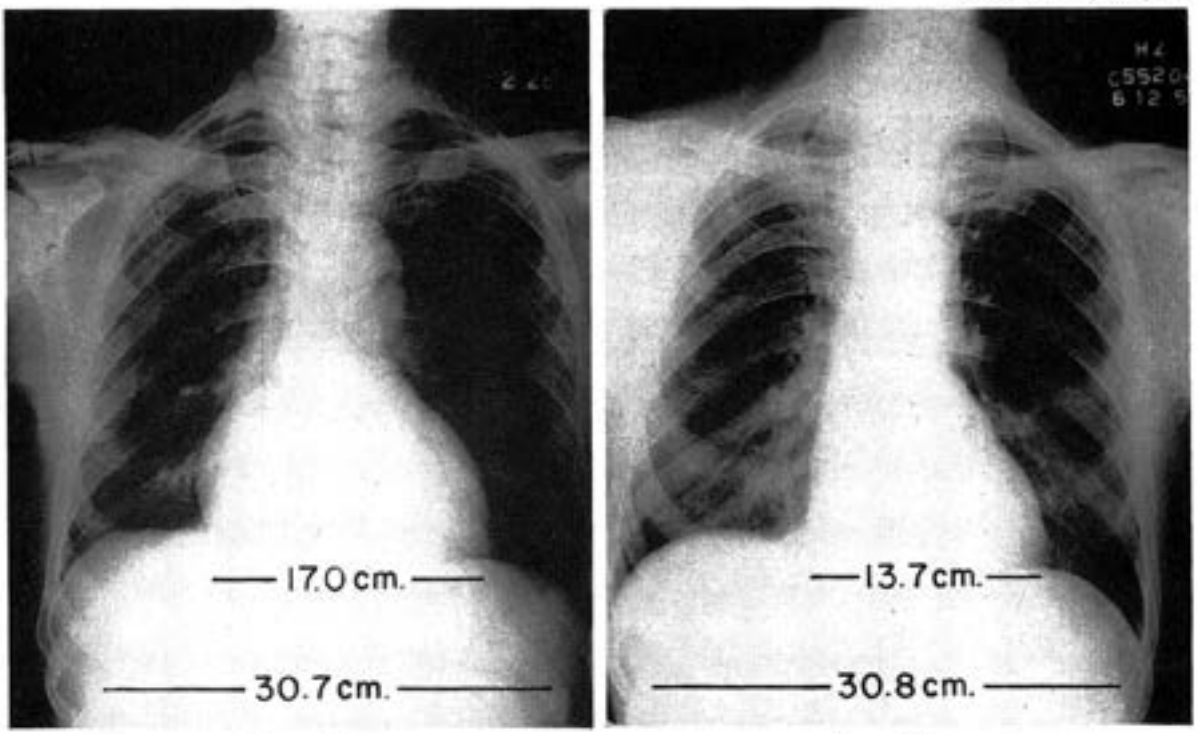

February, 1949 June, 1950

Figure 17. Heart enlargement in arteriosclerosis decreased by rice diet (R.J.B.-m. 79).

Other Effects of the Rice Diet

Old age is considered by most of us a kind of bankruptcy caused by the accumulation of vascular, cardiac, and renal debts. Accordingly, the arteriosclerotic and hypertensive vascular processes are accepted as results of degenerative disease, an inevitable and almost physiologic accompaniment of advancing years. The reversibility of some of these processes in many of my older patients proves, however, that this attitude of resignation is today no longer necessary.

The systolic blood pressure of a person of 75, just as well as that of a person of 30, should be below 130, the diastolic below 90. A consoling remark such as, "A blood pressure of 175/110 is good enough at this age," is an unwarranted admission of defeat and should not be substituted for active treatment. It denotes an attitude reminiscent of the days when similar excuses were given with regard to the "diseases of early infancy," instead of treating specific diseases by specific methods. *Figure 17* shows the decrease in heart size, with a change of 20 per cent in the transverse diameter of the heart, in a 79-year-old patient with hypertensive and arteriosclerotic vascular disease. *Figure 18* shows the improvement in the electrocardiogram of an 81-year-old patient with the same diagnosis: the left bundle branch block has disappeared.

In a series of 120 patients with hypertensive vascular disease, the T_1 wave in the electrocardiogram was inverted when the rice diet was started (no digitalis, no evidence of infarction). It remained inverted in sixty-eight patients, after an average of seven months on the diet; in fifty-two it changed from inverted to upright, after an average of ten months (*Figures 19 and 20*). In a control series of 300 patients, T_1 was upright when the rice diet was started. In none of these patients did it change from upright to inverted, after an average period of eleven months on the diet.

In a series of 500 patients who followed the rice diet for an average of five months, the heart became larger in 20 (4 per cent), the average increase in the transverse diameter of the heart being 2 per cent. In 480 of the 500 patients (96 per cent), the heart became smaller, the average change in the transverse diameter being 11.8 per cent (6 per cent in 218 patients, 14 per cent in 207 patients, and 25 per cent in 55 patients).

However, such encouraging results do not mean that once they are obtained, the treatment should be discontinued. It is true that the diet can be made more liberal after a patient's hypertension, heart enlargement, abnormal electrocardiogram, retinopathy, azotemia, or hypercholesterolemia have sufficiently improved. But additions should be made gradually, dependent upon eyeground photographs, heart films, electrocardiograms, blood pressure readings, blood chemical findings, and kidney function tests. In this way guess work is avoided, and objective evidence is obtained as to whether the patient has recovered enough to tolerate the additions he has been given so far, whether he can have further additions, or if his diet should be made stricter again.

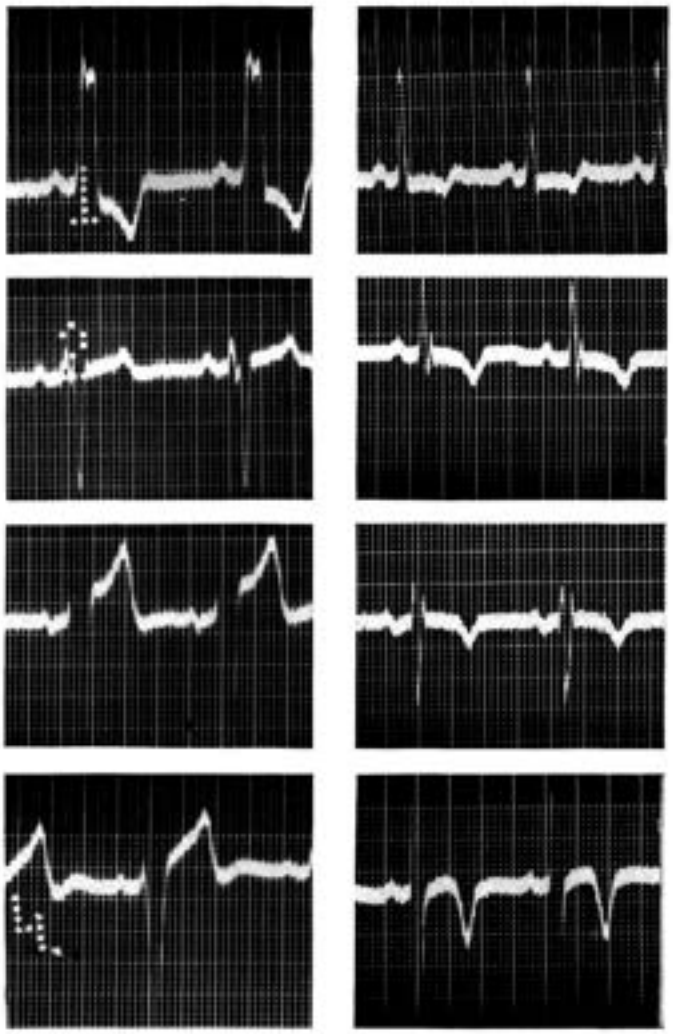

Figure 18. Disappearance of left bundle branch block in hypertensive cardiovascular disease treated with the rice diet (M.F.-f. 80).

Figure 21 shows in seven chest films a sad example of the way modifications should not be made, but which, unfortunately, has the greatest appeal to all too many patients. H. W., a patient with arterio- and arteriolonephrosclerosis was 60 years old when

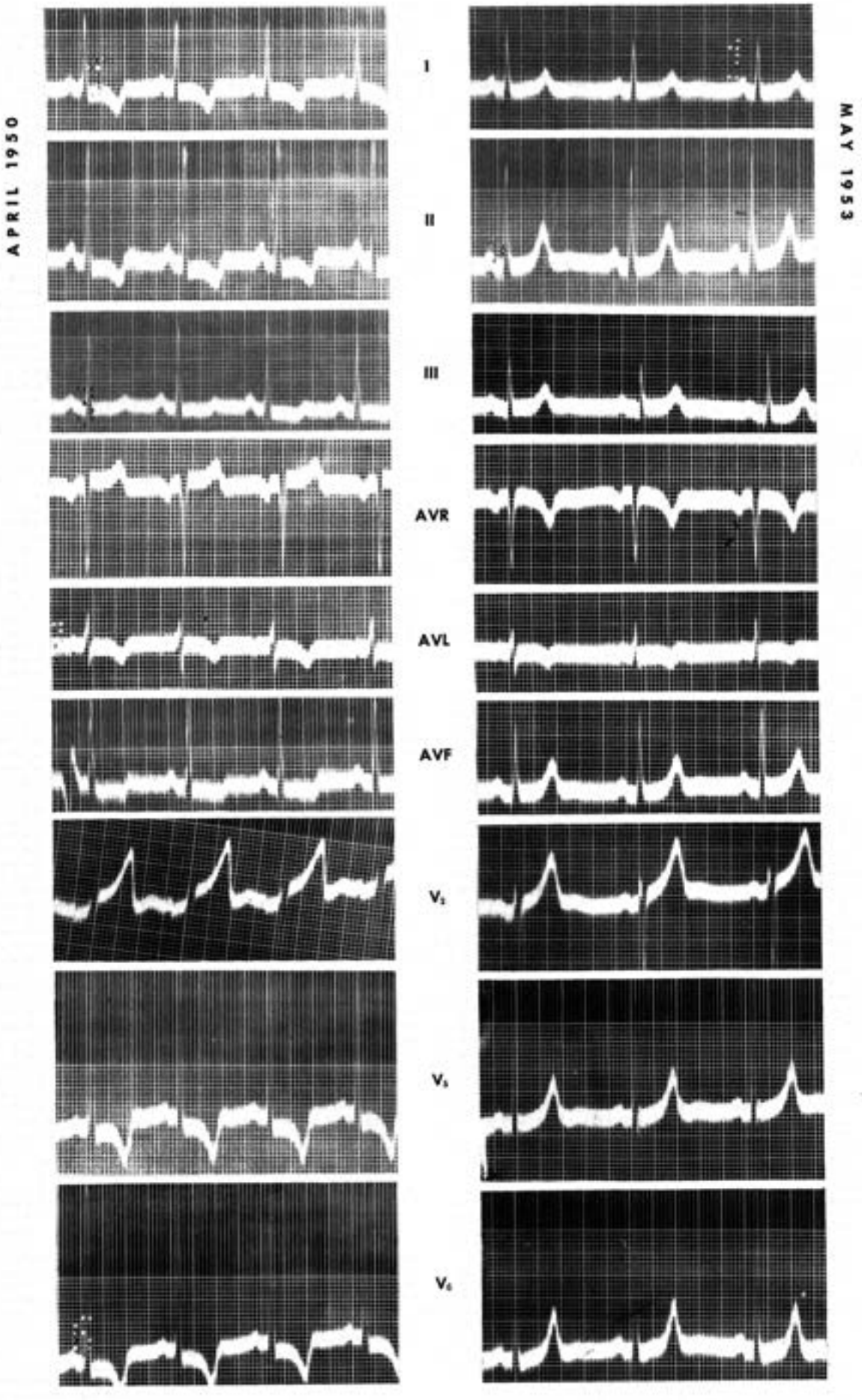
APRIL 1950
I
II
III
AVR
AVL
AVF
V1
V5
V6
MAY 1953

Figure 19 (on facing page). Disappearance of left ventricular strain pattern in hypertensive cardiovascular disease treated with the rice diet (C.H.B.-m. 48).

Figure 20. Disappearance of first degree heart block and T_1 inversion in hypertensive cardiovascular disease treated with the rice diet (E.P.-m. 44).

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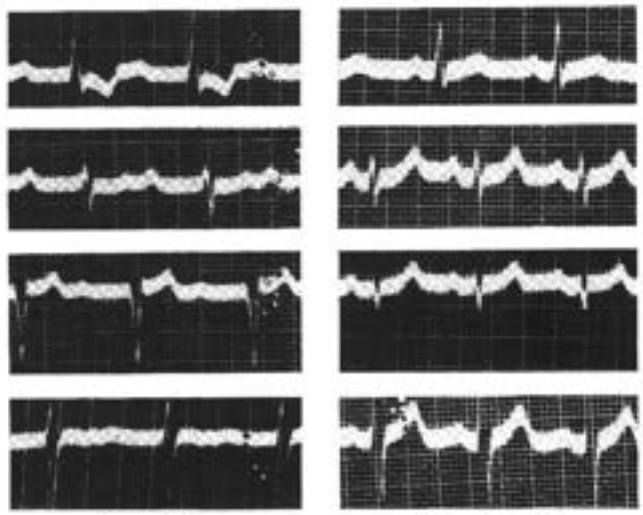


April, 1949 December, 1951

he came to us for the first time. He had been treated with a salt-restricted diet, digitalis, potassium nitrate, theobromine, and mercurials. In spite of this, his heart had become progressively larger, and the signs and symptoms of cardiac failure had increased. When all the drugs except digitalis were discontinued and the salt-poor diet (198 mg. NaCl per 100 cc. of urine) replaced by the strict rice diet (23 mg. NaCl per 100 cc. urine), his heart became decidedly smaller, and all the signs and symptoms of cardiac failure disappeared. As long as he had any discomfort, he adhered strictly to the rice diet, but the better he felt the more careless he grew, making additions of his own choice. After some time, all his former symptoms would gradually return, and each time this happened he would come back here to make a fresh start on the strict regimen. When the salt figure decreased, the heart became smaller in size; when the salt figure increased, the heart became larger again. This pattern repeated itself for six years until finally the heart failure was no longer reversible. The weight of the heart at autopsy was 900 grams.

Another patient with hypertensive vascular disease had been treated successfully, first with a strict then with an increasingly liberalized rice diet over a period of six years. Then he abandoned all dietary restrictions, ate everything he wanted, and gained from 183 to 220 pounds. In spite of this, he did not have a relapse. His disease apparently had healed so that he was able to tolerate a general diet. When I discussed the situation with him, he said: "Doctor, I really have eaten like a pig, but I promise that I will not do it again." I answered: "Your blood pressure is normal, your heart size and electrocardiogram are normal. Perhaps it is all right now for you to eat like a pig." However, we finally agreed that the weight should be reduced and that fat and salt should be restricted.

Retinal Changes

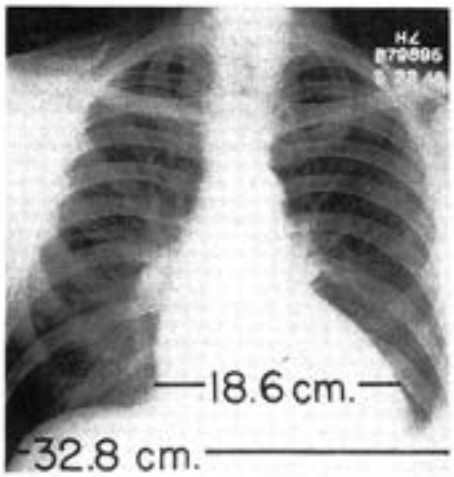
Advanced hemorrhagic and exudative vascular neuroretinopathy had always been considered an ominous sign indicative of the terminal stage of an irreparable disease. Cecil's *Textbook of Medicine,* in its seventh edition, stated: "Hemorrhages associated with white spots in the retina (hypertensive neuroretinopathy) are ominous signs. Death commonly follows within a year." Malignant hypertension, even with advanced neuroretinopathy, when treated with the rice diet, may either revert to the benign type of hypertension or disappear completely.

Figure 22 shows the eyeground photographs of a woman who was 45 when she came to us in 1944 with a history of hypertension of four months' duration, apparently malignant from the onset. The eyegrounds showed a typical hemorrhagic exudative neuroretinopathy. The patient followed the rice diet for one year—then a more liberal, though still salt- and fat-poor, regimen. The blood pressure during the first four weeks of strict bed rest after admission to the hospital, including three weeks of treatment with the rice diet, was 221/152 (average of daily readings of twenty-eight days). At her most recent re-examination, July, 1951, the blood pressure average was 162/105. She was pursuing her normal activities and had no complaints. Not only was she alive seven years (now ten years) after exhibiting all the signs of a full blown malignant hypertension, but the neuroretinopathy, the exudates, and the hemorrhages had completely disappeared.

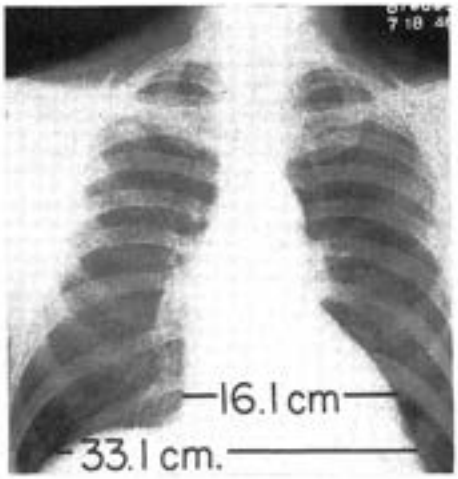
Figures 23, 24, and 25 are three more examples of complete recovery on the rice diet from advanced vascular retinopathy, although in each case the general course of the hypertensive vascular disease was entirely different.

The patient, A. A. H., was admitted to the hospital with severe retinopathy. The blood pressure was 190/119 (average June 20–28, 1944). The T_1 wave in the electrocardiogram was inverted. He followed the strict rice diet for four months and a

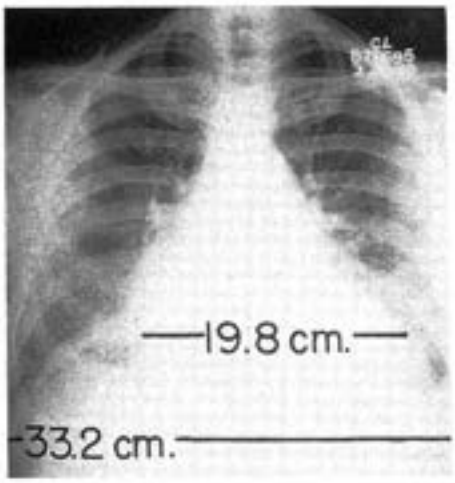
Figure 21 (H.W.-m. 60).



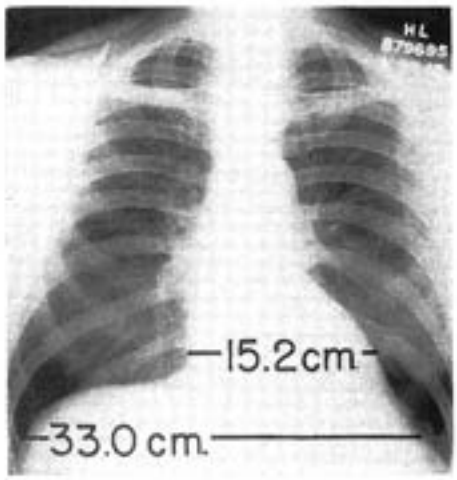
May, 1946. 198 Mg. NaCl.



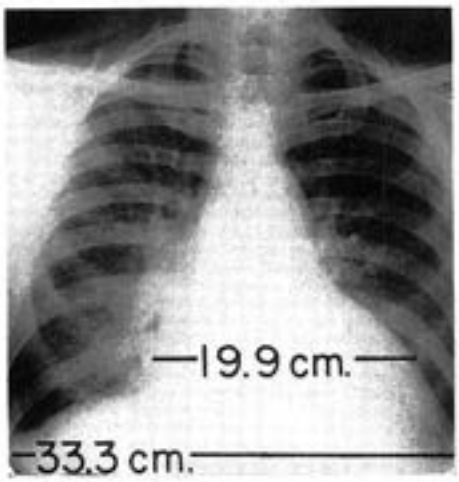
July, 1946. 23 mg. NaCl.



March, 1948. 500 mg. NaCl.

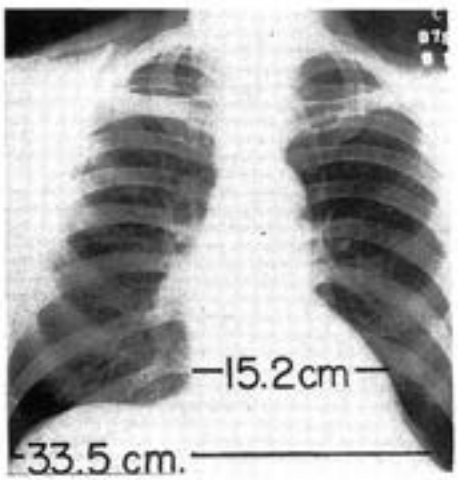


September, 1948. 19 mg. NaCl.

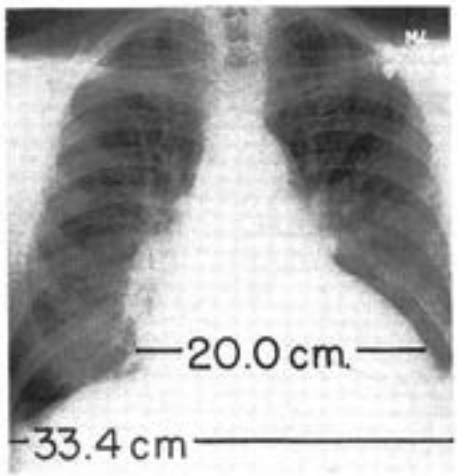


April, 1950. 237 mg. NaCl.

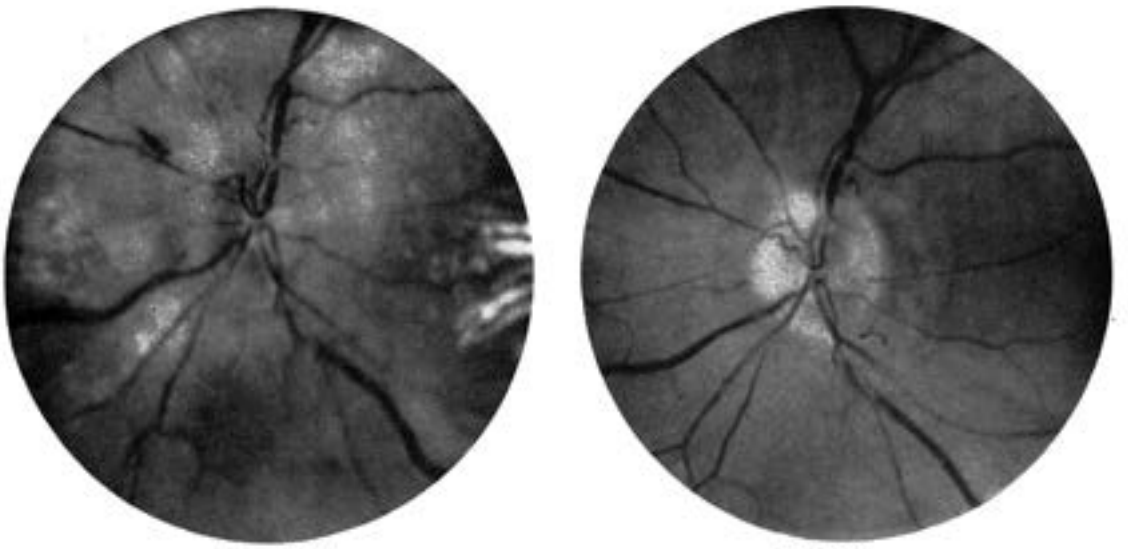
August, 1950. 15 mg. NaCl.



September, 1952. 177 mg. NaCl.

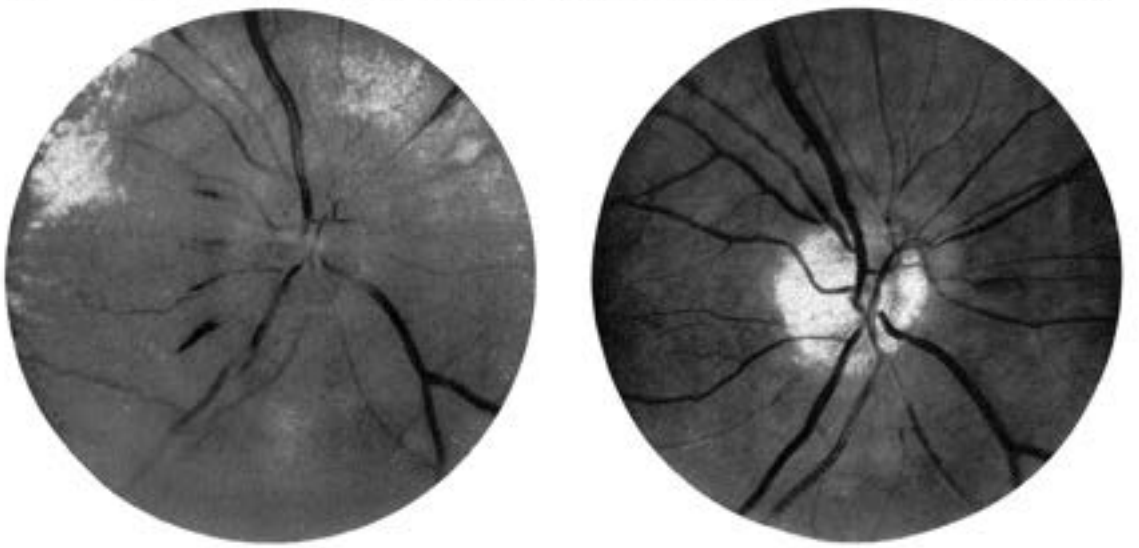


Patient died October, 1952. Autopsy findings: Heart—weight, 900 Gm.; both ventricles dilated and hypertrophied.



August, 1944 July, 1951

Figure 22. Disappearance of papilledema, hemorrhages, and exudates in malignant hypertension treated with the rice diet (L.W.-f. 45).

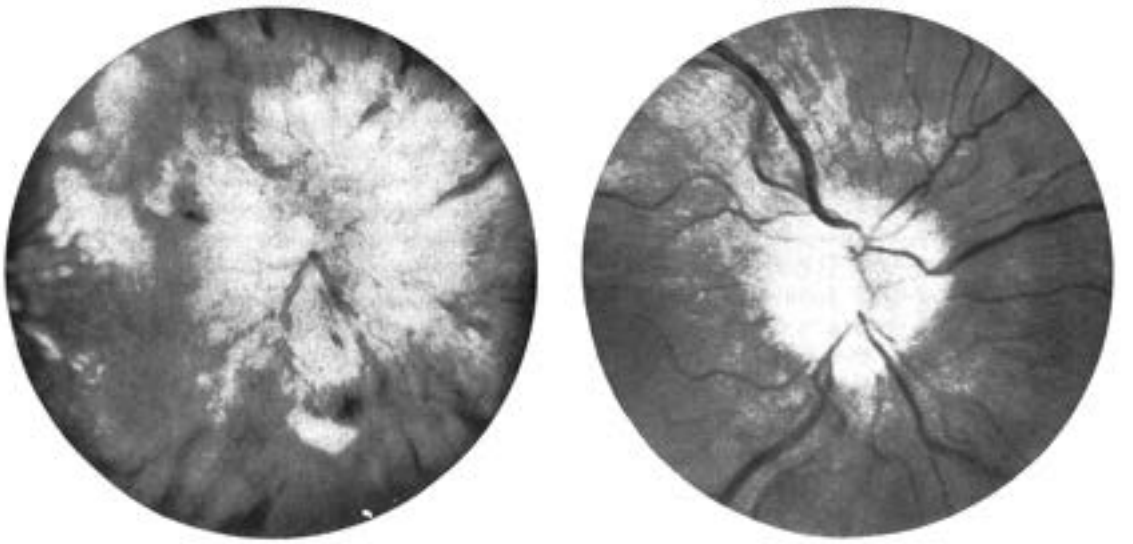


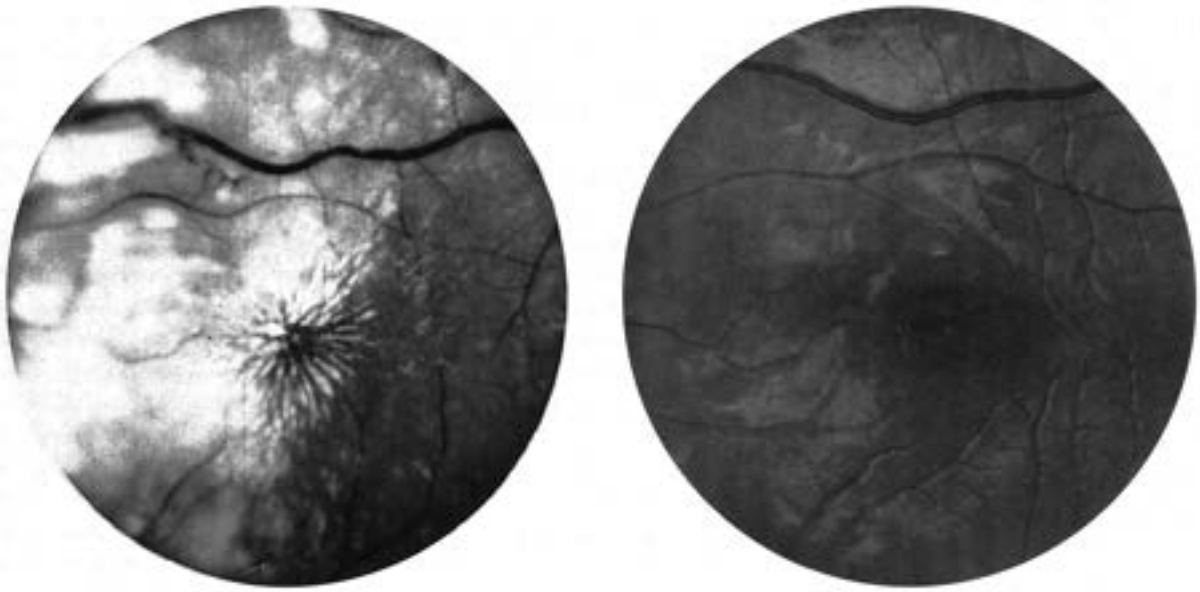
June, 1944 June, 1952

Figure 23. Disappearance of papilledema, hemorrhages, and exudates in malignant hypertension treated with the rice diet (A.A.H.-m. 47).

Figure 24. Disappearance of papilledema, hemorrhages, and exudates in malignant hypertension treated with the rice diet (L.B.-f. 24).

November, 1944 December, 1949





August, 1948 January, 1952

Figure 25. Disappearance of macular star in malignant hypertension treated with the rice diet (D.T.-f. 20).

modified rice diet afterward. The T_1 wave in the electrocardiogram became upright, the retinopathy disappeared, but the blood pressure though lower never became normal. During 1947–1949, the average was 171/109; during 1951–1952, 158/100.

The patient, L. A. B., was admitted to the hospital with severe retinopathy. The blood pressure was 220/150 (average October 30–31, 1944). The heart was enlarged. After four months on the rice diet, the blood pressure was 120/87. The heart was normal in size. The retinopathy had completely disappeared.

After one year, the patient gave up the diet. The blood pressure rose again. In October, 1948, it was 194/132, in November, 1949, 228/138. In spite of this the retinopathy did not recur.

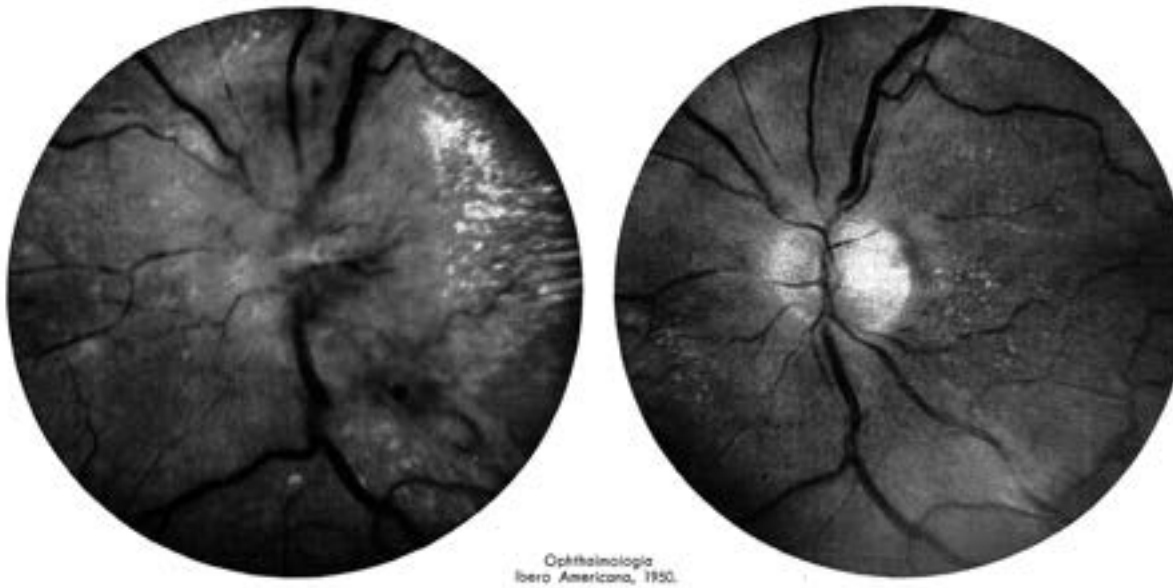
The patient, D. T., was admitted to the hospital with severe retinopathy. The blood pressure was 205/151 (average August 6–12, 1948). After four months on the rice diet, it was 105/78. The retinopathy healed and did not recur although the patient continued the diet for only one more month. The blood pressure remained normal: 120/80 (January, 1952, three years after the diet was discontinued).

These histories also show that the rice diet is not only a treatment of compensation, effective as long as it is given, like insulin in diabetes or liver in pernicious anemia, but that it often produces permanent results which may persist after the diet has been greatly modified or discontinued altogether.

The picture of vascular neuroretinopathy is sometimes such that it is almost impossible to rule out a diagnosis of brain tumor. In these cases the rice diet may be used as a therapeutic test.

Figures 26 and 27 are the eyeground photographs of two patients, where Dr. Banks Anderson, our ophthalmologist, thought that an expanding intracranial lesion in a patient with hypertension was the most likely diagnosis. In both instances, the response to the rice diet showed that the entire picture was caused by malignant hypertension. When Dr. Anderson saw the patients again after some months on the rice diet, he wrote in his consultation notes: "A. H. (February, 1950): This patient's eyegrounds are improved to an unbelievable degree. I have never previously seen such an extensive papilledema subside with such minimal retinal scarring, nor for that matter do I think I have ever seen a patient with this degree of hypertensive retinopathy alive after this length of time.

"B. R. (June, 1953): Review of notes indicates that when I saw this patient last I was of the opinion that the papilledema was too great to have been due exclusively to hypertension. I was wrong. Fundoscopic examination through the undilated pupils shows no evidence of papilledema at this time . . . There are no areas of exudate, hemorrhage or pigmentation."



November, 1948 February, 1950

Figure 26. Disappearance of papilledema, hemorrhages, and exudates in malignant hypertension treated with the rice diet (A.H.-f. 45).

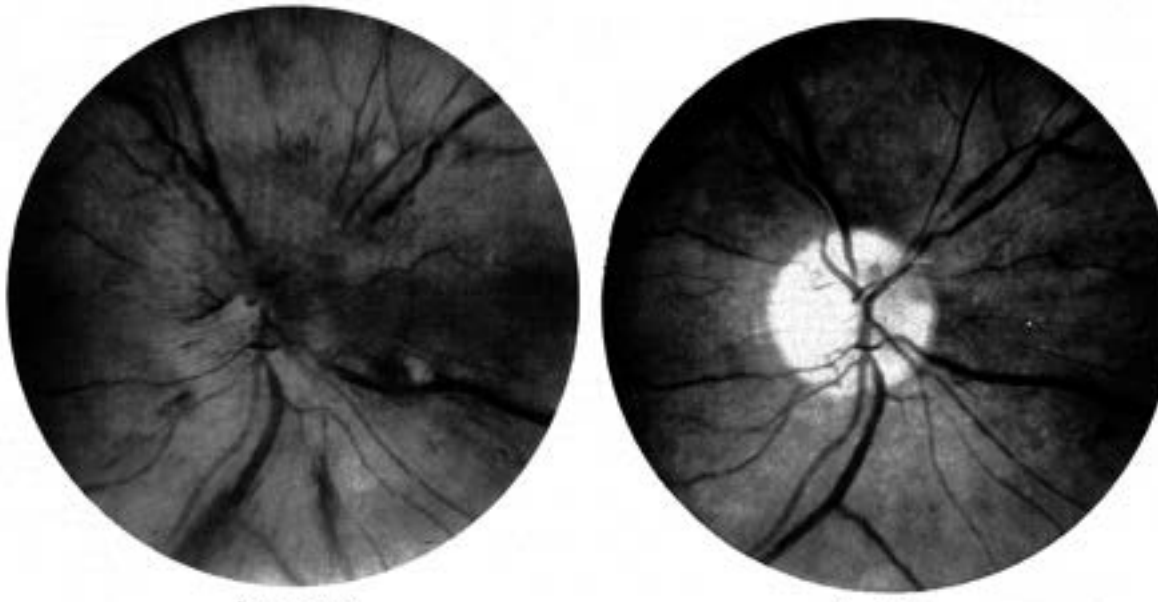
It was the eyeground photographs more than anything else that bothered those who had insisted that diet was of no value in the treatment of hypertensive vascular disease. Since eyegrounds are as individual as finger prints and the photographs compared, therefore, were obviously of the same patient, some people actually went so far as to accuse us of having reversed the dates, intimating that the pictures of the normal eyegrounds were the first ones and those of the abnormal eyegrounds had been taken later.

The following quotation from Dr. Goldring's chapter on the "rice diet in the treatment of hypertension" in the closing paper of the Hypertension Seminars of the *American Journal of Medicine,* 1948, expresses this view more politely: "Proponents of the rice diet in the treatment of hypertension point to the astonishing incidence of reversal of the so-called 'hypertension pattern' of the electrocardiogram toward normal, diminution of the size of the heart and regression of papilledema. It is these objective evidences of the effect of the rice diet which are urgently in need of explanation. However, these striking data come from the one source which has reported brilliant results with the rice diet treatment and as yet there has been no confirmation from other observers. Until such confirmation is available, the rice diet does not warrant any more than casual interest."

In the intervening years such confirmation has been made available by a number of research projects both in this country and abroad.

Among our own patients we have a series of 388 patients with advanced vascular retinopathy (papilledema, hemorrhages, or exudates) in whom it has been possible to take eyeground photographs before and after one to one hundred months on the rice diet. Forty-four of the 388 patients had chronic nephritis, 344 had hypertensive vascular disease. One hundred and twenty-five of the 388 had papilledema when the rice diet was started. In four of these, there was no change; in two the papilledema disappeared partially, in 119 completely. Two hundred and ninety-six patients had hemorrhages. In seven cases, the hemorrhages increased; in twelve there was no change; in forty-six the hemorrhages disappeared partially and in 231 completely. Three hundred and twenty-eight had exudates. They increased in five; in eighteen there was no change; in seventy-nine the exudates disappeared partially and in 226 completely.

The reversibility of the blood vessel damage shown by the healing of the retinal disease is even more impressive than the reversibility of heart and kidney disease. It was for me the most convincing evidence that the old school of thought was wrong in insisting that these diseases were of necessity progressive and degenerative and that, in patients with malignant hypertension, death within a short time was inevitable. The course of these diseases



August, 1952 May, 1953

Figure 27. Disappearance of papilledema, hemorrhages, and exudates in malignant hypertension treated with the rice diet (B.R.-f. 60).

can be changed by the very simple procedure of replacing the various foods commonly eaten by a diet of rice, fruit, and sugar.

But, the more convincing these results are, the more obvious it becomes that intensive dietary treatment should be started when the disease is still at an early stage and not postponed until an emergency is created by some vascular catastrophe. The general practitioner is usually the one in a position to pick up the signs and symptoms long before they are alarming. He has every opportunity to prevent much unnecessary invalidism and many untimely deaths by enforcing immediate and radical treatment.

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Trattamento Radicale Dietetico delle Malattie Vascolari Ipertensive ed Arteriosclerotiche, di quelle Cardiache e Renali e delle Retinopatie Vascolari

[Italian translation of preceding article]

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Trattamento radicale dietetico delle malattie vascolari ipertensive ed arteriosclerotiche, di quelle cardiache e renali e delle retinopatie vascolari

Da "General Practitioner", *March 1954, volume IX, Number 3.*

Grazie alla cortesia del Dr. Walter Kempner, l'Ente Nazionale Risi è lieto di poter riprodurre integralmente questo recente ed interessante studio sul « trattamento radicale dietetico » nella grande serie delle affezioni cardiovascolari che fanno capo all'aterosclerosi. Come è noto, tale trattamento si basa quasi esclusivamente su una dieta il cui principale componente è il riso.

Gli evidenti e brillanti risultati che sono stati ottenuti nei numerosi casi seguiti clinicamente nell'Università di Durham (U.S.A.), stanno a confermare la razionalità e l'efficacia terapeutica di tale dieta, conosciuta appunto con il nome di Kempner.

L'Ente Nazionale Risi congeda quindi il presente lavoro certo di far cosa grata ai Sigg. Medici cui esso è principalmente indirizzato e, nel contempo, di rendere omaggio all'opera appassionata del Dr. Kempner.

Ringrazia altresì l'Editore della rivista « General Practitioner » per averne autorizzata la riproduzione.

Maggio 1957

La percentuale dei decessi per malattie vascolari ipertensive, per forme di arteriosclerosi, per malattie renali che portano ad insufficienze cardiache, a trombosi coronarie, a sincopi oppure ad uremie è maggiore di quella determinata da altri gruppi di malattie. Secondo le più recenti statistiche, tale gruppo di malattie provoca casi di mortalità tre volte maggiori di quelli causati dal cancro, sette volte maggiori in confronto a quelli dovuti ad incidenti e venti volte maggiori di quelli determinati dalla tubercolosi. Oltre a procurare un più grande numero di decessi le malattie di origine vascolare determinano più numerosi casi di invalidità croniche, quali: disturbi cardiaci di carattere asmatico, sindrome anginosa, idropisia, disturbi renali con stati uremici, cecità causate da retinopatia vascolare e casi di paralisi con incapacità di parola o balbettio o con limitazione nell'uso degli arti.

È passato il periodo in cui il problema poteva essere accantonato in base alla considerazione che queste malattie rappresentavano l'inevitabile cammino della degenerazione progressiva. Proprio come è ingiustificabile il rimandare la cura nei casi di cancro o di tubercolosi, così è molto più da considerarsi una cattiva pratica per un medico il trattare i pazienti ammalati di ipertensione o di forme cardiache croniche o di affezioni renali con frasi generiche come « non dateci peso », « non preoccupatevi » oppure « non fateci caso ».

Quando nel periodo compreso fra l'aprile ed il luglio del 1944 apparvero i primi 3 rapporti sulla dieta di riso, i risultati furono accolti con una buona percentuale di scetticismo. Questi rapporti illustravano gli effetti di tale dieta su 150 pazienti trattati tra il 1939 ed il 1944. I principali risultati erano stati i seguenti: in una larga percentuale si era verificata una marcata diminuzione nella pressione del sangue, i diametri cardiaci si erano normalizzati, l'onda T 1 invertita dagli elettrocardiogrammi si era regolarizzata, le neuroretinopatie essudative emorragiche erano scomparse e l'elevata quota di azoto non proteico del sangue insieme al colesterolo serico erano stati ridotti ai normali livelli.

Gli anni compresi fra il 1944 ed il 1954 ci hanno permesso non solo di confermare e di estendere con la osservazione di più di duemila casi i risultati ottenuti nei primi 150 pazienti, ma hanno anche determinato un completo cambiamento nell'atteggiamento di coloro che, al-

cuni anni prima, avevano stabilito che la dieta non poteva avere un posto nel trattamento delle malattie ipertensive vascolari e della arteriosclerosi.

Sarà fornito un breve riassunto dei fatti che hanno portato gradualmente a questo cambiamento di opinioni non per un interesse accademico o storico, ma perchè una conoscenza delle basi scientifiche di questo tipo di trattamento dietetico ha una diretta influenza sul successo terapeutico quando si ha a che fare con il singolo paziente. Senza queste conoscenze, il medico non è capace di imporre la dieta e di seguire con intelligenza l'ammalato. Inoltre, nessun trattamento dietetico che implichi delle così drastiche restrizioni e dei sacrifici giornalieri, è concepibile senza grande autodisciplina e forza di volontà da parte del paziente e nessun medico potrà convincere l'ammalato della necessità di questa dieta senza che egli stesso ne sia convinto da argomenti di carattere scientifico.

Restrizione del sale

La restrizione del sale in diversi gradi era di uso comune al principio del secolo nel trattamento delle malattie di cuore, di quelle renali, delle forme di ipertensione ed era ancora usata nel 1920 da Allen in America e da Volhard in Europa.

Nel 1922 Allen pubblicò un rapporto su 180 pazienti affetti da forme ipertensive. La loro dieta fu considerata come « priva di sale »,

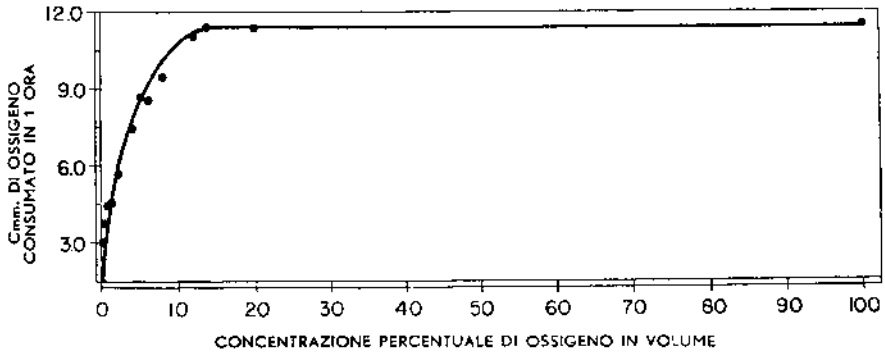


Fig. 1. Aspetti delle varie concentrazioni di ossigeno sui livelli respiratori (1 mg. di batterio tubercolare, 38 °C).

allorquando il contenuto in cloruri delle urine (espresso come cloruro di sodio) non superava i 500 milligrammi al giorno. In 125 ammalati venne registrata una diminuzione della pressione del sangue.

I commenti al lavoro di Allen furono scoraggianti. Il « Journal of the American Medical Association » in un editoriale fece il seguente commento: « Infine, alcuni successi terapeutici sono stati messi in correlazione con delle diminuzioni nell'assunzione di sale da parte dei pazienti. Quale sarà la nuova moda nelle prescrizioni di diete, resta ancora

da sapere ». Altri dissero che è difficile credere che una restrizione nell'assunzione di sale da 2 grammi a 0,5 grammi si dimostrasse più efficace di una restrizione da 10 grammi a 2 grammi, come era stato frequentemente provato.

Questa osservazione dimostra chiaramente la principale difficoltà che molti medici e la maggior parte degli ammalati hanno nel capire il significato della parola « restrizione », sebbene vi siano numerosi processi biologici nei quali si potrebbe trovare una analogia. Per esempio, una riduzione della concentrazione di ossigeno da 100 a 10 per cento abbassa solamente la saturazione in ossigeno dell'emoglobina da 100 a 90 per cento. Per produrre un significativo abbassamento della saturazione in ossigeno, la concentrazione di ossigeno dovrebbe essere ancor maggiormente ridotta. La dipendenza della respirazione cellulare dalle variazioni della concentrazione di ossigeno è un altro fenomeno di questo genere. Anche in tale caso non si ottiene un risultato a meno che si riducano le concentrazioni di ossigeno ai valori minimi (fig. 1).

I medici che hanno familiarità con la cura delle varie forme allergiche potrebbero fornire esempi simili.

Tenendo presente ciò dovrebbe essere comprensibile che in alcune malattie un aumento di sale da 10 a 20 grammi al giorno oppure una diminuzione dello stesso da 10 a 2 grammi possa virtualmente essere di nessun effetto e che, cionondimeno, possano verificarsi significative modificazioni se l'assunzione giornaliera di sale viene diminuita da 2 grammi a 0,3 grammi o meno.

La dieta di riso

La restrizione di sale nella dieta di riso è più rigida che in ogni altro schema dietetico usato nella cura delle malattie renali acute o croniche, delle forme ipertensive, dell'arteriosclerosi, delle malattie di cuore e delle retinopatie vascolari. Questa dieta contiene in 2.400 calorie da 70 a 120 milligrammi di sodio e da 140 a 240 milligrammi di cloruri. Questi ultimi possono essere ulteriormente ridotti eliminando tutte le frutta ed i succhi di frutta, ammettendo nella dieta solamente riso bianco, the e zucchero raffinato. Una dieta di tal genere contiene, in 2.400 calorie, 20 milligrammi di Na e 70 milligrammi di Cl. In un certo numero di casi abbiamo anche usato in aggiunta delle resine scambiatrici per rimuovere il sodio dal tratto gastro-intestinale.

Però, questa pubblicazione non contempla i risultati ottenuti con la dieta « ipoalcalina » e neppure quelli ottenuti con l'uso addizionale di resina, ma si limita agli effetti della dieta di riso « normalmente alcalina », senza nessuna medicazione eccetto l'aggiunta di vitamine A, B, C, D. La dieta di riso è monotona, ma ha il grandissimo pregio della

semplicità; non si rendono necessarie elaborate prescrizioni e la sua preparazione è facile.

La escrezione urinaria di cloruri dopo uno o due mesi di dieta alcalina di riso è fra 2 e 10 milligrammi per cento centimetri cubici di urina (espressa come cloruro di sodio: circa 100 milligrammi al giorno). La escrezione di sodio per le vie urinarie varia da 0,3 a 2 milligrammi per cento centimetri cubici. Percentuali più alte di questa, eccetto che per i pazienti in fase di sblocco degli edemi o nei casi in cui è presente una perdita di sali in via cronica o acuta, dimostrano che sono stati compiuti degli errori nella dieta intenzionalmente oppure inavvertitamente.

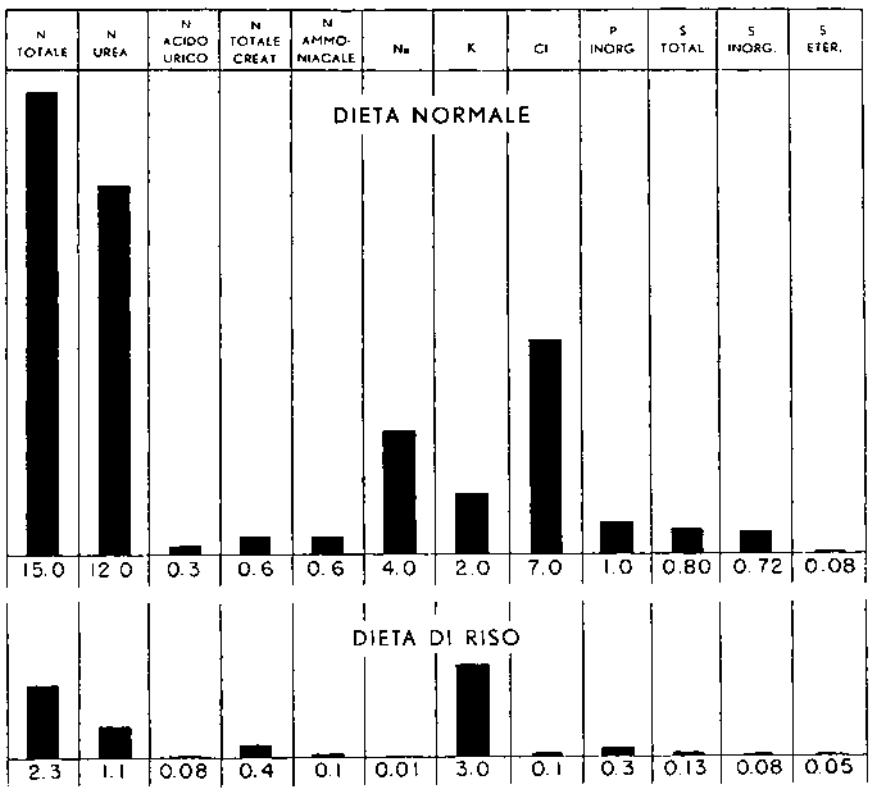


Fig. 2.
Escrezione urinaria (grammi 24 h) a dieta normale ed a dieta di riso (da 2 a più mesi).

Il principale pericolo di una rigida restrizione di cloruro di sodio nella dieta è rappresentato dalla « perdita di sale » con le conseguenti ipocloremia e/o iponatremia, che possono frequentemente essere congiunte alla ipercalemia, alla alcosi oppure alla iperazotemia.

In 19 ammalati su 20 che non offrono sintomi di avanzato scompenso renale, l'estrema restrizione di cloruro di sodio della dieta di riso è ben tollerata perchè una normale ed indisturbata funzione regolatrice renale raggiunge una massima ritenzione del sodio e dei cloruri ed è mantenuto l'equilibrio sierico. Possono venire riscontrati una moderata caduta nei cloruri del siero ed un corrispondente aumento in bicarbo-

nati. Il sodio, il potassio e le concentrazioni ioniche totali rimangono essenzialmente invariate. Ciononostante, in uno su 20 casi, si sviluppano dei disturbi di carattere elettrolitico, malgrado il fatto che i reperti urinari, come le prove di funzionalità renale, indichino una inalterata funzione dei reni.

Nella maggior parte degli ammalati con gravi scompensi renali primari o secondari, si possono invece prevedere delle difficoltà poichè il meccanismo regolatore del rene è alterato. La perdita di sodio e di cloruri nell'urina supera le quantità assunte con gli alimenti e ciò può condurre alla ipocloremia ed alla iponatremia, accompagnate da una o più delle seguenti manifestazioni cliniche: stati apprensivi, atteggiamenti psicotici, sonnolenza, debolezza, cefalea, anoressia, nausea, diarrea, cram-

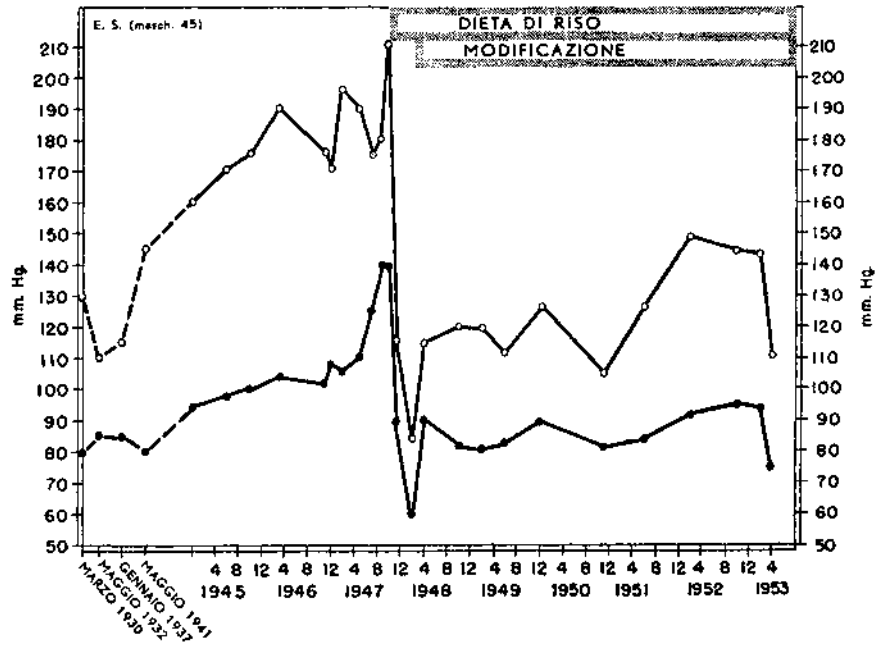


Fig. 3.
Pressione sanguigna in un caso di ipertensione maligna ridotta con dieta di riso (pericolosa ipotensione corretta con aggiunte dietetiche).

pi muscolari, spasmi, tachicardia, collassi circolatori periferici, uremia (figg. 3 e 4). Si può anche verificare un pericoloso aumento nel potassio serico; che si associa a paralisi dei muscoli periferici (le quali sono particolarmente serie se implicano i muscoli respiratori) ed a danneggiamenti del muscolo cardiaco, sino a giungere all'arresto del cuore stesso.

Si deve inoltre tenere presente che le perdite di sale possono essere causate anche da fattori extra renali, come la intensa sudorazione, la eccessiva secrezione da parte del tratto respiratorio, il drenaggio biliare oppure la secrezione gastrica. Se tali disturbi di natura elettrolitica non sono diagnosticati abbastanza presto, le conseguenze possono essere serie; alcuni scritti medici degli ultimi anni ripetutamente sottolineano i pericoli delle diete a basso tenore di sodio per la possibile e fatale apparizione di uno stato carenziale di sali.

Perciò, è ovvio che la dieta di riso, la quale rappresenta la più drastica forma di restrizione del sale, è una cura pericolosa. Questo non è un argomento contro la cura stessa, ma è solamente un argomento contro l'impiego di essa quando non vi siano le possibilità di un costante controllo clinico e chimico e quando il paziente non voglia o non sia capace di sottomettersi ad un periodo di prova piuttosto lungo. Quindici anni fa pensavamo che fosse sufficiente un periodo di prova di 2-3 settimane. Più tardi questo periodo fu esteso da 2 a 3 mesi ed attualmente usiamo tenere gli ammalati sotto controllo giornaliero per 4 mesi. I pazienti non sono ospedalizzati, a meno che non siano in condizioni particolarmente serie oppure che non si verifichino altre speciali ragioni.

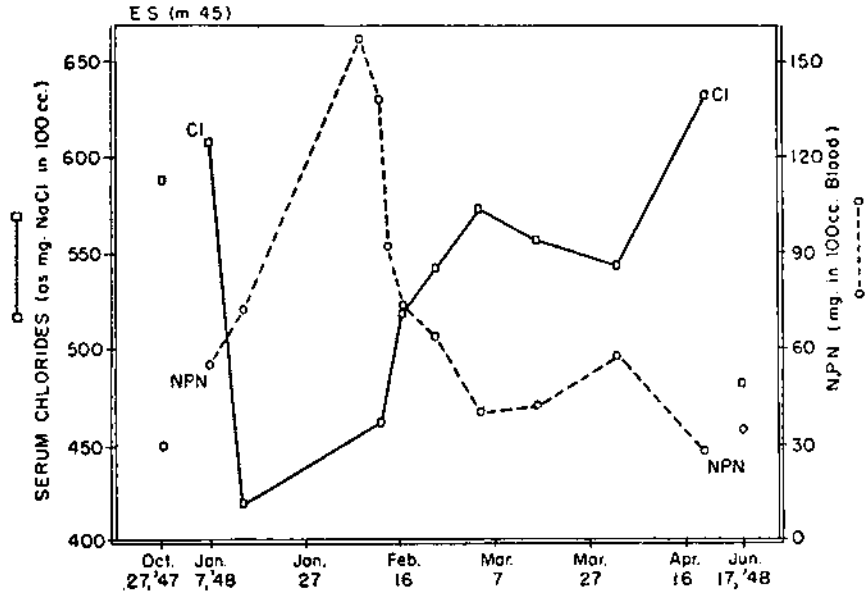


Fig. 4.
Azotemia susseguente ad ipocloremia in un ammalato a dieta di riso (E. S. m. 45).

La maggior parte di essi resta in alberghi, nelle proprie case oppure in una delle « case del riso ».

Quando non vi è una specifica contro-indicazione, essi ricevono la prescrizione di condurre vita normale. Dopo i 4 mesi, gli ammalati ritornano a casa affidati alla cura dei loro medici di famiglia i quali debbono controllarli frequentemente, osservare i loro progressi ed incoraggiarli a seguire con coscienza il regime alimentare appositamente per loro studiato. I pazienti generalmente compiono il proprio lavoro e svolgono le ordinarie attività. Ogni 2-6 mesi, essi dovrebbero ritornare per un periodo di 2-14 giorni in modo che sia possibile determinare se si rendono necessarie ulteriori modificazioni della dieta oppure se alcune delle aggiunte prima indicate debbono essere sospese. Negli intervalli fra gli esami, dei campioni di urina vengono inviati al nostro laboratorio uno o due volte al mese.

Restrizione dei grassi e del colesterolo

Di tutte le diete indicate nella cura delle malattie renali acute e croniche, di quelle ipertensive, della arteriosclerosi, delle malattie di cuore e delle retinopatie vascolari, quella di riso contiene la più modesta quantità di grassi (meno di 5 grammi in 2.400 calorie) e non contiene assolutamente colesterolo.

Secondo Watt e Merrill, 300 grammi di riso bianco (peso secco) contengono 0,9 grammi di grassi; 12 once di succo d'arancia e 12 once di succo d'uva contengono complessivamente 1,5 grammi di grassi; una libbra di mele, una di uva ed una di pesche contengono 2,7 grammi di grassi. In tale maniera l'assunzione giornaliera totale di grassi ammonta a grammi 4,65.

Alcuni tentativi di sostituire la dieta di riso con altre combinazioni alimentari ai fini della restrizione salina sono stati orientati in una giusta direzione; però non è stato mantenuto sufficientemente basso il contenuto in grassi. Anche la sostituzione di un cereale con un altro può decisamente alterarlo; infatti 300 grammi di farina di avena (peso secco), contengono 22,2 grammi di grassi, in confronto ai 0,9 contenuti in una stessa quantità di riso.

Grollman e Harrison cercarono di modificare la dieta di riso e di renderla più appetibile con l'aggiunta di carne, di burro, di uova e di latte dializzato. Questa dieta contiene un quantitativo di cloruro di sodio di sole tre volte maggiore di quello contenuto nella dieta di riso, ma maggiore di ben venti volte per quanto concerne i grassi. Anche se il contenuto di sale in tale dieta fosse minore, l'eccessiva quantità di grasso la renderebbe non adatta per il fatto che più del 70% dei pazienti affetti da malattie ipertensive vascolari, i quali erano curati con la dieta di riso, avevano un livello del colesterolo serico che superava i 219 milligrammi per 100 centimetri cubici di siero (media: 280 milligrammi) prima di iniziare la dieta stessa.

Quando resi pubblica una documentazione la quale illustrava che la dieta di riso abbassa la concentrazione del colesterolo serico nei pazienti con malattie renali ed ipertensive, e questo avvenne dieci anni fa

Tabella 1 - Concentrazione totale del colesterolo serico in 800 casi di ipercolesterolemia trattati con dieta di riso (media di 124 giorni).

	Numero casi	%	Prima della dieta a riso (medie)	Dopo la dieta a riso (medie)
Diminuzioni	747	93	283	205
Da 220 in più	257	32	301	245
Da 219 in meno	490	61	273	184
Aumenti o non mutamenti . . .	53	7	262	287

al Congresso scientifico dell'American Medical Association di Chicago, furono sollevate due obiezioni:

la ipercolesterolemia è di nessuna importanza nelle malattie vascolari;

la concentrazione del colesterolo serico non può essere ridotta con una diminuita assunzione di colesterolo alimentare.

Ora, ognuno parla dell'importanza del colesterolo nelle malattie vascolari, particolarmente in connessione con la sindrome anginosa, con le malattie delle coronarie e con l'infarto cardiaco. Un giornale, il « Circulation », pubblicò nei suoi dodici numeri del 1952 ben 17 articoli originali sul colesterolo. È vero che sovente è impossibile abbassare il livello dei colesterolo serico mediante una moderata restrizione dei grassi e del colesterolo, ma mediante la dieta di riso il colesterolo serico è stato abbassato nel 93% dei nostri casi di ipercolesterolemia (tabella 1). Questo è vero, indipendentemente dal fatto che il colesterolo nell'organismo derivi da sostanze grasse o no, oppure dal tipo di meccanismo che produce un'alta concentrazione di colesterolo serico.

Restrizione delle proteine

Non è fra gli scopi di questa pubblicazione il considerare il ruolo delle proteine nella patogenesi e nella cura delle diverse malattie vascolari. Dieci anni fa, quando venne pubblicato il primo rapporto sulla dieta di riso, fu obiettato che la dieta non aveva alcun valore nei casi di malattie vascolari ipertensive e nella arteriosclerosi. La restrizione del sale, dei grassi, del colesterolo e delle proteine venne considerata non giustificata. Per quanto concerne il sale, i grassi ed il colesterolo, l'argomento è stato superato — essendovi ora un accordo quasi generale circa l'importanza della restrizione di questi componenti dietetici. Per quanto riguarda invece le proteine, l'argomento è ancora in discussione. Qualsiasi possa essere il valore della restrizione delle proteine, fra tutte le diete usate nella cura delle malattie renali acute e croniche, di quelle vascolari ipertensive, dell'arteriosclerosi, delle malattie cardiache e delle retinopatie vascolari, quella di riso contiene la più bassa quantità di proteine (circa 25 grammi in 2.400 calorie).

L'organismo umano richiede un minimo di circa 50 grammi di proteine al giorno per poter prevenire le carenze proteiche, risultanti in ipoproteinemia, anemia ed edema. La base di questa asserzione è il fatto che, *a completo digiuno* la escrezione totale giornaliera di azoto nelle urine e nelle feci è di circa 8 grammi. Poichè per reintegrare una perdita di azoto di 8 grammi è necessaria una quantità di proteine pari a 50 grammi ($8 \times 6{,}25$), quest'ultima quantità è con-

siderata l'indispensabile ed è chiamata « quota minima giornaliera ».

Tuttavia, se nella completa carenza di proteine, sono assunti sufficienti carboidrati perchè forniscano le necessarie calorie, la totale escrezione di azoto può scendere da 8 grammi a meno di 2 grammi. Questo fenomeno è conosciuto come « effetto di risparmio delle proteine operato dai carboidrati » ed è uno dei principi seguiti nella dieta di riso. La totale escrezione giornaliera di azoto nelle feci e nelle urine con un'assunzione proteica giornaliera di 125 grammi è di 20 grammi (a digiuno completo è di circa 8 grammi), dopo una media di 88 giorni di dieta di riso è invece di 4 grammi. Questi ammalati sono in equilibrio nei riguardi dell'azoto con un'assunzione di proteine di 25 grammi ($4 \times 6{,}25$). Non vi sono fatti anemici; al contrario vi è generalmente un leggero aumento nella concentrazione emoglobinica, il tasso proteico del plasma è mantenuto normale o leggermente aumentato, l'edema non solo non si manifesta, ma, se è presente, quasi sempre scompare.

Tuttavia, se un abbassamento del metabolismo dell'azoto è desiderabile, come in molti casi di nefriti sia acute che croniche e di nefrosclerosi, allora la dieta con scarsissime escrezioni totali di azoto risulta essere la più idonea. È evidente che una dieta proteinopriva (cura raccomandata da Volhard per le glomerulonefriti acute), con una escrezione di azoto pari ad 8 grammi, è preferibile ad una dieta usuale con una escrezione di 20 grammi. La dieta di riso, però, con una escrezione di 4 grammi, è ancora più efficace della precedente e può essere continuata per mesi oppure per anni (tabella 2).

Tabella 2 - Confronto tra i reperti del sangue e dell'urina nella dieta di riso ed a digiuno.

	DIGIUNO	DIETA DI RISO
Emoglobina	diminuita	invariata
Calcio serico	diminuita	invariata
Proteine totali del plasma: rapporto A/G	diminuita	aumentate
Azoto non proteico del sangue; urea	aumentato	diminuiti
Zucchero nel sangue	diminuito	invariato
Tolleranza ai carboidrati	diminuito	aumentata
Riserva alcalina del plasma	diminuito	aumentata
Volume del sangue; volume fluido interstiziale	invariati	diminuiti
Equilibrio dell'azoto	negativo	in equilibrio
Creatina, ammoniaca ed acidi organici dell'urina	aumentati	diminuiti

L'effetto della dieta di riso sull'azoto non proteico del sangue e su quello ureico di 950 pazienti non uremici con malattie ipertensive vascolari è riportato nella tabella 3. L'azoto non proteico medio è del 17% più alto con una dieta ordinaria che non con una dieta di riso, essendo l'azoto ureico medio del sangue pari al 62%.

Anche nei pazienti senza malattie renali, che hanno concentrazioni

normali di azoto proteico ed ureico, è consigliabile all'inizio di diminuire l'assunzione di proteine alimentari quando la quota di sale è drasticamente ristretta poichè, come è noto, nei casi di profusa sudorazione, di diarrea o di morbo di Addison, una diminuzione dei cloruri o del sodio nel siero si è spesso seguita da un aumento dell'azoto non proteico e dell'urea nel sangue.

Nessuno mette in dubbio che l'assunzione di proteine dovrebbe essere ridotta al minimo nei pazienti con avanzata insufficienza renale

Tabella 3 - Effetti della dieta di riso sull'azoto non proteico e sull'azoto ureico di 950 casi non uremici (azoto non proteico 45 o meno) (valori medi).

	Prima della dieta di riso	Dopo tre giorni di dieta di riso (medie)
Azoto non proteico (m. g./100 cc. di sangue)	34,0	29,0
Azoto ureico (m. g./100 cc. di sangue)	14,1	8,7

ed uremia, senza considerare se questo scompenso sia la conseguenza di malattie parenchimali o vascolari. Generalmente questa restrizione è iniziata solo dopo che la totale escrezione PSP in 2 ore è scesa sotto al 10% e l'azoto non proteico ha superato i 100 milligrammi. Nelle malattie ad andamento progressivo come le nefriti croniche e le malattie renali di carattere ipertensivo ed arteriosclerotico, appare evidente la necessità di iniziare la restrizione prima che si verifichino le finali e fatali conseguenze.

Indicazioni

Cinque anni fa, nel discutere le indicazioni della dieta di riso, io scrissi:

« La dieta di riso è indicata in tutte le forme serie di nefriti acute, nei disturbi cardiaci che non traggono giovamento dalle normali cure a base di restrizione salina e di medicinali, nelle malattie vascolari arteriosclerotiche ed ipertensive con complicazioni cardiache, retiniche e renali.

La dieta di riso dovrebbe essere provata nelle forme più semplici di malattie vascolari ipertensive quando un più libero regime alimentare (scarsità di grassi e di sali, regolazione del peso, diminuzione delle attività, regolazione dell'alvo, cure calmanti, ecc.) non ha dato risultati ».

Queste osservazioni non erano però sufficientemente radicali. La esperienza fatta su di un grande numero di pazienti colpiti da queste malattie, mi ha convinto che la cura dovrebbe essere più aggressiva, senza compromessi, e dovrebbe iniziare appena la diagnosi può essere con cer-

tezza formulata. Perdite di tempo sono ingiustificabili come lo sarebbero per il cancro e per la tubercolosi ed il timore di inconvenienti non è un motivo sufficiente per dilazionare la cura dietetica « optimum » fino al momento in cui appaiono le complicazioni più spiacevoli e sovente irrimediabili.

Purtroppo, proprio nei casi in cui la dieta è maggiormente necessaria, qualche volta diventa impossibile seguirla sia per uno squilibrio elettrolitico (ipocloremia, iponatremia oppure iperpotassiemia) che rende necessaria la somministrazione di un supplemento di sale sia per un pesistente vomito che impedisce all'ammalato di trattenere qualsiasi tipo di cibo. Particolari difficoltà nella deglutizione dovuta all'anoressia ed

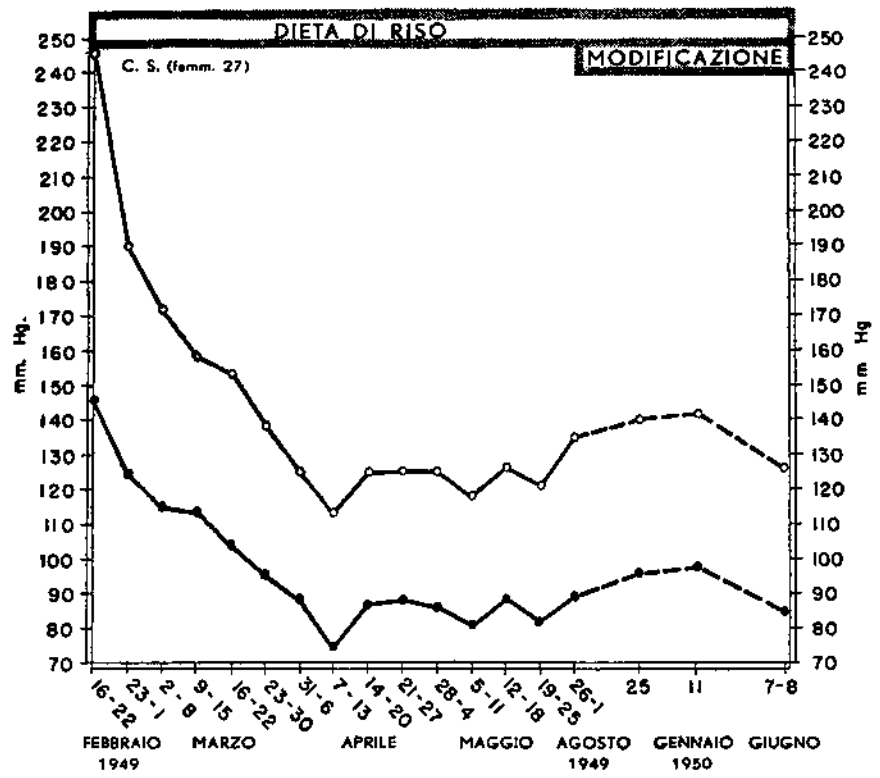


Fig. 5. Ipertensione in glomerulonefrite cronica ridotta con la dieta di riso (escrezione totale di PSP in due ore: 11%).

alla nausea possono essere superate con l'uso della sonda gastrica, attraverso la quale vengono forniti ad ogni ora del giorno e della notte, 100 centimetri cubici (100 calorie) di una preparazione omogeneizzata di riso, frutta, succo di frutta e zucchero. (Un paziente colpito da una lesione cerebrale vascolare, è stato alimentato in questa maniera per più di un anno).

La dieta di riso è indicata nelle nefriti acute ed in quelle croniche. L'alta percentuale di guarigioni spontanee nelle glomerulo nefriti rende difficile una valutazione quantitativa. Ciononostante i benefici effetti della dieta nelle nefriti croniche sono evidenti e facilmente dimostrabili: la

pressione del sangue, l'albuminaria e l'azotemia diminuiscono, gli ingrandimenti del cuore, le emorragie della retina, gli essudati e gli edemi della papilla scompaiono (figg. 5, 6, 7 e 8).

La dieta di riso è indicata anche per le nefrosi. In molti ammalati che presentavano sindrome nefrotica è stata constatata la scomparsa dell'ascite dell'edema, della proteinuria, della ipercolesterolemia malgrado la notevole restrizione proteica della dieta, le proteine del plasma sono tornate normali (fig. 9).

La dieta di riso è inoltre indicata negli ingrandimenti del cuore e nella insufficienza cardiaca sia che questa dipenda da una malattia valvolare, sia che tragga origine da arteriosclerosi, da malattie ipertensive vascolari, da malattie renali, da febbre reumatica, da lupus eritematoso diffuso oppure da altri stati patologici. Le figg. 10, 11 e 12 mostrano le diminuzioni nelle dimensioni del cuore ottenute in pazienti affetti da malattie delle valvole, delle arterie e da ipertensione maligna.

Gli ammalati di ipercolesterolemia sia di origine familiare che derivante da altre cause dovrebbero essere trattati con dieta di riso, così come quelli colpiti da angina pectoris o da infarto miocardico. In questi casi la terapia ha due scopi: contrastare o prevenire i processi che portano ad una diminuzione dell'afflusso del sangue nelle coronarie e ridurre le necessità di lavoro, e quindi di affaticamento, del miocardio.

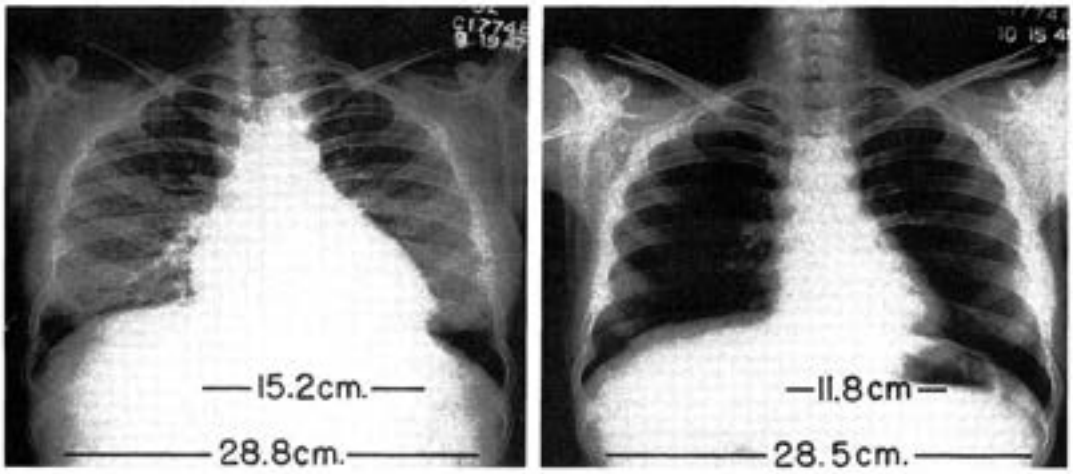
La dieta di riso è stata efficace nelle malattie arteriosclerotiche ed in quelle ipertensive vascolari. Un gran numero di pazienti con ipertensione benigna, accompagnata o no da serie complicazioni ha tratto un notevole beneficio dalla dieta stessa. Così è stato anche per molti ammalati la cui forma di ipertensione era del tipo maligno, accompagnata da gravi lesioni cardiache, renali o retiniche.

Casistica

Il caso di un soggetto di 47 anni, proveniente dallo Stato di New York, è considerato come esempio (fig. 13). Questo paziente era stato colpito due anni e mezzo prima da ipertensione; era stato curato con una dieta ristretta e con sedativi. A causa di una grave e debilitante cefalea, fu mandato dal suo medico al Dott. Raisbeck del New York Medical College. Il Dott. Raisbeck trovò una pressione del sangue di 257/173 millimetri di Hg (media di 7 letture) e fece diagnosi di ipertensione cardiovascolare in fase maligna. Fece immediatamente iniziare all'ammalato la dieta di riso e lo consigliò di recarsi al più presto a Durham. Gli esami ivi compiuti una settimana più tardi, indicarono che la pressione era già leggermente diminuita: 233/161 millimetri di Hg. Il diametro trasversale del cuore tra di 13,8 centimetri. Erano inoltre presenti delle profonde modificazioni vascolari nel fundus oculi, degli edemi della

papilla bilaterali, delle emorragie e degli essudati cotonosi (fig. 14).

Dopo 110 giorni a dieta di riso la media dei valori della pressione (media di 10 giorni) era di 124/89 millimetri di Hg. Il diametro trasversale del cuore era diminuito a 12,4 centimetri; gli edemi della papilla, le emorragie e la maggior parte degli essudati erano scomparsi come lo era la cefalea. Il paziente ritornò a casa con la indicazione di seguita una dieta leggermente modificata. Egli si sentiva benissimo e ricominciò il proprio lavoro. Fu riesaminato dopo due mesi; la pressione del sangue media durante un periodo di prova di tre giorni fu di 120/83 millimetri di Hg. Il diametro trasversale del cuore era di 12,4 centimetri. Il paziente era completamente asintomatico; tutti i sintomi della inoltrata retinopatia causata dalla ipertensione maligna erano scomparsi.



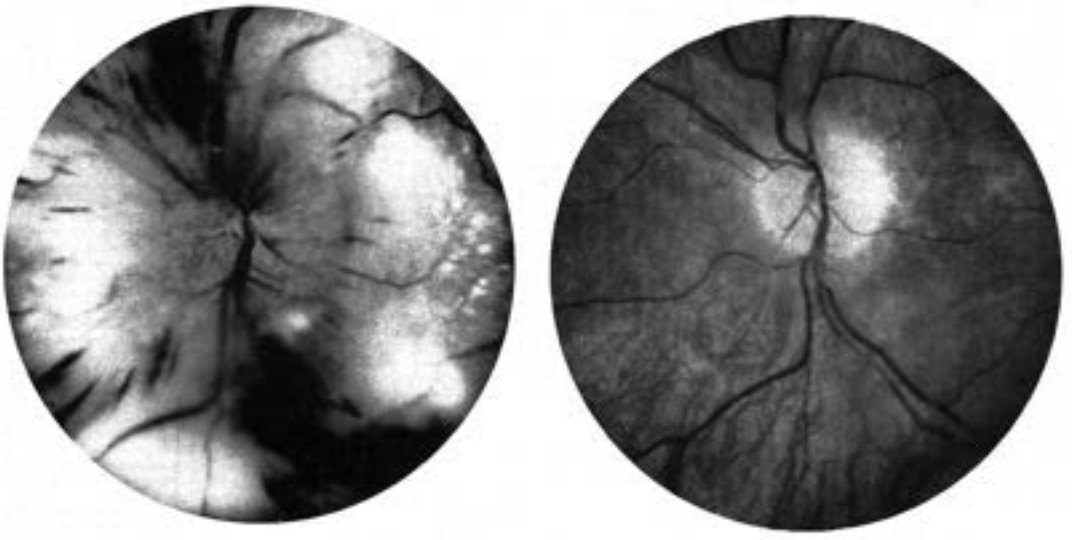
200/98 Settembre 1947 120/80 Ottobre 1948

Fig. 6. Ingrandimento del cuore in nefrite cronica ridotto con dieta di riso.

In questo caso l'ammalato fu riportato in normali condizioni di pressione in quattro mesi.

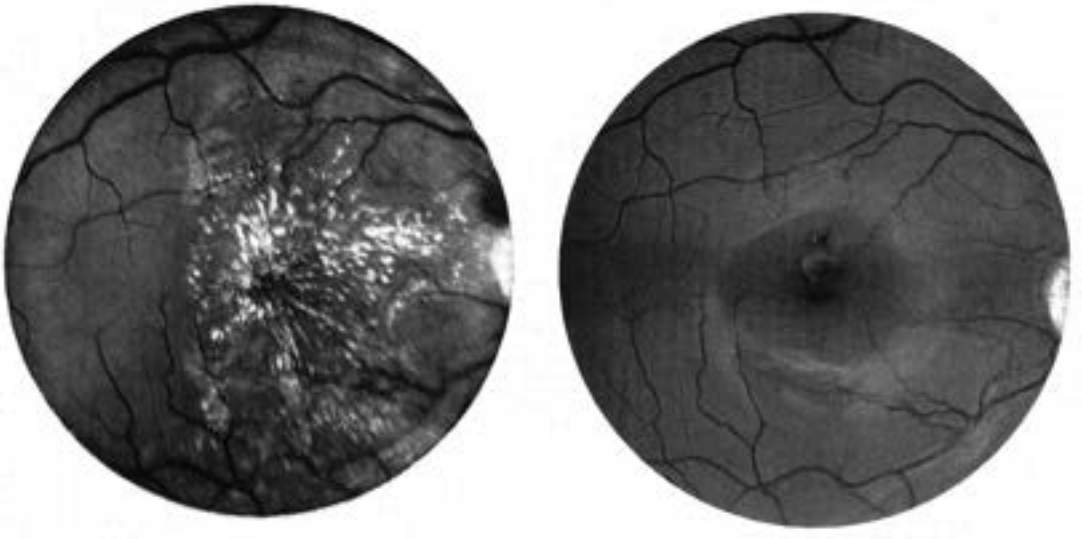
La fig. 15 rappresenta il diagramma della pressione del sangue di una donna affetta da ipertensione benigna, rilevata per quattro anni. La ipertensione era iniziata nel 1939; nel settembre del 1943 la pressione del sangue era 203/109 - 214/110 ed il Dott. Smithwick aveva compiuto una simpatectomia bilaterale lombo-dorsale. La pressione dopo l'intervento si era abbassata, ma ritornò al livello preoperatorio nel volgere di un anno. Dall'ottobre del 1947 la pressione fu di 245/120. Il Dott. Wright le fece iniziare una dieta modificata di riso e poichè dopo pochi mesi non vi era stato alcun significativo miglioramento le consigliò di recarsi a Durham.

La paziente aveva 41 anni; la pressione del sangue, (media delle letture effettuate in posizione di riposo dal 27-2 al 6-3 1948) era di



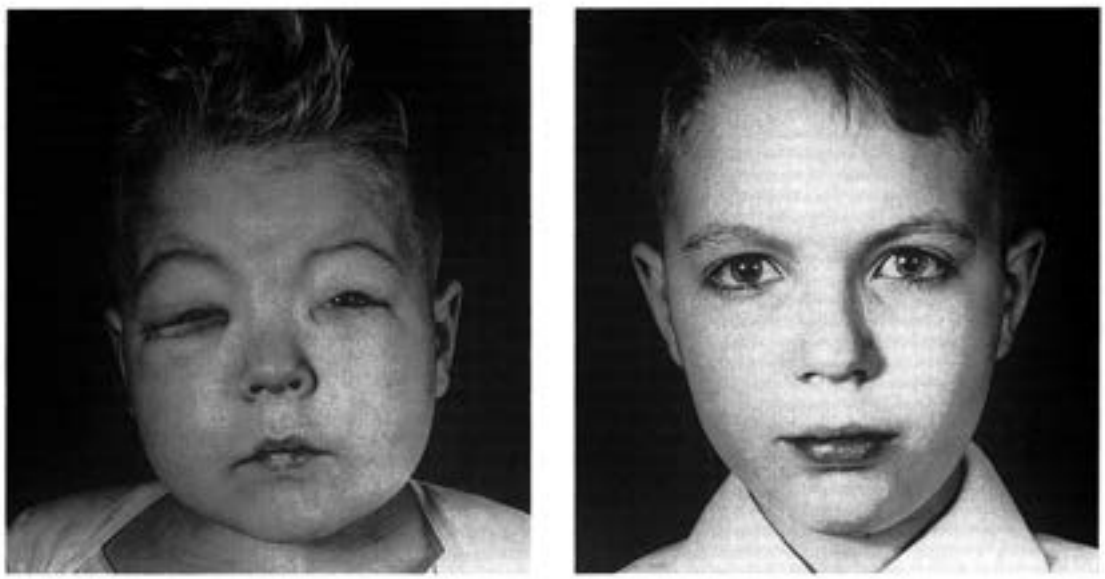
Ottobre 1948 Novembre 1949

Fig. 7. Scomparsa dell'edema della papilla, delle emorragie e degli essudati nella fase finale di una glomerulonefrite trattata con dieta di riso (H. R. - m, 39).



Febbraio 1949 Maggio 1952

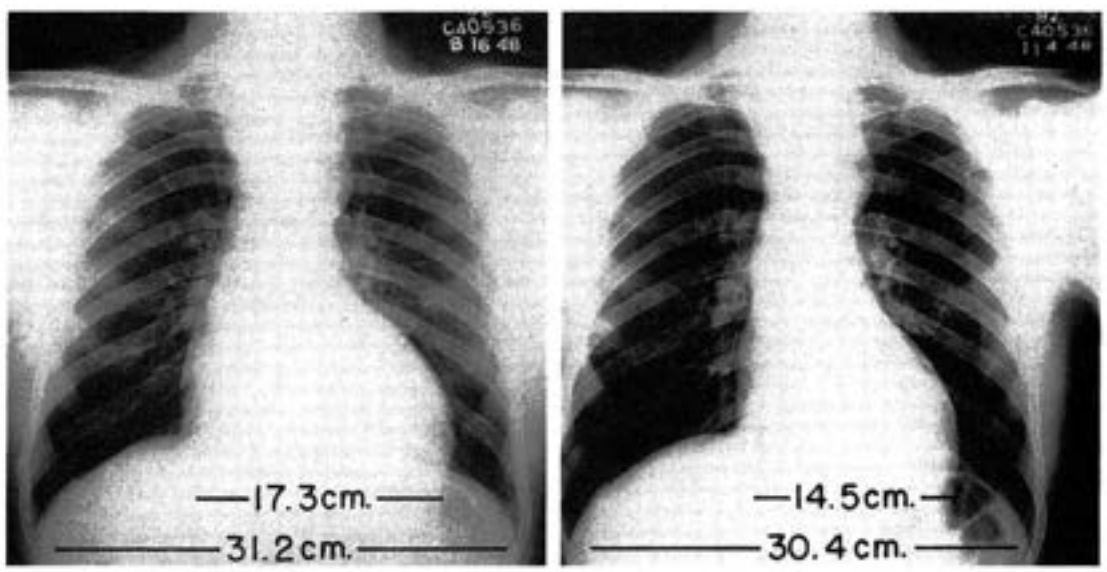
Fig. 8. Scomparsa della stella maculare nella fase finale di una glomerulonefrite cronica (m, 22).



Dicembre 1948 Maggio 1953

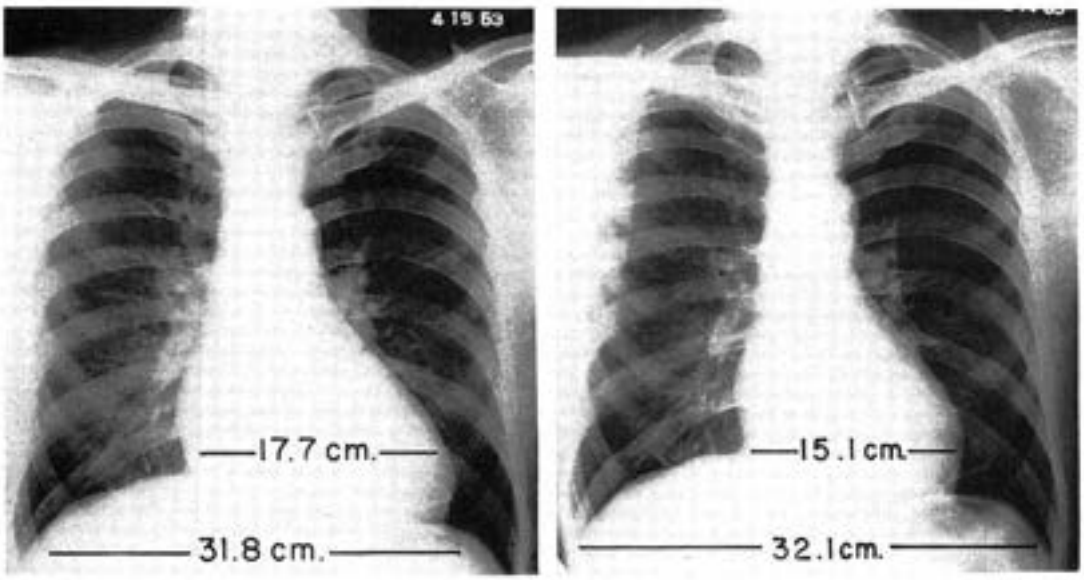
Fig. 9. Nefrosi trattata con dieta di riso (D. H., 5 e 10).

1,100	Colesterolo (mg. per 100 cc. di siero) . .	249
3,9	Proteine totali (Gm. per 100 cc. di plasma)	6,8
42,—	Escrezione totale di PSP in 2 ore % . . .	77
4,0	Proteine (Gm. per 1000 cc. di urina) . . .	0,2



130/64 mm. 8-1-48 120/70 mm. 11-4-48

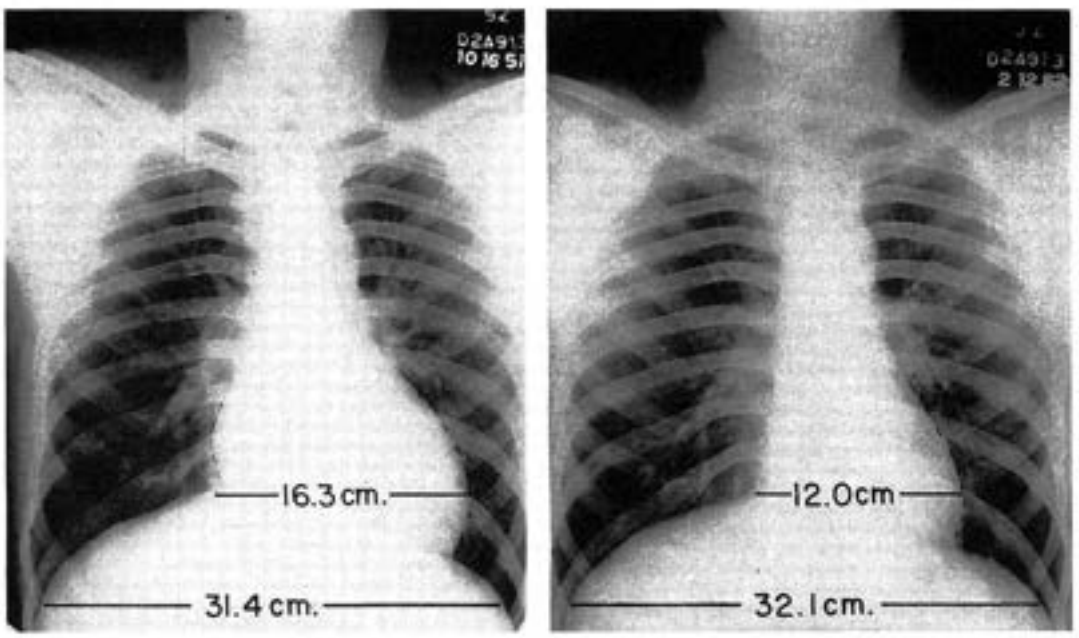
Fig. 10. Ingrandimento cardiaco in steno-insufficienza aortica con blocco cardiaco parziale-completo, ridotto con la dieta di riso (H. G. W., m. 55).



120/80 Aprile 1953

106/77 Agosto 1953

Fig. 11. Diminuzioni delle dimensioni del cuore in un caso di coronaropatia curata con dieta di riso.



Ottobre 1951

Febbraio 1952

Fig. 12. Diminuzione delle dimensioni del cuore in un caso di ipertensione maligna trattata con dieta di riso (S. L., m. 26).

222/131. Il solo reperto positivo a fianco dell'ipertensione era un lieve rumore aortico diastolico. La concentrazione dei cloruri nell'urina, come cloruro di sodio, era di 114 milligrammi su 100 centimetri cubici in confronto dei 5/15 milligrammi presenti quando fu seguita una stretta dieta di riso. Quest'ultima venne iniziata nel febbraio del 1943; dopo 105 giorni la pressione del sangue era di 213/122 millimetri di Hg. e dopo 180

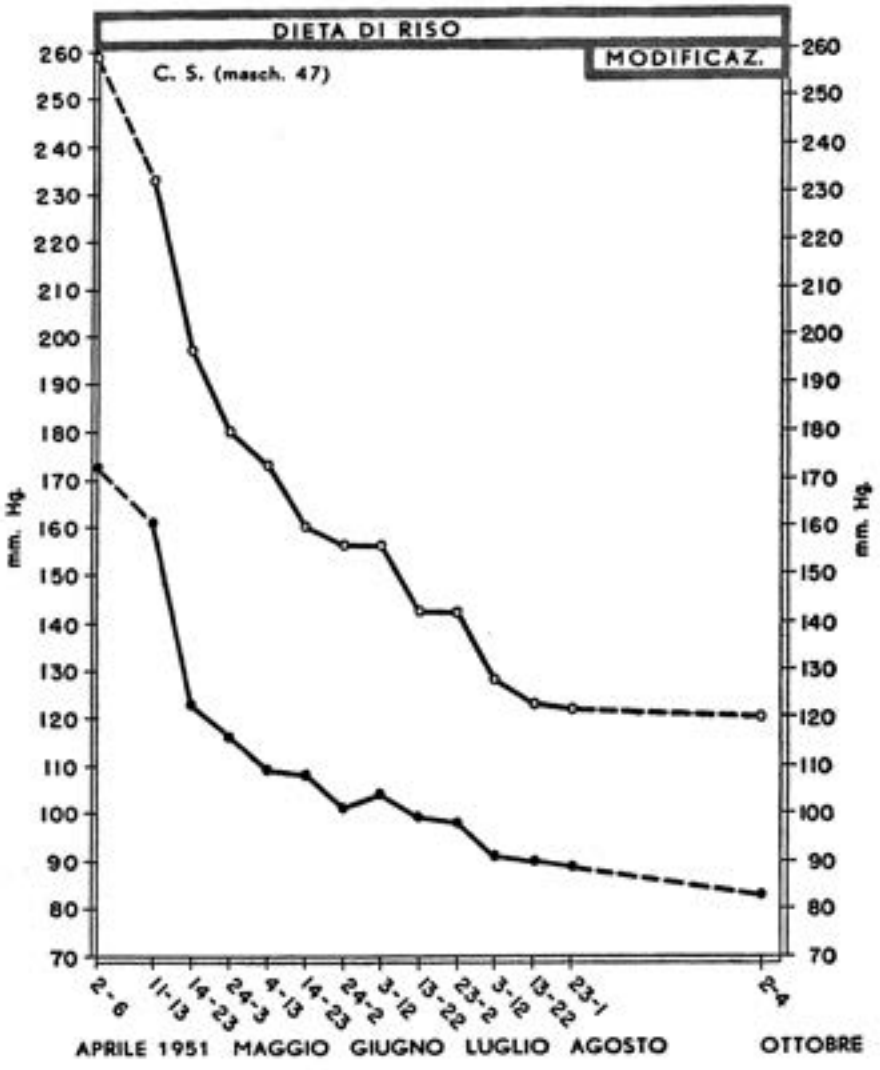
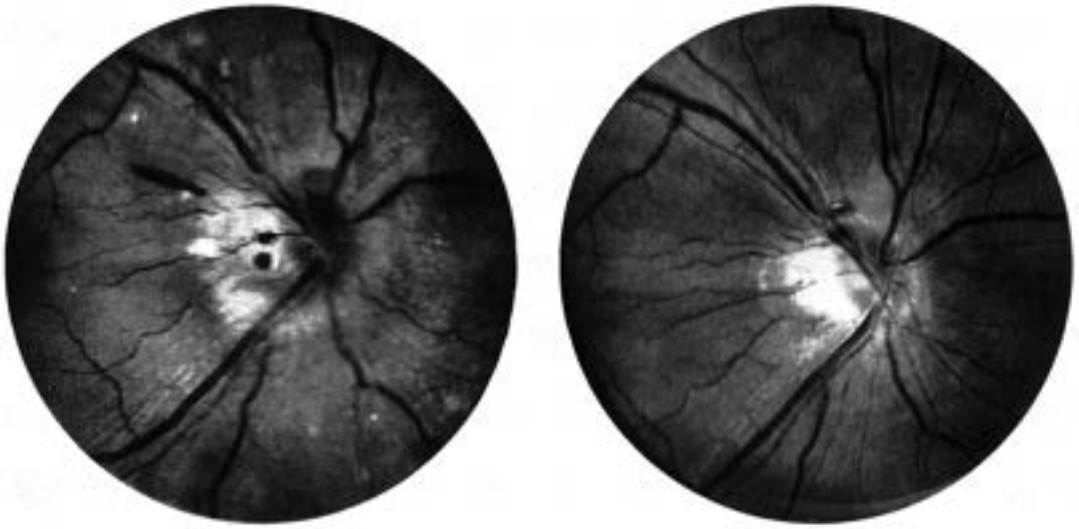


Fig. 13. Pressione sanguigna in un caso di ipertensione maligna ridotta con dieta di riso.

giorni di 212/121 millimetri di Hg. La concentrazione dei cloruri nell'urina, sempre come cloruro di sodio a questo momento risultò essere ancora di 82 milligrammi.

Da quel momento, la paziente si attenne rigorosamente alla dieta di riso alla quale vennero fatte delle minime aggiunte. La concentrazione salina delle urine era notevolmente inferiore ai 20 milligrammi. Tuttavia, dopo un anno di dieta di riso, la pressione del sangue era ancora di



Aprile 1951 Gennaio 1952

Fig. 14. Scomparsa dell'edema della papilla, della emorragia e degli essudati in un caso di ipertensione maligna (C. S., m. 47).

192/126 e, dopo due anni, di 167/130. È stato solamente nel gennaio del 1952, cioè circa quattro anni dopo l'inizio della dieta di riso, che si è ottenuta la prima lettura quasi normale della pressione del sangue: 135/82.

Da allora la pressione si è mantenuta quasi sempre normale; la media di 16 letture dal gennaio al settembre del 1953 è stata di 120/75, in confronto a 209/124 (media di 102 letture durante i primi quattro

Fig. 15. Diminuzione graduale della pressione durante cinque anni di cura con dieta di riso.

mesi della dieta di riso) di cinque anni prima. L'ammalata è attualmente molto attiva e completamente senza sintomi.

La tabella 4 illustra gli effetti della dieta di riso sulla pressione del sangue in un gruppo di 860 pazienti colpiti da malattie vascolari ipertensive sottoposti a cura per 90 o più giorni (mediamente 146 giorni). In 709 casi (82,4%) vi è stato un deciso abbassamento della pressione da un valore medio di 195/114 ad uno di 145/91. In 291 casi la pressione è discesa ai livelli normali: da 180/106 a 127/81 (valori medi). La percentuale dei risultati positivi aumenta con la durata del periodo di cura.

La dieta del riso nel diabete mellito

Gli ammalati di diabete mellito non solo tollerano bene la dieta di riso, ma in un significativo numero di casi, viene ad essere diminuito il tasso zuccherino del sangue e ad essere attenuata la necessità di somministrazione dell'insulina. La dieta può anche avere uno speciale valore nella cura di molti casi di diabete mellito a causa del pericoloso ruolo che la ipercolesterolemia giuoca in questa malattia.

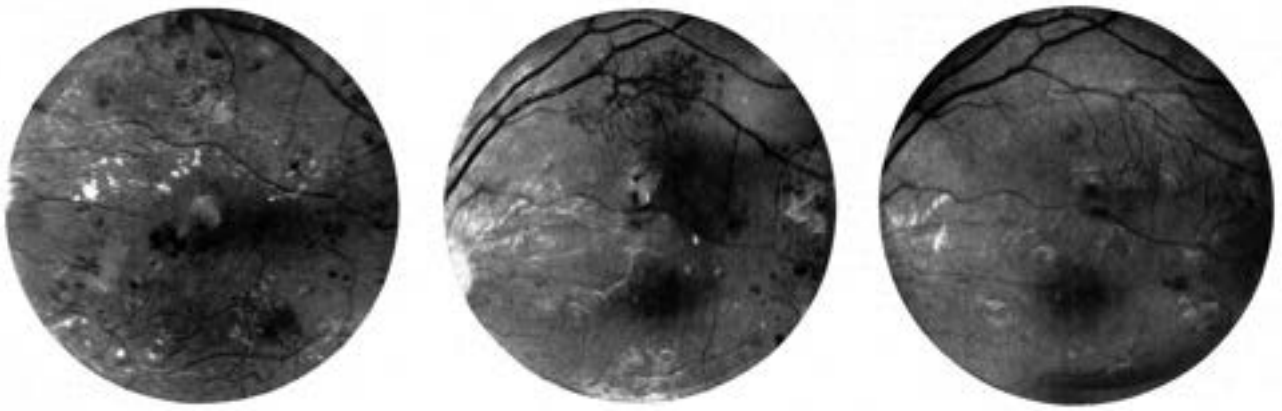
Sono stati sottoposti alla dieta di riso 48 pazienti affetti da diabete mellito con complicazioni renali o vascolari. Il periodo di osservazione è andato da 8 settimane a circa 6 anni, mediamente 59 settimane). In 17

Tabella 4 - Effetti della dieta di riso sula pressione del sangue di 350 casi di ipertensione vascolare (trattati in 90 o più giorni: media di 146 giorni).

	Numero dei casi	%	Pressione prima della dieta riso (medie)	Pressione dopo la dieta riso (medie)
Non migliorati	151 (*)	17,6	179/108	194/114
Migliorati	709	82,4	145/91	195 114
Diminuiti a meno di 140/90 . .	291	33,8	127/81	180/106

(*) Sono inclusi otto ammalati deceduti (la pressione non è considerata nelle medie).

dei 48 casi si è verificato un cambiamento superiore a 30 milligrammi del tasso zuccherino del sangue, in tre di essi è aumentato, mentre in quattordici è diminuito. Gli altri casi hanno registrato delle marcate variazioni nel tasso zuccherino del sangue oppure hanno registrato delle variazioni minori. Ventinove dei 48 casi non hanno dimostrato alcun cambiamento per quanto concerne la necessità di somministrazione di insulina, mentre negli altri 19 vi è stato un ben definito cambiamento in ciò. In quattro pazienti vi è stato un aumento (da una media di 20 unità iniziali a una media di 41 unità con un incremento massimo da 0 a 30 unità); in 15 vi è stata ua diminuzione (da una media di 45 unità iniziali ad una media di 22 unità con una diminuzione massima da 90 a 30 unità).



Agosto 1950 Giugno 1951 Luglio 1953

Fig. 16. Scomparsa della retinopatia in diabete mellito (F. F., m. 24).

Il favorevole risultato ottenuto su questi pazienti ed il fatto che un grande numero di diabetici muore per malattie vascolari od almeno è fortemente debilitato da queste, suggerisce che la dieta di riso dovrebbe essere usata nei diabetici in cui si manifestano i primi sintomi di malattie cardiache, retiniche, renali o del sistema vascolare periferico.

La figura 16 mostra l'effetto della dieta di riso sulla retinopatia di un soggetto di 24 anni colpito da diabete mellito.

Altri effetti della dieta di riso

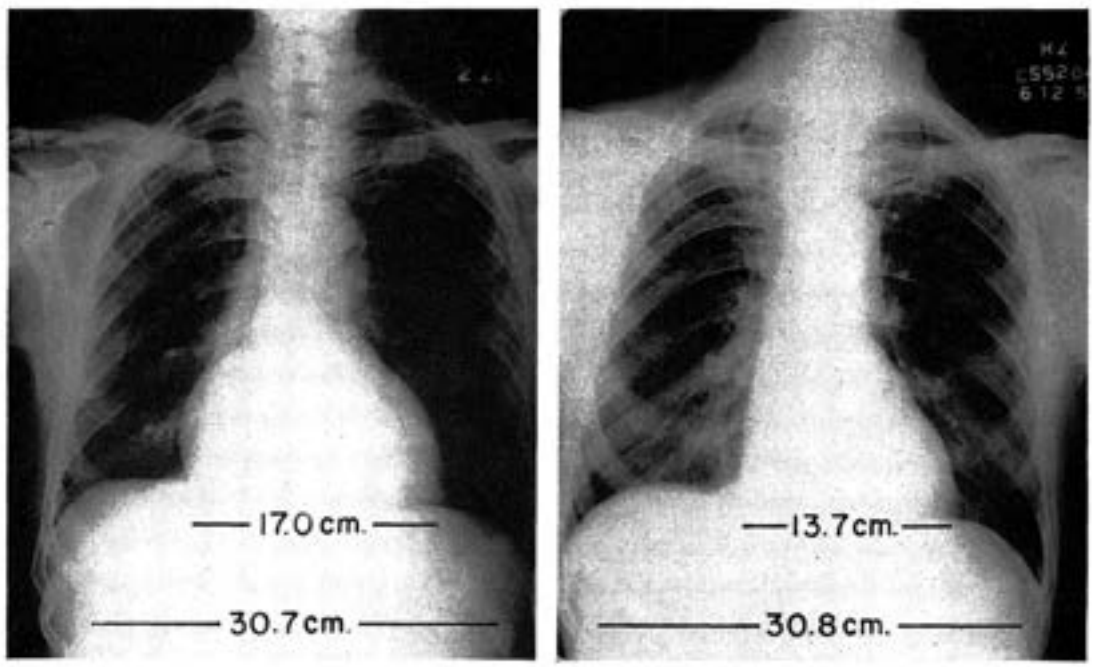
La vecchiaia è considerata dalla maggior parte di noi una specie di bancarotta causata da un accumulo di debiti vascolari, cardiaci e renali. Concordemente, i processi arteriosclerotici ed ipertensivi vascolari sono accettati come il risultato di una malattia degenerativa, un inevitabile e quasi fisiologico fatto collegato all'avanzare dell'età. La reversibilità di alcuni di questi processi in molti dei miei più vecchi pazienti prova, tuttavia, che questa specie di rassegnazione non è oggi più ammissibile. La pressione sanguigna sistolica di un soggetto di 75 anni, al pari di quello di uno di 30 anni, può essere inferiore a 130 e quella diastolica a 90. Un consolabile commento come « una pressione del sangue di 175/100 è abbastanza buona per questa età » è una ammissione gratuita e non dovrebbe sostituire la cura efficace. Tutto questo denota un'attitudine reminescente del tempo in cui simili scuse erano fornite per le « malattie della prima infanzia », al posto di intervenire con specifici metodi contro specifiche malattie.

La figura 17 illustra la diminuzione delle dimensioni del cuore, con un cambiamento del 20% nel diametro trasversale di esso, in un

soggetto di 79 anni ammalato di arteriosclerosi e di ipertensione. La figura 18 illustra il miglioramento dell'elettrocardiogramma in un soggetto di 81 anni con analoga diagnosi: il blocco di branca sinistra è scomparso.

In un gruppo di 120 casi affetti da malattie ipertensive vascolari, l'onda T1 dell'elettrocardiogramma era invertita all'inizio della cura a base di dieta di riso (niente digitale, niente evidenti sintomi di infarto).

In 68 pazienti essa è rimasta invertita dopo una media di sette mesi di dieta; in 52 essa invece si è normalizzata dopo una media di 10 mesi (figure 19 e 20). In un gruppo di controllo di 300 casi l'onda T1 era regolare quando la dieta di riso ebbe inizio; in nessuno di questi ammalati



Febbraio 1949 Giugno 1950

Fig. 17. Ingrandimento cardiaco in arteriosclerosi ridotto con cura di riso (R.J.B., m. 79).

essa si è invertita dopo un periodo medio di 11 mesi di dieta di riso.

In un gruppo di 500 pazienti che seguirono la dieta di riso per una media di 5 mesi, il cuore divenne più grande in 20 casi (4%), con un incremento medio del diametro trasversale pari al 2%. In 480 dei 500 pazienti (96%) il cuore divenne più piccolo con una riduzione media del diametro trasversale dell'11,8% (6% in 218 casi, 14% in 207 e 25% in 55).

Tuttavia tali risultati incoraggianti non significano che si debba sospendere il trattamento dietetico appena essi vengono ottenuti. È vero che la dieta può divenire più elastica dopo che la ipertensione, l'ingran-

dimento del cuore, il cardiogramma irregolare, la retinopatia, l'azotemia oppure l'ipercolesterolemia sono sufficientemente migliorati nel paziente; ma le aggiunte debbono essere gradualmente fatte in quanto esse dipendono dalle osservazioni fotografiche del fundus oculi e del cuore, dagli elettrocardiogrammi, dalle letture della pressione, dai reperti chimici del sangue e dalle prove di funzionalità renale. In tale maniera si ottiene una obbiettiva conoscenza per individuare se l'ammalato è abbastanza ben ristabilito per tollerare le aggiunte che per lungo tempo gli sono state

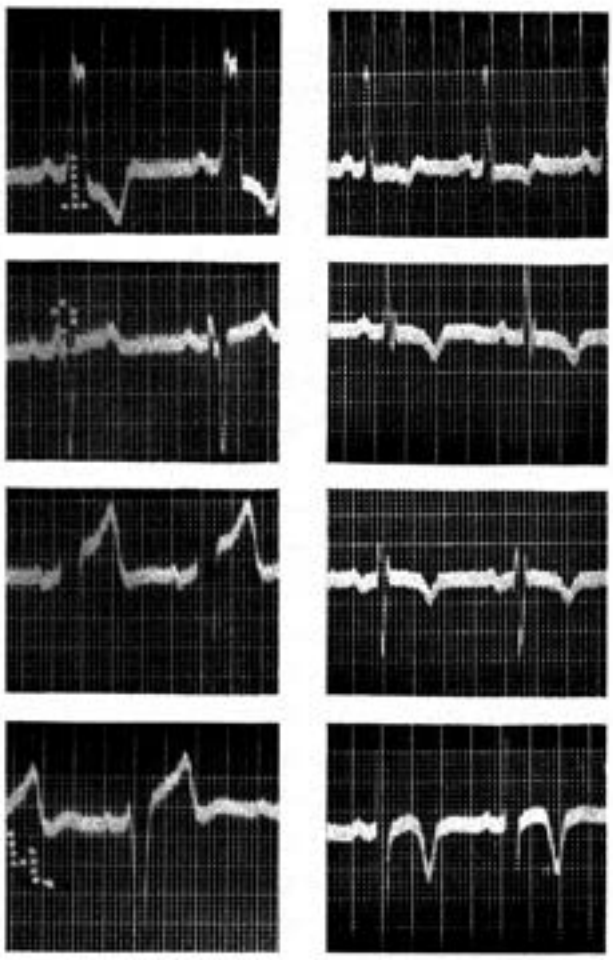


Fig. 18.
Scomparsa del blocco di branca sinistra in un caso di ipertensione cardiovascolare trattata con dieta di riso (M. F., f. 80).

proibite e per sapere se egli può tollerare ulteriori aggiunte oppure se la dieta deve nuovamente diventare rigorosa.

La figura 21 mostra con sette fotografie del torace un triste esempio del modo in cui non debbono essere eseguite queste modifiche della dieta.

H. W., affetto da arterio-arteriolonefrosclerosi, era sessantenne quando venne per la prima volta da noi; era stato curato con una dieta ristretta di sale, con digitale, con nitrato di potassio, con teobromina e con composti mercuriali. Tuttavia il suo cuore si era fatto progressivamente

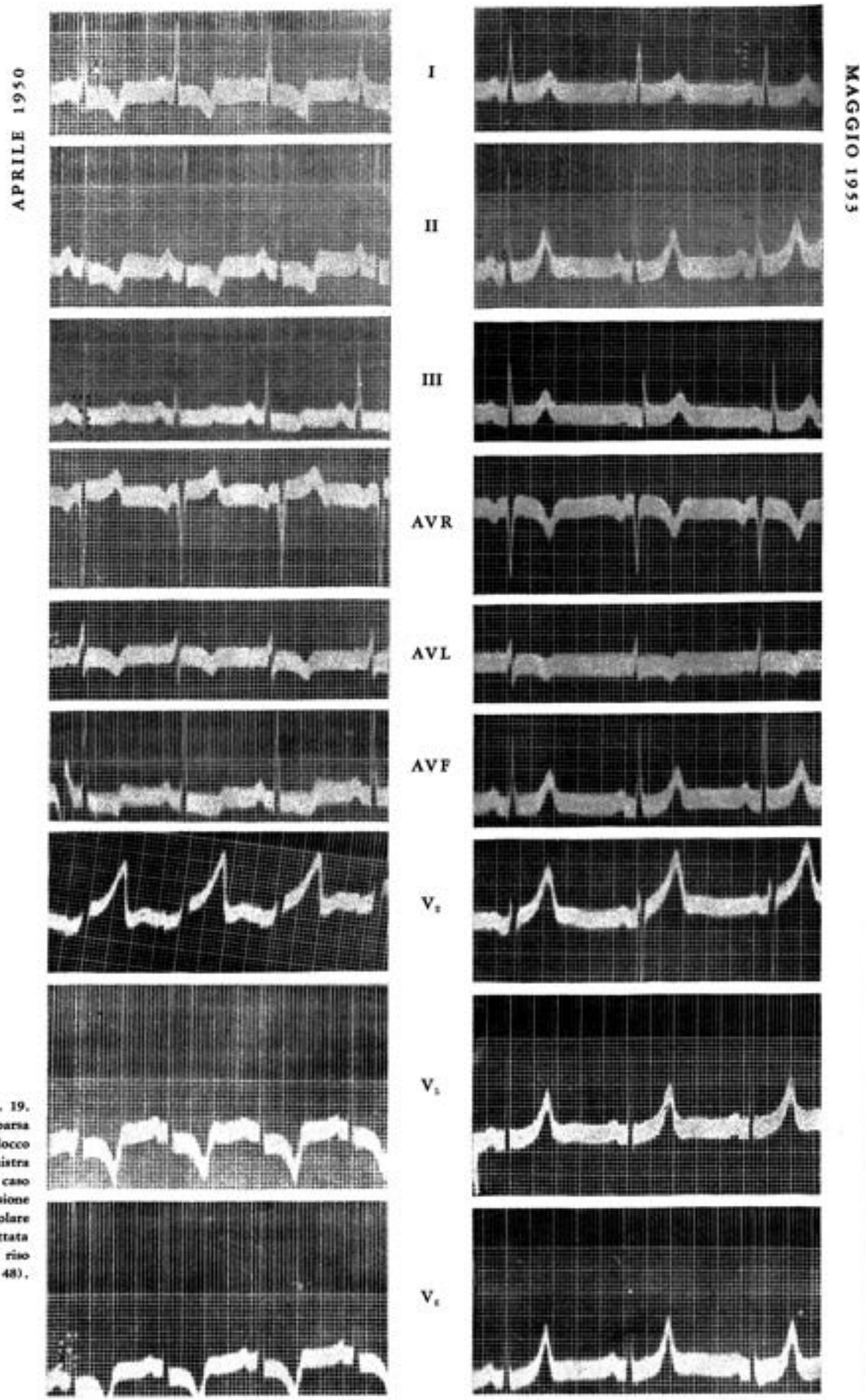


Fig. 19. Scomparsa del blocco di branca sinistra in un caso di ipertensione cardiovascolare trattata con dieta di riso (C. H. B., m. 48).

più grande ed erano aumentati i sintomi della insufficienza cardiaca. Quando tutte le medicine, eccetto la digitale, furono sospese e la dieta fu ristretta di sale (198 milligrammi di cloruro di sodio in 100 centimetri cubici di urina), il suo cuore si fece decisamente più piccolo ed i segni ed i sintomi dell'insufficienza cardiaca scomparvero. Fino a che ebbe qualche disturbo si attenne alla dieta di riso, ma via via che migliorava, fece di sua iniziativa delle aggiunte alla dieta. Dopo qualche tempo i suoi precedenti sintomi gradualmente ritornarono ed egli fu costretto a tornare da noi per ripartirne di nuovo con delle rigide indicazioni dietetiche. Quando la percentuale di sale diminuiva, il cuore diveniva di dimensioni più piccole, quando invece cresceva, il cuore tornava a farsi più grande. Questo fatto si è ripetuto per sei anni fino a quando l'insufficienza cardiaca è divenuta incurabile. Il peso del cuore all'esame autoptico è stato di 900 grammi.

Un altro paziente colpito da ipertensione è stato trattato con suc-

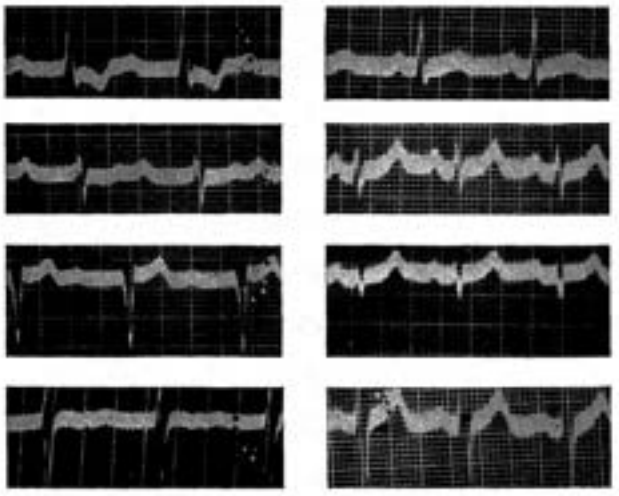
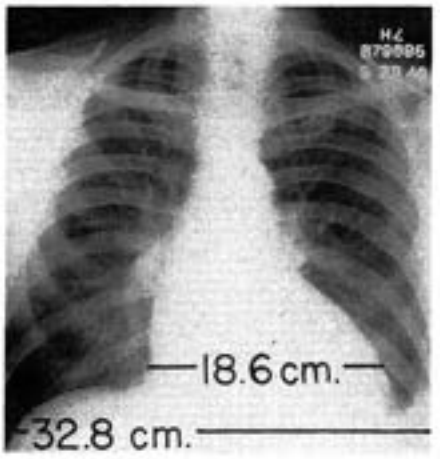


Fig. 20.
Scomparsa del blocco cardiaco di primo grado e della inversione di T1, in un caso di ipertensione cardiovascolare trattata con dieta di riso (E. P., m. 44).

cesso con una dieta stretta e poi con una dieta di riso progressivamente meno rigida nel corso di sei anni. A quel momento egli abbandonò ogni restrizione dietetica, mangiò ogni cosa che desiderava ed aumentò di peso da 183 a 220 libbre. Nonostante ciò non ebbe alcuna ricaduta. La sua malattia era stata vinta poichè era stato capace di sopportare una dieta comune.

Quando io discussi la situazione con lui, mi disse: « Dottore, realmente ho mangiato moltissimo, ma prometto che non lo farò mai più ». Io risposi: « La sua pressione del sangue è normale, il suo cuore ha dimensioni regolari e regolare è pure l'elettrocardiogramma; perciò lei può mangiare quanto vuole ». Alla fine però convenimmo che il peso doveva essere diminuito e che doveva essere anche ristretta la quantità di grassi e di sale nell'alimentazione.



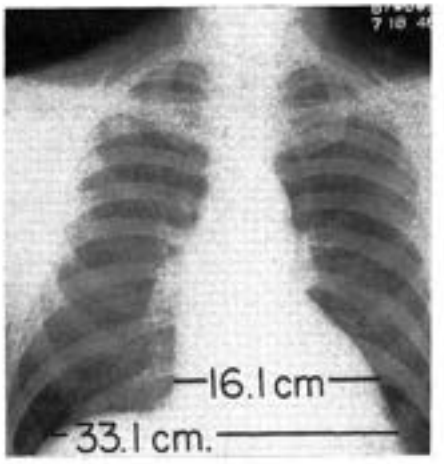
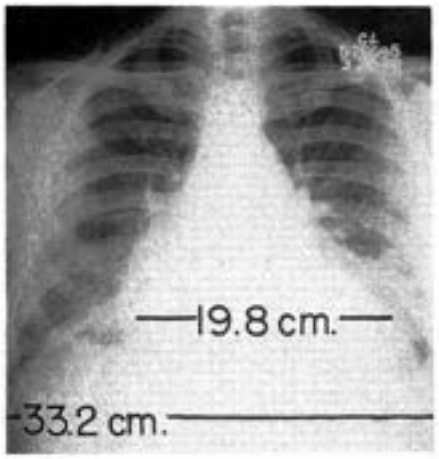
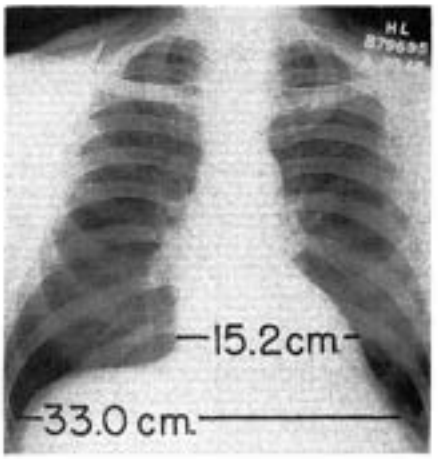
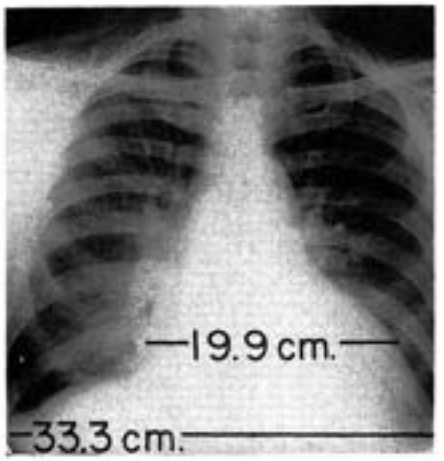
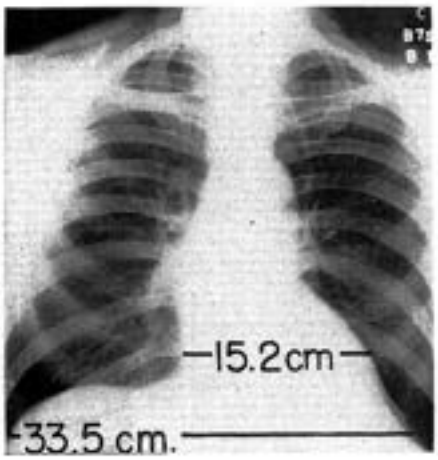


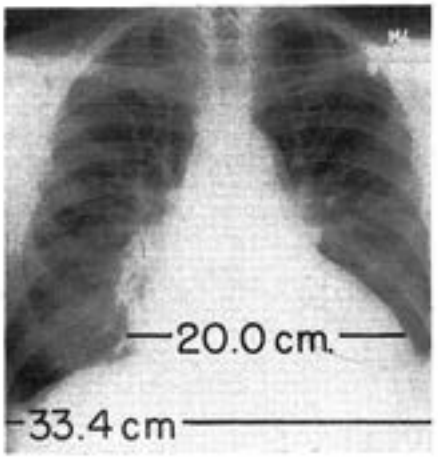
Fig. 21. (H. W., m. 60).
Il paziente è morto nell'ottobre del 1952.
Reperti autopici:
peso del cuore gm. 900;
entrambi i ventricoli dilatati ed ipertrofici.











Modificazioni retiniche

Le avanzate neuroretinopatie vascolari emorragiche ed essudative sono sempre state considerate un importante sintomo indicativo dello stadio finale di una malattia irreparabile. Il Textbook of Medicine di Cecil nella sua settima edizione dice: « Le emorragie associate con macchie nella retina (neuroretinopatie ipertensive) sono preoccupanti sintomi. La morte generalmente sopravviene entro un anno ».

Le ipertensioni maligne anche con neuroretinopatie in fase avanzata, se curata con la dieta di riso, possono regredire allo stadio benigno oppure completamente sparire.

La figura 22 illustra il fundus oculi di una donna che aveva 45 anni quando nel 1944 venne da noi con una forma di ipertensione apparentemente maligna che si protraeva da quattro mesi.

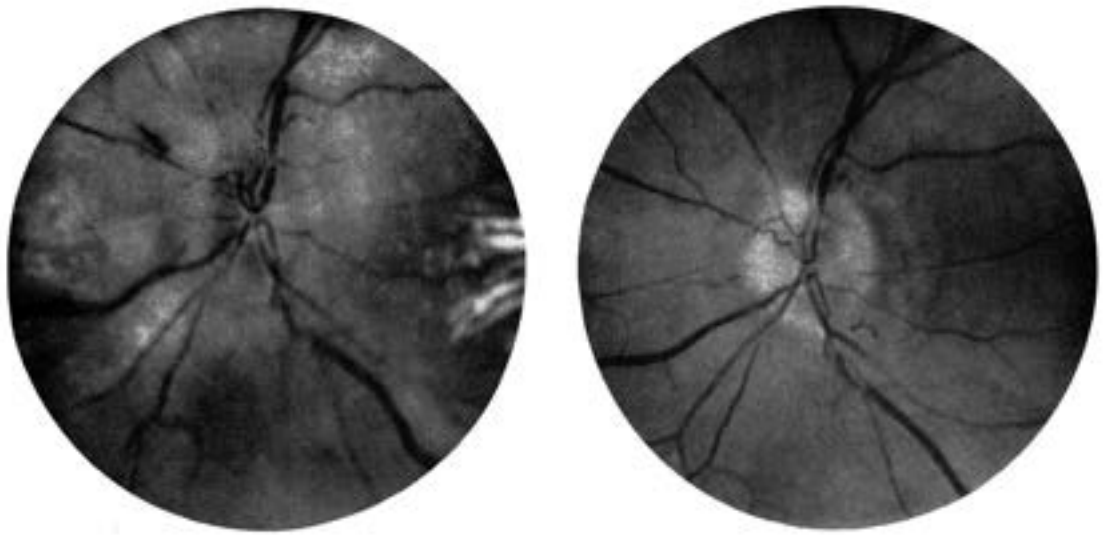
L'esame del fundus oculi mise in evidenza una tipica neuroretinopatia emorragica essudativa.

La paziente seguì la dieta di riso per un anno, poi, una dieta più libera, seppure ancora povera di sale e di grassi. La pressione del sangue durante le prime quattro settimane di assoluto risposo in letto subito dopo l'ospedalizzazione, comprendenti tre settimane di trattamento con la dieta di riso, fu di 221/152 (media delle letture giornaliere di 28 giorni). Al più recente riesame, luglio 1951, la pressione si aggirava su un valore medio di 162/105, la donna svolgeva le sue normali occupazioni. Essa non solo è sopravvissuta sette anni (ora 10) dopo l'apparizione della ipertensione maligna, ma la neuroretinopatia, gli essudati e le emorragie sono completamente scomparsi.

Le figure 23, 24 e 25 sono altri esempi di guarigione completa ottenuta con la dieta di riso in casi di avanzate retinopatie vascolari, sebbene in ognuno di essi il corso generale dell'ipertensione fosse interamente diverso.

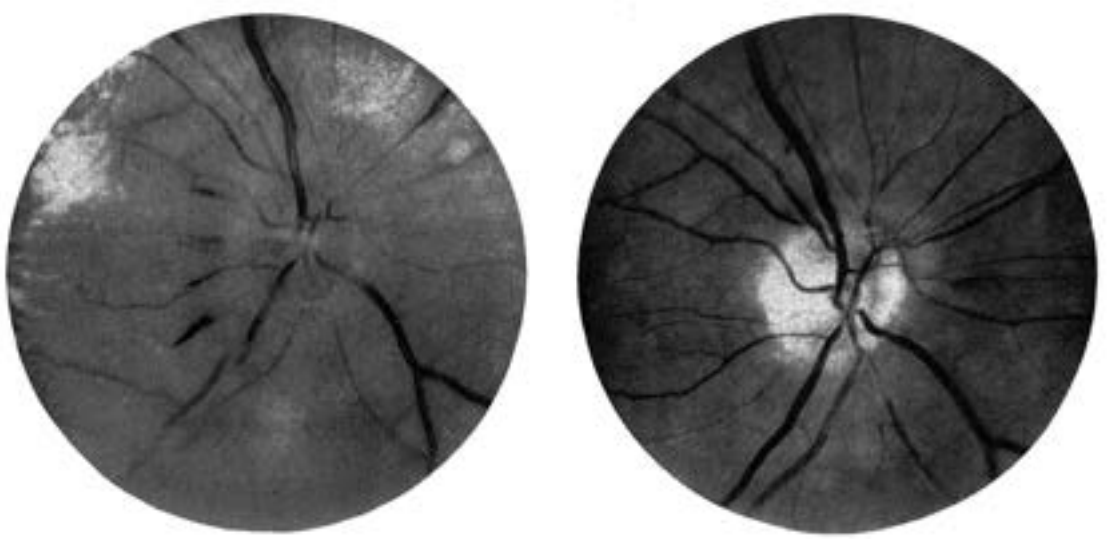
L'ammalato A. A. H. fu ammesso all'ospedale con una grave retinopatia. La pressione del sangue era di 190/119 (media del giugno 1944, dal 20 al 28 del mese). L'onda T1 dell'elettrocardiogramma era invertita. Egli seguì una rigida dieta di riso per quattro mesi, e dopo tale periodo, questa venne modificata. L'onda T1 dell'elettrocardiogramma si fece regolare, la retinopatia scomparve, ma la pressione del sangue, sebbene più bassa non divenne mai normale. Durante il periodo 1947-49 il valore medio di essa fu 171/109; durante il 1951-52 fu 158/100.

L'ammalato L. A. B. fu ammesso all'ospedale con una grave forma di retinopatia. La pressione del sangue era di 220/150 (valore medio del 30-31 ottobre 1944); il cuore era ingrandito. Dopo quattro mesi di riso la pressione era di 120/87; il cuore aveva inoltre assunto dimensioni



Agosto 1944 Luglio 1951

Fig. 22. Scomparsa dell'edema della papilla, delle emorragie e degli essudati in un caso di ipertensione maligna trattata con dieta di riso (L., W., f. 45).



Giugno 1944 Giugno 1952

Fig. 23. Scomparsa dell'edema della papilla, delle emorragie e degli essudati in un caso di ipertensione maligna trattata con dieta di riso (A. A. H., m. 47).

normali e la retinopatia era completamente scomparsa. Dopo un anno il paziente abbandonò la dieta. La pressione risalì; nell'ottobre del 1948 essa era di 194/132, nel novembre del 1949 di 228/138. Ciononostante la retinopatia non riapparve.

L'ammalato D. T. fu ammesso all'ospedale con una grave retinopatia; la pressione era di 205/151 (media dal 6 al 12 agosto 1948). Dopo quattro mesi di dieta di riso essa era di 105/78. La retinopatia scomparve e non tornò sebbene il paziente avesse continuato la dieta solo per un altro mese. La pressione rimase normale: 120/80 (nel gennaio del 1952, cioè tre anni dopo che la dieta di riso era stata sospesa).

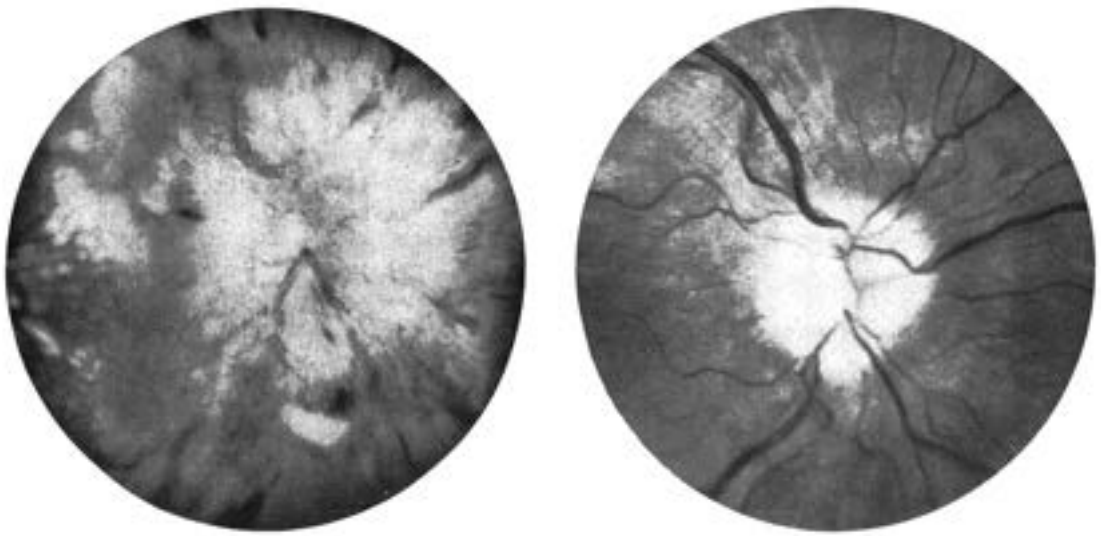
Questi casi dimostrano anche che la dieta di riso non è solo un trattamento « compensatorio », valido cioè fin che essa viene osservata, come l'insulina per il diabete od il fegato per l'anemia perniciosa, ma produce anche degli effetti permanenti che possono appunto persistere dopo che la dieta è stata profondamente modificata oppure addirittura sospesa.

La rappresentazione fotografica della neuroretinopatia vascolare è talvolta tale che è quasi impossibile la diagnosi differenziale con un tumore cerebrale. In questi casi la dieta di riso può essere usata come « test » terapeutico.

Le figure 26 e 27 sono le rappresentazioni fotografiche del fundus oculi di due pazienti, osservando le quali il Dr. Banks Anderson, nostro oftalmologo, pensò che una lesione espansiva intracranica in un ammalato di ipertensione fosse la più sicura diagnosi. In entrambi i casi risultati ottenuti con la dieta di riso mostrano che le alterazioni evidenti nelle rappresentazioni fotografiche erano causate da ipertensione maligna. Quando il Dr. Anderson vide di nuovo i pazienti dopo alcuni mesi di dieta di riso, scrisse nelle sue note di consultazione: « A. H. febbraio 1950 — il fundus oculi di questo paziente è migliorato in un modo incredibile. Non ho mai visto prima d'ora un simile edema della papilla, estensivo, permanere in tali condizioni e neppure ho mai visto un ammalato affetto da retinopatia ipertensiva di questo grado restare in vita dopo tanto tempo ».

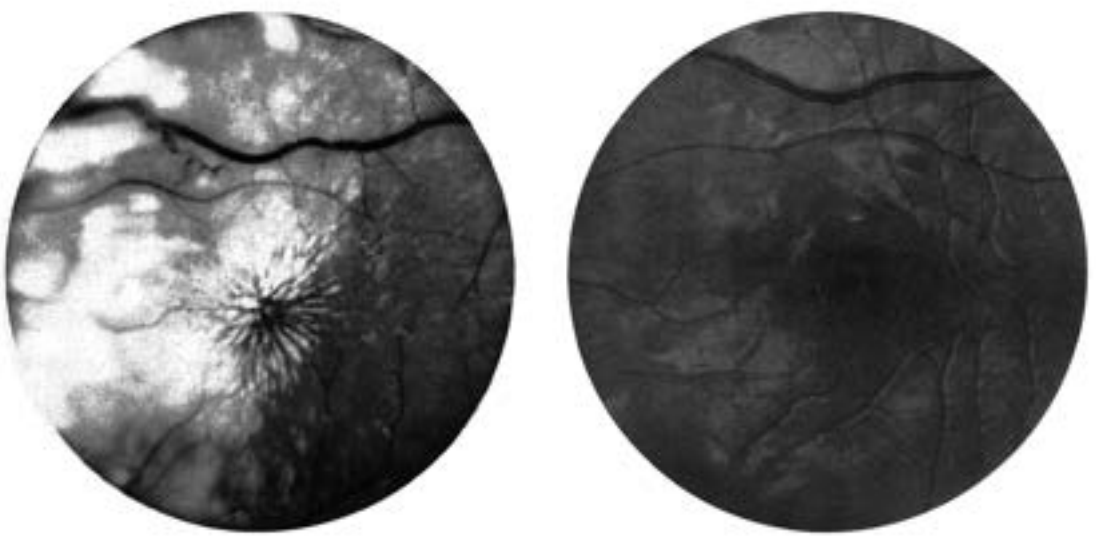
« B. R. giugno 1953 — appunti mi dicono che quando io vidi questo ammalato l'ultima volta ero dell'opinione che l'edema della papilla fosse troppo marcato per essere dovuto esclusivamente alla ipertensione. Mi sono sbagliato. L'esame fundoscopico attraverso le pupille non dilatate mostra che non vi è nessun sintomo di edema della papilla... Non vi sono neppure aree di essudato, di emorragia o di pigmentazione ».

È stata la rappresentazione fotografica del fundus oculi che più di ogni altra cosa ha convinto coloro che avevano asserito che la dieta non ha nessuna efficacia nelle malattie vascolari ipertensive. Seppure il fundus oculi sia tipico per ogni individuo come lo sono le impronte digitali ed



Novembre 1944 Dicembre 1949

Fig. 24. Scomparsa dell'edema della papilla, delle emorragie e degli essudati in un caso di ipertensione maligna trattata con dieta di riso (L. B. F., 24).



Agosto 1948 Gennaio 1952

Fig. 25. Scomparsa della stella maculare in un caso di ipertensione maligna trattata con dieta di riso (D. T., f. 20).

inoltre le fotografie messe a confronto siano dello stesso paziente, qualcuno arriva attualmente ad accusarci di avere alterato i dati, sostenendo che le fotografie dei fundus normali erano state prese prima e quelle dei fundus anormali erano state invece prese più tardi.

La seguente affermazione del Dott. Goldring, nel capitolo sulla « dieta di riso nel trattamento della ipertensione » che fa parte della conclusione del Hypertension Seminars dell'American Journal Medicine del 1948, esprime più chiaramente questo punto di vista. Coloro che propongono la dieta di riso nel trattamento dell'ipertensione puntano sulla strabiliante incidenza della reversione del cosiddetto abito ipertensivo dell'elettrocardiogramma ai livelli normali, sulla diminuzione delle dimensioni del cuore e sulla regressione dell'edema della papilla. Questi aspetti dell'effetto della dieta di riso abbisognano urgentemente di una spiegazione. Infatti questi clamorosi dati vengono da una sola fonte che ha riportato dei brillanti successi con la dieta di riso ed essi non sono ancora stati confermati da altra fonte di osservazione. Finchè mancherà una simile conferma, la dieta di riso non avrà che un interesse casuale ».

Negli anni successivi tale conferma è stata fornita da un certo numero di ricerche compiute sia in America che altrove.

Fra i nostri stessi ammalati abbiamo un gruppo di 388 casi con avanzate retinopatie vascolari (edema della papilla, emorragie oppure essudati), nei quali è stato possibile fare fotografie delle cavità orbitali (prima e dopo, mese per mese), nei 100 mesi di dieta di riso. Quarantaquattro dei 388 pazienti avevano nefriti croniche, 344 avevano malattie ipertensive vascolari. Centoventicinque dei 388 casi avevano l'edema della papilla quando fu iniziata la dieta di riso. In quattro di questi, non vi è stato nessun cambiamento; in due l'edema della papilla è scomparso parzialmente, in 119 completamente. Duecentonovantasei pazienti avevano emorragie. In sette casi le emorragie sono aumentate, in dodici non vi è stato nessun cambiamento, in 46 le emorragie sono scomparse parzialmente ed in 231 completamente. Trecentoventotto pazienti avevano degli essudati; questi sono aumentati in cinque casi, in diciotto non vi è stato nessun cambiamento, in 79 gli essudati sono scomparsi parzialmente ed in 226 completamente.

La reversibilità del danneggiamento dei vasi sanguigni dimostrata dalla guarigione delle malattie retiniche è ancor più indicativa che non quella delle alterazioni cardiache e renali. Questa è stata per me la più convincente prova che la vecchia scuola errava nell'insistere che queste malattie erano necessariamente progressive e degenerative e che, nei pazienti affetti da ipertensione maligna, la morte era inevitabile in breve tempo. Il corso di queste malattie può essere cambiato con la semplicissima procedura che consiste nel sostituire i vari cibi normalmente inge-

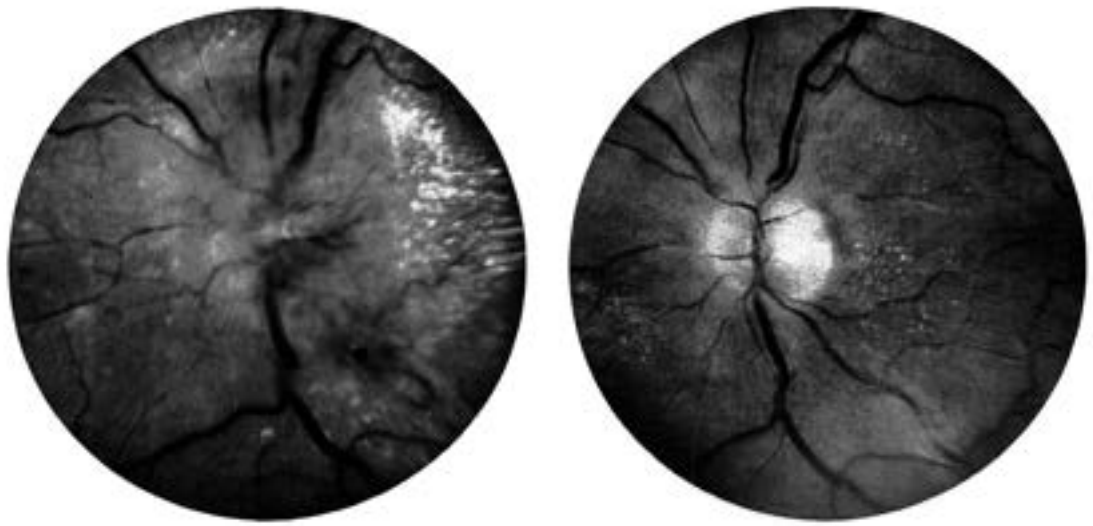


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Fig. 26. Scomparsa dell'edema della papilla, delle emorragie e degli essudati in un caso di ipertensione maligna trattata con dieta di riso (H. A., f. 45).

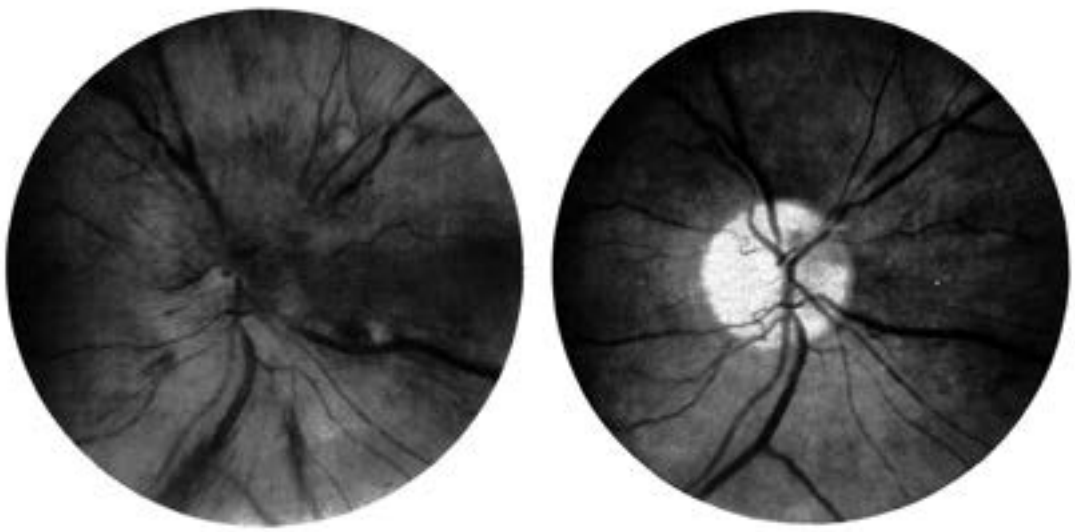

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Fig. 27. Scomparsa dell'edema della papilla, delle emorragie e degli essudati in un caso di ipertensione maligna trattata con dieta di riso (B. R., f. 60).

riti con una dieta a base di riso, di frutta, di zucchero. Ma più convincenti si fanno questi risultati più ovvio diventa che il trattamento dietetico intensivo deve iniziare quando la malattia è ancora nelle primissime fasi e non deve essere rimandato sino al momento, veramente di emergenza, rappresentato da qualche disastro vascolare. Il medico generico è il solo, normalmente, che si trova nella posizione di percepire i segni ed i sintomi molto prima che essi diventino allarmanti. Egli ha anche ogni occasione per prevenire tale forma di invalidità non obbligatoria e molte morti precoci nel consigliare energicamente un trattamento immediato e radicale.

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Wirkung der Reisdiät bei Experimenteller Hypertonie und bei Patienten mit Herz-, Nieren- und Gefässkrankheiten

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Wirkung der Reisdiät bei experimenteller Hypertonie und bei Patienten mit Herz-, Nieren- und Gefäßkrankheiten

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Wirkung der Reisdiät bei experimenteller Hypertonie und bei Patienten mit Herz-, Nieren- und Gefäßkrankheiten*, **.

Von
WALTER KEMPNER.

Mit 18 Textabbildungen.

(Eingegangen am 31. Oktober 1953.)

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** GUSTAV VON BERGMANN zum 75. Geburtstag mit vielen guten Erinnerungen und herzlichen Wünschen.

Die Lebensdauer von Ratten mit experimentell erzeugter Hypertonie kann durch Veränderung der Diät auf über das Zehnfache verlängert werden.

Wir haben die Wirkung der einzelnen Diätfaktoren an mehreren tausend Ratten untersucht, bei denen eine Niere eingekapselt und die andere entfernt worden war. Neben der Erhöhung des systolischen Blutdrucks von 100—110 auf 160—250 mm Hg kamen bei diesen Tieren alle Begleiterscheinungen vor, die wir von der schweren Hochdruckkrankheit beim Menschen kennen: Herzvergrößerung, Dekompensation, Arrhythmien, Schlaganfälle mit Lähmungen, Augenhintergrundsveränderungen, Konvulsionen, Urämie. Die erkrankten Tiere starben bei gewöhnlicher Rattenkost nach durchschnittlich 20 Tagen. (Die Lebensdauer gesunder Ratten ist ungefähr 1000 Tage.)

Ersetzte man die gewöhnliche Rattenkost durch andere Nahrung und hielt dabei einen konstanten Kochsalzgehalt von 25 mg täglich ein, so ergaben sich folgende Zahlen für die durchschnittliche Lebensdauer nach Beginn der Krankheit:

Fleisch	28 Tage
Reis	200 Tage;

bei einem konstanten Kochsalzgehalt von 100 mg täglich:

Fleisch	17 Tage
Erbsen	25 Tage
Brot	38 Tage
Reis	57 Tage;

bei Reisdiät mit verschieden großen Kochsalzzulagen:

bei 125 mg NaCl täglich	28 Tage
bei 100 mg NaCl täglich	57 Tage
bei 75 mg NaCl täglich	91 Tage
bei 50 mg NaCl täglich	129 Tage
bei 25 mg NaCl täglich	200 Tage.

Wir haben die Reisdiät bei mehr als 2000 Patienten mit Herz-, Nieren- und Gefäßkrankheiten angewandt. Chemische und klinische Resultate sind in ausführlichen Arbeiten in amerikanischen Zeitschriften veröffentlicht KEMPNER (1—13), PESCHEL (1950, 1952, 1953), STARKE (1950). Der vorliegende Beitrag für die Festschrift zu Ehren des 75. Geburtstags von G. VON BERGMANN soll kurz neben neuem Zahlenmaterial einige der Grundprinzipien und die Indikationen dieser radikalen Diätbehandlung besprechen.

Keiner meiner Patienten hat die Reisdiät gern gegessen und es erfordert Mühe und Geduld, sie bei Menschen mit durchschnittlicher Willenskraft länger als 2—3 Monate durchzuführen[1]. Die umfassendsten Arbeiten aus anderen Kliniken, in denen unsere Resultate bestätigt wurden, wie dem Rockefeller Hospital (DOLE und Mitarbeiter) und dem Goldwater Memorial Hospital (WATKIN und Mitarbeiter) in New York, dem Hospital T. de Alvear (DE SOLDATI und Mitarbeiter) in Buenos Aires, den Hôpitaux Henri-Rouselle und Lariboisière (LICHTWITZ und Mitarbeiter) in Paris und den Universitätskliniken in London, Manchester und Edinburgh (Report to the Medical Research Council), mußten sich deshalb auf Studien an im Höchstfall 100 Patienten beschränken.

[1] Mit FRANZ VOLHARD, dem die Schwierigkeiten der Diätbehandlung wohlbekannt waren, hatte ich darüber folgenden Briefwechsel:

Frankfurt, 9. 1. 50: „... Ich bin tief beeindruckt von Ihrer Arbeit Treatment of heart and kidney disease and of hypertensive and arteriosclerotic vascular disease with rice diet in den Annals of Internal Medicine, und ich wäre für einen Sonderabdruck sehr dankbar. Ich habe seit ca. 30 Jahren die *streng* salzfreie Kost mit bisweilen sehr gutem Erfolg durchgeführt, aber die Erfolge von Ihrer Reisdiät scheinen mir noch größer zu sein. Aber was mich wundert ist, daß Ihre Patienten Wochen und Monate lang diese eintönige Diät zu sich nehmen und nicht revoltieren. Haben Sie vielleicht auch diese Diät bei Diabetes mit Hochdruck und nephrotischem Syndrom (KIMMELSTIEL und WILSON) versucht? Ihre Methode imponiert mir sehr, noch mehr aber die Folgsamkeit Ihrer Patienten ..."

Durham, 18. 2. 50: „... Die Patienten zum strengen Befolgen der Reisdiät zu veranlassen, ist nicht immer leicht. Die meisten sind während der ersten drei oder vier Monate hier in Durham unter täglicher Kontrolle. Das wird nach der Entlassung in gewissem Ausmaß fortgesetzt durch periodische Urinuntersuchungen auf Natrium, Chlor etc. Die Patienten, die die schwersten Herz-und Augenhintergrundserscheinungen gehabt haben, folgen der Diät am besten. Bei Diabetikern ergab sich, daß sie nicht nur diese Diät gut vertragen, sondern daß die Insulinmenge herabgesetzt werden mußte. Eine Bemerkung darüber ist auf S. 561 der Arbeit 1948 ..."

Frankfurt, 28. 2. 50: „... Die Erfolge der Reisdiät sind ja überzeugend und insofern wohl besser als die meiner strengen kochsalzfreien Kost, insofern als es bei dieser gemischten Kost sehr viel schwerer ist, Fehler zu vermeiden und zu erreichen, daß die 24stündige Chloridausscheidung unter 1 g sinkt. Haben Sie denn beim essentiellen und malignen Hochdruck ohne Diabetes auch Furcht vor dem Cholesterin, weshalb Sie salzfreie Butter vermeiden, und warum verbieten Sie salzfreien Toast? Haben Sie auch einmal bei Patienten, die Übelkeit und Erbrechen bekommen haben, Zustände von Hypochlorämie bei der Reisdiät beobachtet? Die größte Schwierigkeit finde ich darin, daß die Patienten die eintönige Kost nicht weiter essen wollen oder können, weil sie ihnen widersteht ..."

Der Gehalt an Kochsalz, Fett, Cholesterin und Eiweiß ist in der Reisdiät weit geringer als in jeder anderen Diät zur Behandlung der Hypertonie, Arteriosklerose, Herz-, Nieren- und vasculären Netzhautkrankheiten. Sie besteht ausschließlich aus Reis, Zucker, Früchten und Fruchtsäften und enthält in 2400 Calorien 25 g Eiweiß, weniger als 5 g Fett, kein Cholesterin, 70—120 mg Natrium und 140—240 mg Chlorid (Abb. 1). Die Calorienmenge, die ein Patient jeweils erhält, richtet sich danach,

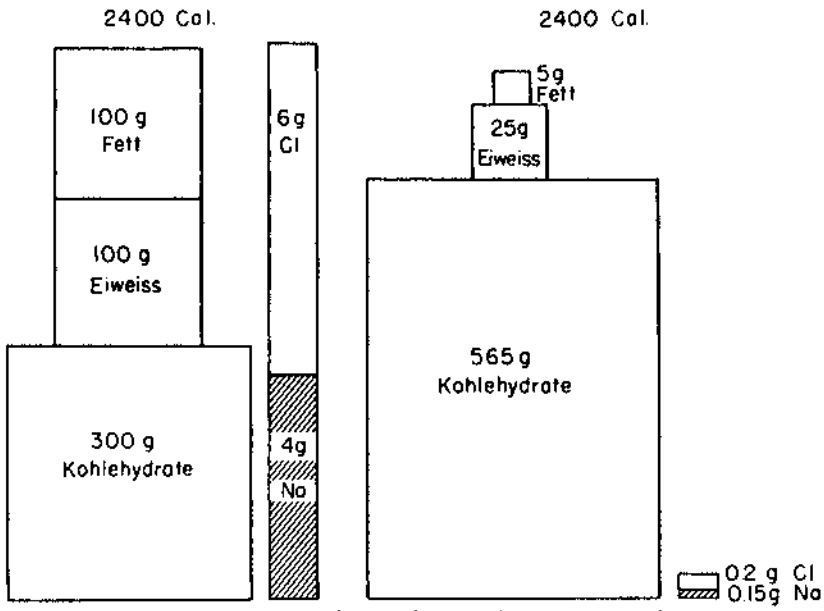


Abb. 1. Zusammensetzung der Reisdiät, verglichen mit normaler Diät.

ob Gewichtszunahme oder -abnahme erwünscht ist. Natrium-, Chlorid- und Fettzufuhr kann noch verringert werden, wenn Früchte und Fruchtsäfte fortgelassen und nur weißer Reis, Tee und Zucker gegeben werden. In 2400 Calorien einer solchen „Minimal"-Diät sind nur noch 20 mg Natrium, 70 mg Chlorid und 0,9 g Fett. In einer Anzahl von Fällen haben wir zusätzlich Kationenaustauschpräparate angewandt, um das Natrium aus dem Magendarmkanal zu entfernen. Jedoch enthält diese Arbeit weder die Resultate der „Minimal"-Diät, noch die der Kombination mit Kationenaustauschharz. Wir beschreiben hier lediglich die Wirkung der gewöhnlichen Reisdiät — ohne alle Medikamente außer den Vitaminen A, B, C, D.

Die Reisdiät ist eintönig, aber sie hat den praktischen Vorteil der Einfachheit. Keine umständlichen Anweisungen sind notwendig und sie ist leicht zuzubereiten. Die Chloridausscheidung im Urin beträgt nach

1—2 Monaten Diät 20—100 mg, die Natriumausscheidung 3—20 mg in 1000 cm³ Urin. Zahlen, die höher sind, ausgenommen bei Patienten, die Ödeme verlieren oder die chronische oder akute „Salzverlierer" sind, zeigen, daß — wissentlich oder unwissentlich — Fehler in der Diät begangen worden sind.

Kochsalzeinschränkung.

Die Hauptgefahr einer so radikalen Kochsalzeinschränkung ist die Möglichkeit einer Hypochlorämie oder Hyponaträmie (möglicherweise mit Erhöhung des Reststickstoffs), häufig kombiniert mit Hyperkalämie und Alkalose.

Tabelle 1. *Einfluß der Nierenfunktionsschädigung auf die Häufigkeit von Elektrolytstörungen im Serum (80 Reisdiät-Patienten mit schwerem Nierenschaden).*

Serum-Elektrolytstörung	Zahl der Patienten	Rest-N mg in 100 cm³ (Durchschnitte)	PSP %-Ausscheidung in 2 Std (Durchschnitte)
Keine, nach 3 Monaten Diät	36	61	29
Nach 3 Monaten . . .	6	52	28
Nach 2 Monaten . . .	15	77	21
Nach 1 Monat	14	121	14
Nach $^1/_2$ Monat . . .	6	72	14
Vor Beginn der Diätbehandlung	3	117	2

95% unserer Patienten, die keine Zeichen einer vorgeschrittenen Nierenschädigung zeigten, konnten die extreme Kochsalzeinschränkung gut vertragen. Die normale, ungestörte Regulationsfunktion der Niere bewirkt eine maximale Einsparung der Elektrolyte; das Serumchlorid sinkt etwas ab, das Bicarbonat steigt entsprechend an, Natrium, Kalium und Gesamtionen bleiben praktisch unverändert. Jedoch bei 5% der Patienten kam es zu Störungen der Elektrolytkonzentrationen, obgleich eine ernstere Nierenschädigung nicht nachweisbar war (PESCHEL 1952). Bei Patienten mit schlechter Nierenfunktion erhöhte sich dieser Prozentsatz auf 55% (PESCHEL 1953). In jedem Falle ist deshalb die ständige klinische und chemische Kontrolle bei der Reisdiät unerläßlich. Tabelle 1 zeigt, wie weit die Höhe des Reststickstoffs und das Ergebnis der Nierenfunktionsprüfungen eine Voraussage zulassen, ob der Patient die Reisdiät in ihrer strikten Form ohne Na- oder Cl-Zusätze vertragen kann.

Cholesterin- und Fetteinschränkung.

Die Erzeugung von Arteriosklerose durch Cholesterinfütterung bei Kaninchen ist seit den Versuchen von ANITSCHKOW bekannt. Die Bedeutung der Cholesterinämie beim Menschen in Fällen von Arteriosklerose, Coronarinsuffizienz, Diabetes und exsudativer Netzhauterkrankung ist auch bekannt. Wir haben bei 70% unserer Patienten mit Hochdruckkrankheit eine Hypercholesterinämie gefunden.

Tabelle 2. *Wirkung der Reisdiät auf den Cholesteringehalt im Serum bei 800 Patienten mit Hypercholesterinämie (Durchschnittliche Dauer der Diät 124 Tage).*

	Zahl der Patienten	%	Cholesterin	
			vor Reisdiät (Durchschnitt)	nach Reisdiät (Durchschnitt)
Abnahme	747	93	283	205
Auf 220 oder darüber .	257	32	301	245
Auf 219 oder darunter	490	61	273	184
Zunahme oder keine Änderung	53	7	262	287

Es ist vielfach behauptet worden, Cholesterineinschränkung in der Diät habe keinen Einfluß auf eine bestehende Hypercholesterinämie. Diese Behauptung ist so wahr wie diejenige, daß Salzeinschränkung keinen Einfluß auf die Hypertonie habe. Die Cholesterin- und Fetteinschränkung, genau so wie die Salzeinschränkung, muß allerdings radikal sein, d. h. sie muß, wie in der Reisdiät, praktisch einem völligen Entzug gleichkommen, um die beabsichtigte Wirkung hervorzubringen. Von 800 Patienten mit Hypercholesterinämie, die wir mit der Reisdiät behandelt haben, ist der Cholesteringehalt im Serum bei 93% niedriger geworden (Tabelle 2). Diese Tatsache ist bedeutsam, gleichgültig welche Mechanismen als Ursache dafür anzusehen sind. Neben der Cholesterin- und Fettarmut der Diät mögen, worauf H. RÜSTOW hingewiesen hat, der Reichtum an Vitamin C und die Salzarmut, durch Beeinflussung der Nebennieren, eine Rolle spielen.

Die Reisdiät bewirkt sowohl eine Abnahme des freien Cholesterins als der Cholesterinester im Serum. Das Verhältnis von Lipoidphosphor im Serum zum Cholesterin ändert sich zugunsten des Lipoidphosphors.

Eiweißeinschränkung.

Die Rolle des Eiweißes in der Entstehung und Beeinflussung der verschiedenen Gefäßerkrankungen soll nicht in dieser Arbeit erörtert werden. Als vor 10 Jahren die Erfahrungen an den ersten 150 Reisdiät-Patienten veröffentlicht wurden, war es die allgemeine Ansicht, daß die diätetische Behandlung von Hypertonie und Arteriosklerose wertlos sei: die Einschränkung von Salz, Fett, Cholesterin und Eiweiß erschien unangebracht. In bezug auf Salz, Fett und Cholesterin hat sich dieser Standpunkt geändert; die Wichtigkeit dieser Diätfaktoren ist jetzt allgemein bekannt. Über die Rolle des Eiweißes besteht noch keine Übereinstimmung.

Welchen Wert auch immer die Eiweißeinschränkung haben mag: von allen Diäten zur Behandlung der Hypertonie und Arteriosklerose, der Krankheiten des Herzmuskels, der Niere und der Netzhaut hat die Reisdiät den geringsten Gehalt an Eiweiß, in 2400 Calorien etwa 25 g.

Auch heute begegnet man noch der Ansicht, ein Minimum von 50 g Eiweiß pro Tag sei notwendig zur Verhütung eines Eiweißdefizits mit folgender Anämie, Hypoproteinämie und Ödemen. Diese Ansicht beruht darauf, daß bei völligem Hungern die Gesamtstickstoffausscheidung in Stuhl und Urin etwa 8 g täglich beträgt; um diesen Verlust zu ersetzen, müsse man dem Körper die entsprechende Menge Eiweiß wieder zuführen: $8 \times 6{,}25 = 50$ g, das sog. Erhaltungseiweiß. Wenn jedoch bei völligem Fehlen von Eiweiß in der Nahrung genügend große Mengen von Kohlenhydraten vorhanden sind, um den Calorienbedarf zu decken, so sinkt die Gesamtstickstoffausscheidung von 8 g auf weniger als 4 g. Diese eiweißsparende Wirkung der Kohlenhydrate ist ein wichtiger Faktor in der Reisdiät.

Bei einer Eiweißzufuhr von 125 g beträgt die tägliche Stickstoffausscheidung in Stuhl und Urin 20 g, im Hungerzustand 8 g, nach durchschnittlich 88 Tagen Reisdiät etwa 4 g (PESCHEL 1950). Die Patienten auf der Reisdiät befinden sich also im Stickstoffgleichgewicht mit einer täglichen Eiweißzufuhr von $4 \times 6{,}25 = 25$ g. Es entwickelt sich keine Anämie, sondern gewöhnlich wird ein geringer Anstieg des Hämoglobins gefunden; der Eiweißgehalt im Serum bleibt der gleiche oder steigt ebenfalls an, und es bilden sich nicht nur keine Ödeme, sondern, falls sie vorhanden sind, werden sie ausgeschwemmt. Wo daher eine Herabsetzung des Stickstoff-Stoffwechsels wünschenswert erscheint, wie in vielen Fällen von akuter und chronischer Nephritis und Nephrosklerose, sollte derjenigen Diät der Vorzug gegeben werden, bei welcher der Gesamtstickstoffumsatz am geringsten ist. Aus den oben angeführten Zahlen ist ersichtlich, daß der völlige Nahrungsentzug (von VOLHARD als Therapie der akuten Glomerulonephritis empfohlen) mit einer Stickstoffausscheidung von 8 g täglich zwar der gewöhnlichen Kost mit einer Stickstoffausscheidung von 20 g vorzuziehen ist; aber die Reisdiät mit einer Stickstoffausscheidung von nur 4 g pro Tag ist wirksamer als Hungern und hat außerdem den Vorteil, daß sie über Monate und Jahre gegeben werden kann (Tabelle 3).

Tabelle 4 zeigt den Einfluß der Reisdiät auf den Reststickstoff und Harnstoff im Blut von 950 nichturämischen Patienten mit Hochdruckkrankheit. Bei gewöhnlicher Kost ist der Reststickstoff im Blut durchschnittlich 17%, der Harnstoff 62% höher als bei der Reisdiät.

Selbst bei Patienten mit gesunden Nieren und normalem Blutharnstoff und Reststickstoff ist es ratsam die Eiweißzufuhr zu verringern,

Tabelle 3. *Unterschiede zwischen Hunger und Reisdiät. Blut- und Urinbefunde und Stickstoffbilanz.*

	Hunger	Reisdiät
Hämoglobin	vermindert	unverändert
Serum Calcium	vermindert	unverändert
Plasma Proteine, Albumin/Globulin	vermindert	unverändert oder erhöht
Blutharnstoff und Rest-Stickstoff	erhöht	vermindert
Blutzucker	vermindert	unverändert
Kohlenhydrattoleranz	vermindert	erhöht
Alkalireserve des Plasmas	vermindert	erhöht
Blut- und Gewebsflüssigkeitsvolumen	unverändert	vermindert
Stickstoffbilanz	negativ	im Gleichgewicht
Kreatin, Ammoniak, organische Säuren im Urin	vermehrt	vermindert

wenn das Salz in der Diät maximal eingeschränkt wird, da ein Absinken von Natrium- oder Chlorionen im Serum (wie man von starken Schweißausbrüchen, Diarrhöen oder der ADDISONschen Krankheit weiß) häufig eine Azotämie zur Folge hat.

Tabelle 4. *Einfluß der Reisdiät auf Blutharnstoff und Rest-N von 950 nichturämischen Patienten (Rest-N unter 45 mg/100 cm³) (Durchschnitte).*

	Vor der Reisdiät	Nach 110 Tagen (Durchschnitt) auf Reisdiät
Reststickstoff (mg/100 cm³ Blut)	34	29
Harnstoff-N (mg/100 cm³ Blut)	14,1	8,7

Niemand zweifelt daran, daß bei fortgeschrittener Niereninsuffizienz und Urämie die Eiweißzufuhr auf ein Minimum zu beschränken ist. Jedoch wird dies meist solange verschoben, bis die Funktionsprüfungen ein weitgehendes Versagen der Niere anzeigen und der Reststickstoff auf über 100 mg gestiegen ist. Mir scheint es zweckmäßiger, bei progressiven Erkrankungen wie chronischer Nephritis oder vasculärer Schrumpfniere, mit allen verfügbaren therapeutischen Maßnahmen an dem Tage zu beginnen, an dem die Diagnose gestellt ist und nicht damit auf die Alarmsignale des endgültigen Nierenzusammenbruchs zu warten.

Indikationen.

Die Reisdiät ist indiziert bei akuter und chronischer Nephritis. Die Häufigkeit der Spontanheilungen bei akuter Glomerulonephritis macht die statistische Auswertung jeder Behandlungsmethode schwierig. Bei der chronischen Nephritis hingegen ist die erfolgreiche Wirkung der Reisdiät leicht nachweisbar: Senkung des Blutdrucks, Besserung des Harnbefundes, Verschwinden von Herzvergrößerung, EKG-Veränderungen, Netzhautblutungen, Exsudaten und Stauungspapille (Abb. 2, 3, 4, 5).

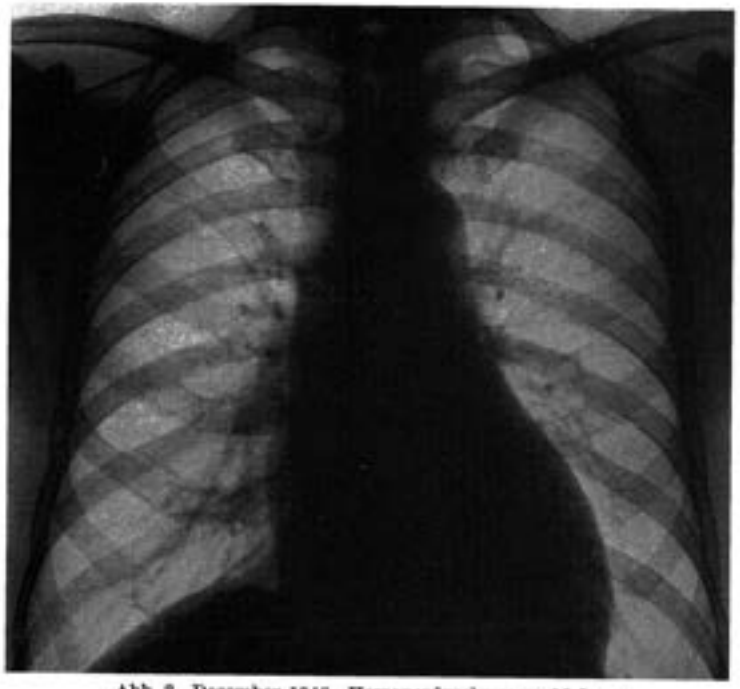


Abb. 2. Dezember 1948. Herzquerdurchmesser 15,5 cm (Brustdurchmesser 30,5 cm).

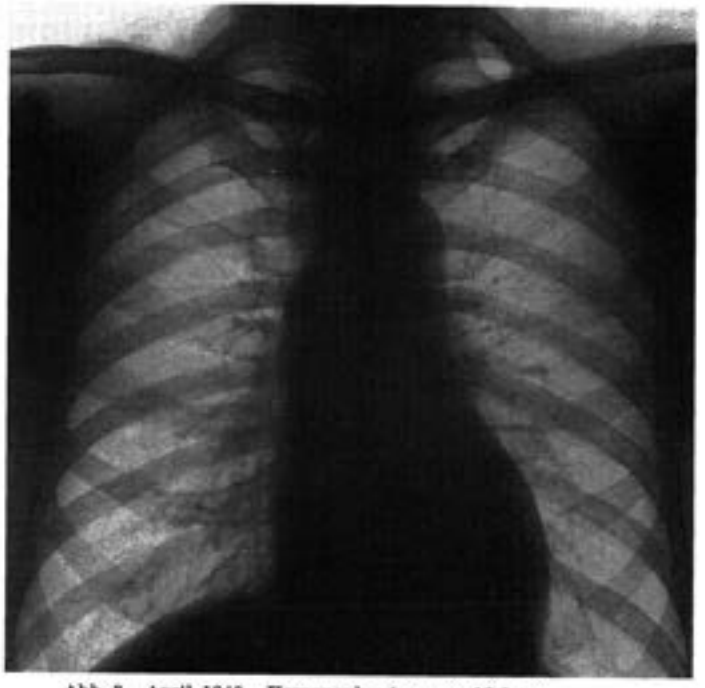


Abb. 3. April 1949. Herzquerdurchmesser 12,5 cm (Brustdurchmesser 29,8 cm).

Abb. 2. u 3. Wirkung der Reisdiät bei chronischer Nephritis; Abnahme der Herzvergrößerung. O. L. (♂, 42 Jahre). Als Kind Scharlach ohne Komplikationen. 1944 „erhöhter Blutdruck"; Proteinurie. Keine Beschwerden. 1945 Kopfschmerzen; „Herzvergrößerung". Seit 1946 salzarme Diät. — Erste Untersuchung in Duke Hospital Dezember 1948: Blutdruck 214/138; Rest-N 52; Phenolsulfonphthaleinausscheidung in 2 Std 35 %; Proteinurie 1,3 g/Liter. Beginn der Reisdiät: 31. Dezember 1948. — April 1949: Blutdruck 180/120; Rest-N 34; Proteinurie 0,28 g/Liter. Herz wesentlich kleiner.

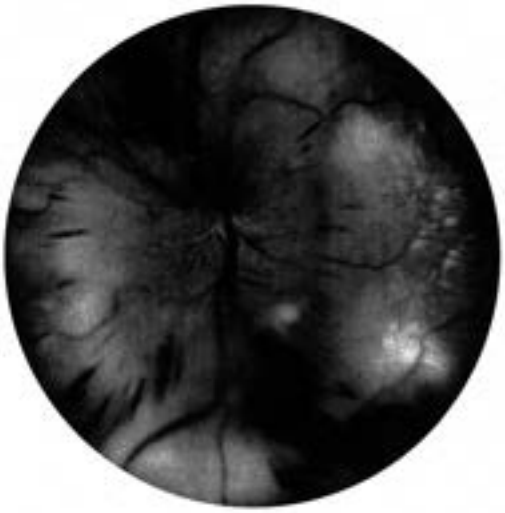


Abb. 4. Oktober 1948.

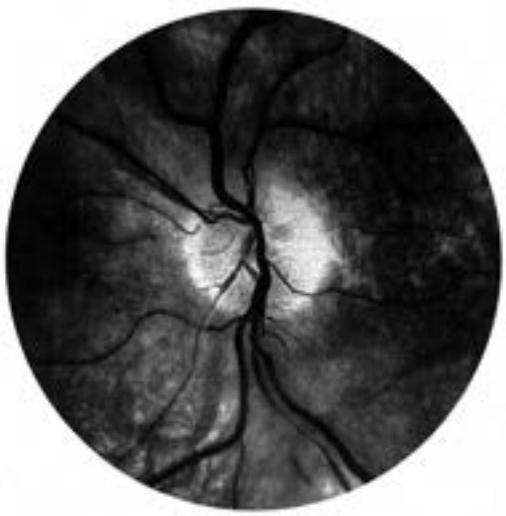
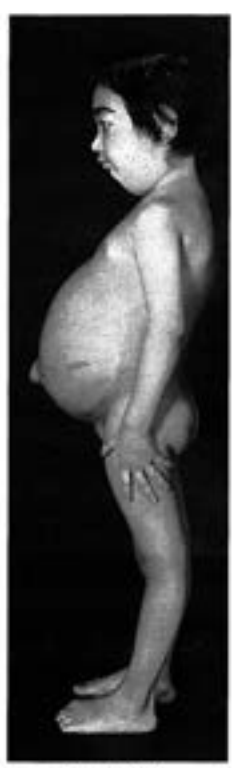
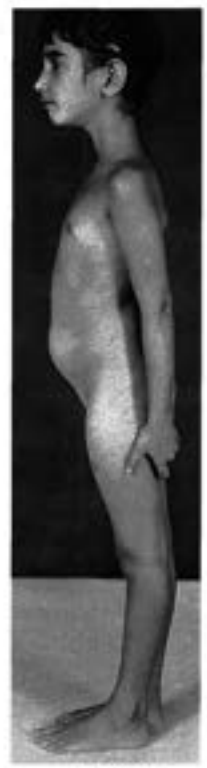


Abb. 5. Juli 1949.

Abb. 4. u. 5. Wirkung der Reisdiät bei chronischer Nephritis; Verschwinden von Stauungspapille, Netzhautblutungen und Exsudaten. H. R. (♂, 39 Jahre). 1919 akute Nierenerkrankung. Seitdem Proteinurie. 1947 normaler Blutdruck. Januar 1948 Krankenhausaufnahme wegen starker Kopfschmerzen; Blutdruck 180 systolisch. Juli 1948 Sehstörung. September 1948 kurze Bewußtlosigkeit; Kopfschmerzen, Übelkeit, Erbrechen und erneute Sehstörungen. — Erste Untersuchung in Duke Hospital 1. Oktober 1948: Blutdruck 240/140; Rest-N 114; Phenolsulfonphthaleinausscheidung in 2 Std 10%. Beiderseitige Stauungspapille, massive Netzhautblutungen und Exsudate. Beginn der Reisdiät Oktober 1948. Bald danach Aufhören von Kopfschmerzen, Übelkeit und Erbrechen. Nach $3^1/_2$ Monaten geringe Diätzulagen. — Juli 1949: Blutdruck 190/114; Rest-N 54; Stauungspapille, Blutungen und Exsudate verschwunden.

Die Reisdiät ist ebenfalls indiziert bei Nephrosen. Bei den meisten Patienten verschwanden Ascites, Ödeme, Albuminurie und Hypercholesterinämie und trotz der stark beschränkten Eiweißzufuhr in der Diät, stieg das Serumeiweiß wieder zu normalen Werten an (Abb. 6, 7),





März 1949.		Juli 1953.
2,4	Proteinurie (g/1000 cm³)	0,09
3,3	Serumeiweiß (g/100 cm³)	7,5
0,6	Albumin (g/100 cm³)	4,9
2,7	Globulin (g/100 cm³)	2,6
510	Serumcholesterin (mg/100 cm³)	242

Abb. 6. u 7. Beeinflussung der Nephrose durch Reisdiät. A. M. (♀, 4 bzw. 8 Jahre).

Die Reisdiät ist indiziert bei Kreislaufdekompensation, gleichgültig ob die Herzinsuffizienz durch Klappenfehler oder durch Arteriosklerose, Hochdruckkrankheit, Nierenerkrankungen, Gelenkrheumatismus, Lupus erythematodes hervorgerufen ist. Abb. 8, 9 zeigt das Verschwinden der Herzvergrößerung bei einem Patienten mit Aorteninsuffizienz und -stenose.

Patienten mit Angina pectoris mit oder ohne Myokardinfarkt sollten mit der Reisdiät behandelt werden. Hier fällt der Therapie eine doppelte

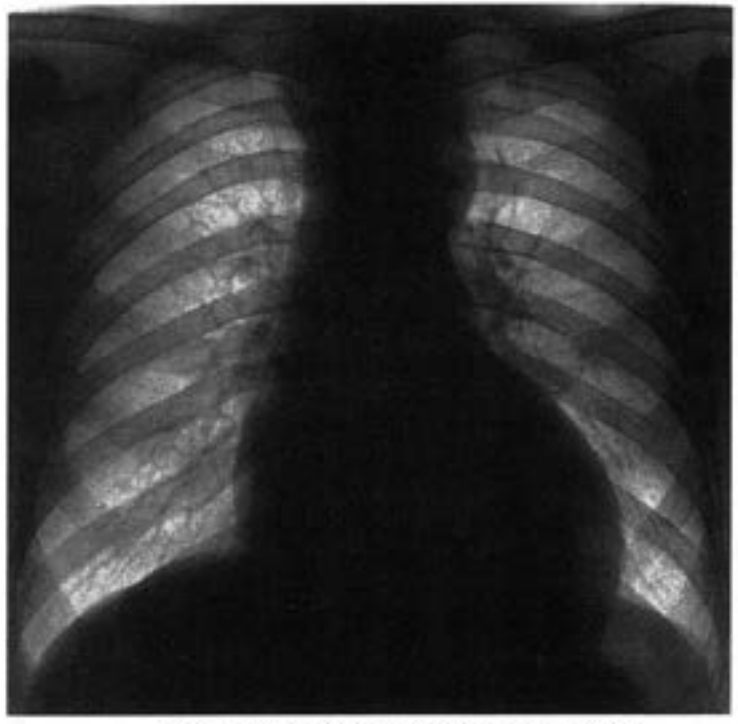


Abb. 8. August 1948. Herzquerdurchmesser 17,3 cm (Brustdurchmesser 31,2 cm).

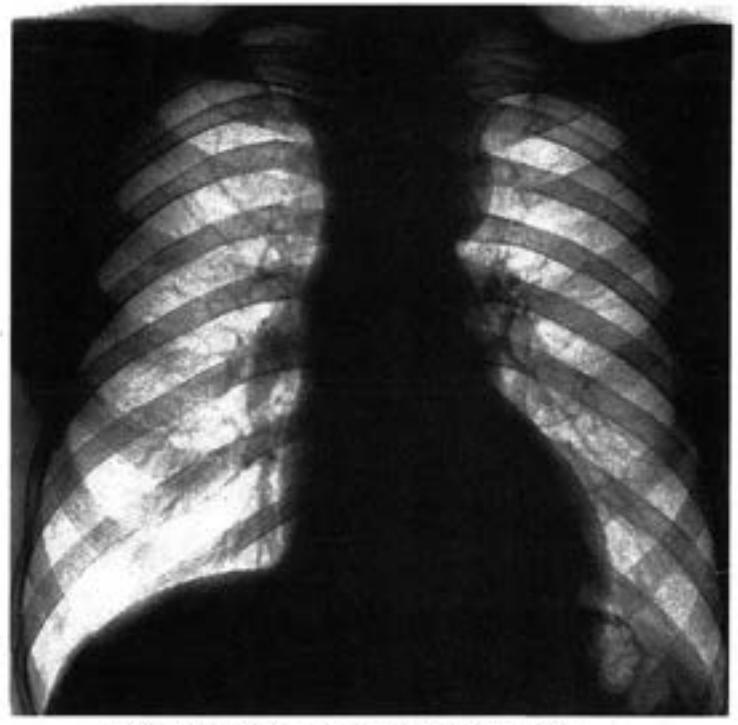


Abb. 9. März 1950. Herzquerdurchmesser 14,6 cm (Brustdurchmesser 30,6 cm).

Abb. 8. u. 9. Wirkung der Reisdiät bei Aorteninsuffizienz und -stenose. Abnahme der Herzvergrößerung. H. W. (♂, 55 Jahre). Gelenkrheumatismus mit 18 Jahren; mehrere Rezidive zwischen 19. und 40. Lebensjahr. Patient weiß von Klappenfehler seit 1938. Keine Beschwerden bis 1942. Seitdem ab und zu „Herzschmerzen" und Atemnot. Juli 1948 heftiger nächtlicher Anfall von „Herzschmerzen". Digitalis. — Erste Untersuchung in Duke Hospital August 1948: Blutdruck 130/64; Herz vergrößert, systolisches und diastolisches Aortengeräusch. Leber nicht vergrößert, keine Ödeme. Wassermann negativ. EKG: verlängerte Überleitungszeit und intraventrikulärer Block. Beginn der Reisdiät 22. August 1948. Digitalis abgesetzt. Nach 3 Monaten Diätzulagen. — März 1950: Patient beschwerdefrei. Herz wesentlich kleiner.

Aufgabe zu: einerseits den Vorgängen entgegenzuwirken, welche zu einer Verringerung der Coronardurchblutung führen (vgl. den Abschnitt über Cholesterin), andrerseits den Energiebedarf des Herzmuskels soweit wie möglich herabzusetzen.

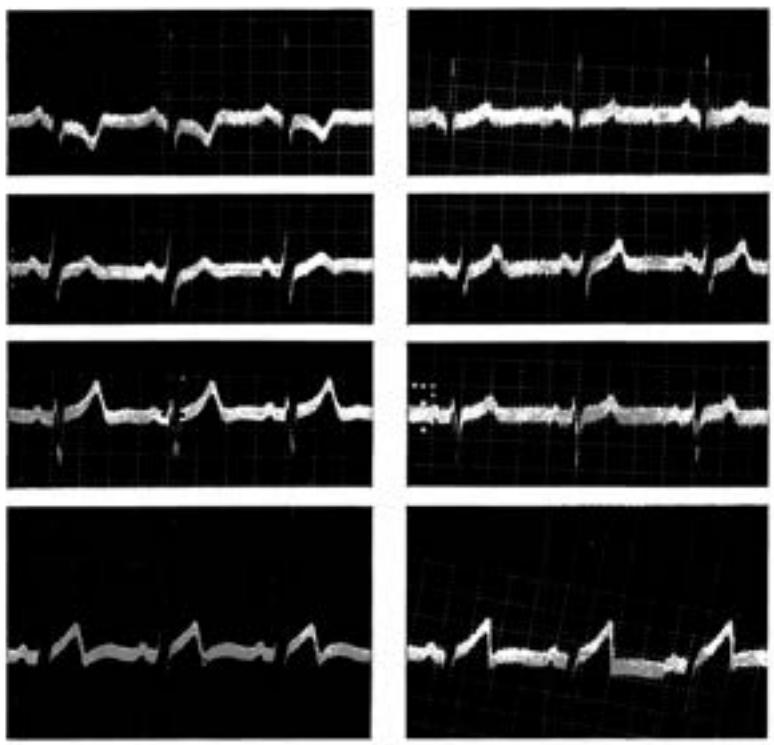


Abb. 10. Februar 1949. Abb. 11. Oktober 1951.

Abb. 10. u. 11. Wirkung der Reisdiät bei Hochdruckkrankheit. Die negative T_1-Zacke im EKG wird positiv. I. W. (♂, 42 Jahre). 1943 starke Kopfschmerzen und Schwindel; Blutdruck 160/105; in den folgenden Jahren um 170/110. 1947 4 Monate salzarme Diät. 1948 Blutdruck 225/120. Kein Digitalis. — Erste Untersuchung in Duke Hospital Februar 1949: Blutdruck 230/146; Netzhautblutungen und Exsudate; Herzvergrößerung; EKG zeigt negatives T_1. Beginn der Reisdiät 10. Februar 1949. Nach 4 Monaten geringe Zulagen. — Oktober 1951: Blutdruck 154/105; Augenhintergrund normal; T_1 positiv.

Die Reisdiät ist indiziert bei Diabetes mellitus mit Nieren- oder Gefäßkomplikationen. Bei den ersten Fällen (die wir wegen schwerer Augenhintergrundsveränderungen behandelten) hatten wir einen Anstieg des Blutzuckers erwartet und rechneten damit, die Insulinmengen erhöhen zu müssen. Doch zeigte sich, daß die Reisdiät von Diabetikern nicht nur gut vertragen wird, sondern daß sogar häufig der Blutzucker sinkt und geringere Insulinmengen benötigt werden.

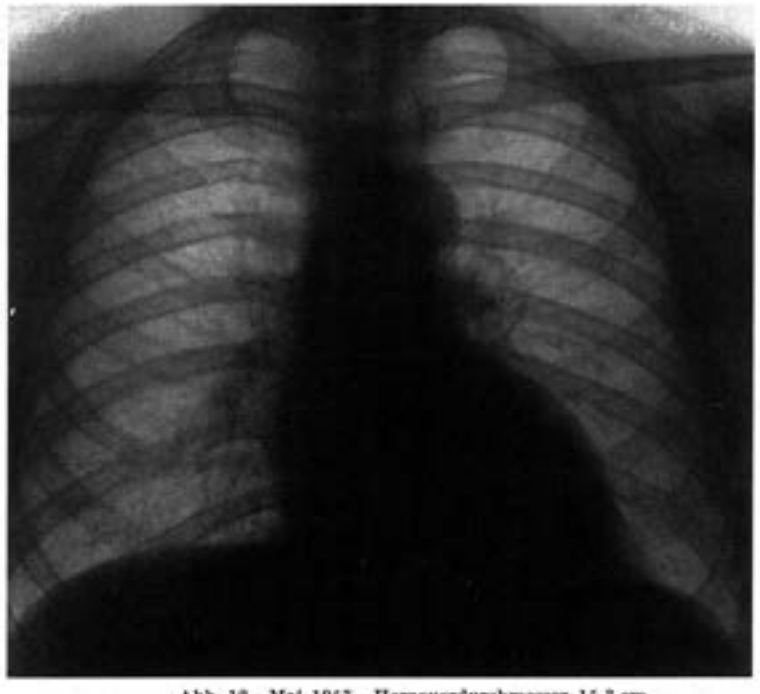


Abb. 12. Mai 1953. Herzquerdurchmesser 15,3 cm (Brustdurchmesser 33,2 cm).

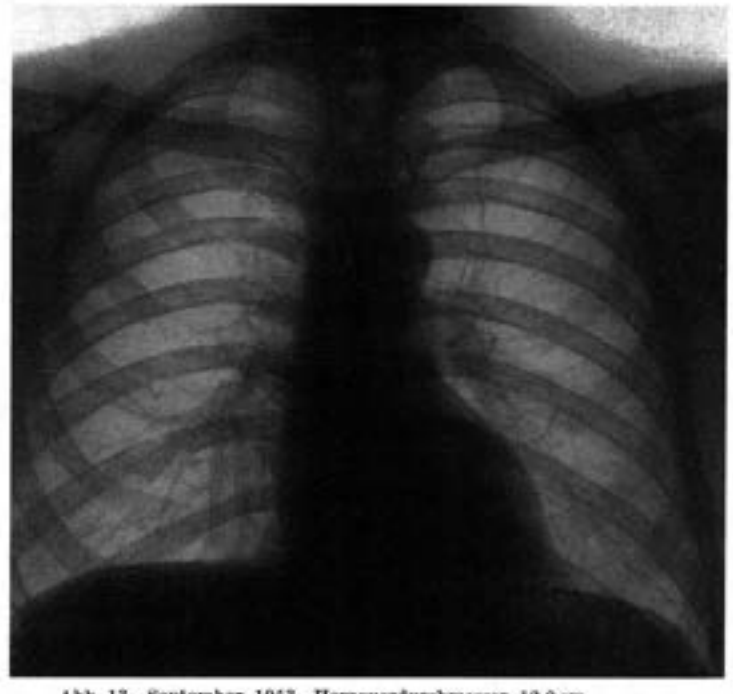


Abb. 13. September 1953. Herzquerdurchmesser 12,0 cm (Brustdurchmesser 32,5 cm).

Abb. 12 u. 13. Wirkung der Reisdiät bei Hochdruckkrankheit. Abnahme der Herzgröße. M. H. (♂, 35 Jahre). 1944 Blutdruck 150/90. 1948 Nierenkolik; Blutdruck 160/100. 1950 „Herzschmerzen", leichte Atemnot, Kopfschmerzen, Netzhautblutungen. War angeblich auf Reisdiät Oktober bis Dezember 1950. Danach „Wohlbefinden". Seitdem mehr oder minder salzarme Diät. — Erste Untersuchung in Duke Hospital 14. Mai 1953: Blutdruck 235/155; Netzhautblutungen und Exsudate; Herzvergrößerung; im EKG negatives T_1. Beginn der Reisdiät 16. Mai 1953. — September 1953: Blutdruck 134/90; Netzhautblutungen und Exsudate verschwunden; positives T_1. Herz wesentlich kleiner.

Wir haben 48 Diabetiker durchschnittlich 14 Monate mit der Reisdiät behandelt. Bei 17 Patienten änderte sich der Blutzucker um mehr als 30 mg; bei 3 nahm er zu, bei 14 ab. Bei 19 von den 48 Patienten mußte

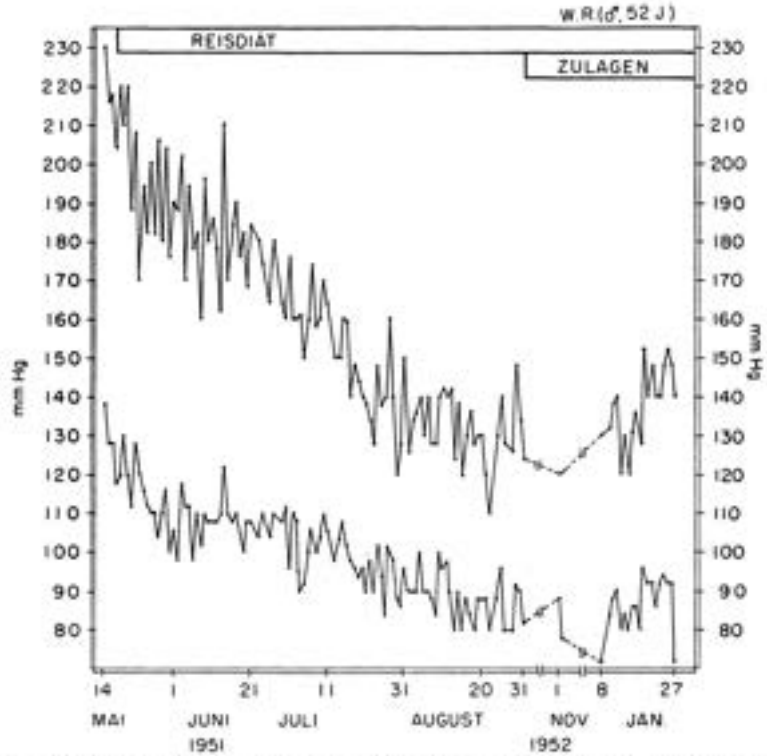


Abb. 14. Wirkung der Reisdiät bei maligner Hochdruckkrankheit. Senkung des Blutdrucks. 1937 „leichte Blutdruckerhöhung". 1945—1948 Blutdruck um 160/90; keine Beschwerden. 1949 Blutdruck 175/107 bis 200/115; „sehr nervös". Seit 1950 Sehstörungen; seit April 1951 können nur noch Konturen erkannt werden. — Erste Untersuchung in Duke Hospital Mai 1951: Blutdruck 230/130; Stauungspapille, Netzhautblutungen und Exsudate. Beginn der Reisdiät 17. Mai 1951. Nach 4 Monaten Blutdruck normal. Augenhintergrund beinahe normal. Blutdruck steigt nach Diätzulagen etwas an; Netzhauterkrankung heilt völlig. — Oktober 1952: alle Zeichen von malignem Hochdruck verschwunden.

die Insulinmenge verändert werden: 4 brauchten mehr, 15 weniger Insulin.

Die Reisdiät ist indiziert bei Arteriosklerose und bei Hochdruckkrankheit. Eine große Anzahl von Patienten mit „benignem" Hochdruck — mit und ohne kritische Komplikationen — konnte durch die Diät entschieden gebessert werden (Abb. 10, 11, 12, 13). Das gleiche gilt für Patienten mit „malignem" Hochdruck mit schweren Schädigungen des Herzens, der Nieren und des Augenhintergrundes. (Abb. 14, 15, 16, 17, 18).

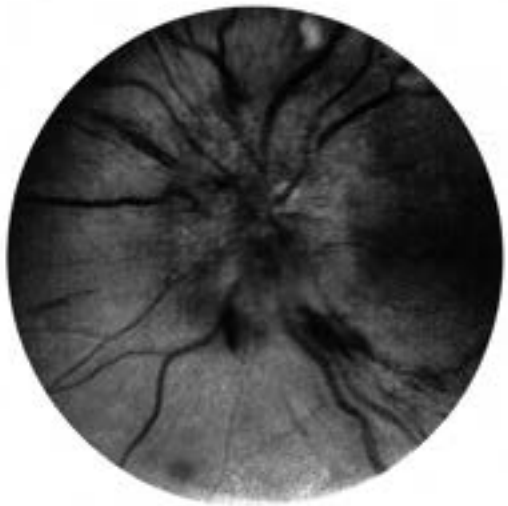


Abb. 15. August 1952.

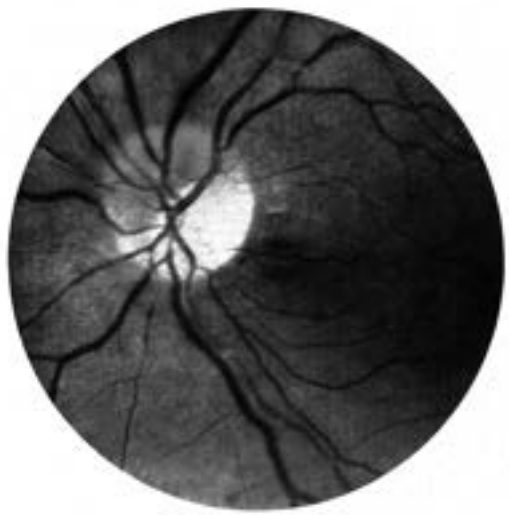


Abb. 16. Dezember 1952.

Abb. 15. u. 16. Wirkung der Reisdiät bei maligner Hochdruckkrankheit. Verschwinden von Stauungspapille, Netzhautblutungen und Exsudaten. B. R. (♀, 60 Jahre). Bei dieser Patientin war die Stauungspapille so hochgradig, daß der Ophthalmologe von Duke Hospital, Dr. Banks Anderson, einen Hirntumor für wahrscheinlich hielt. Als er 10 Monate nach Beginn der Reisdiät die Patientin wieder untersuchte, schrieb er in seinem Bericht: „Wie ich aus meinen Aufzeichnungen ersehe, war ich, als ich die Patientin zuerst sah, der Meinung, daß die Stauungspapille zu ausgedehnt sei, um allein durch Hypertonie erklärt werden zu können. Ich hatte unrecht. Bei der heutigen Untersuchung sind keine Anzeichen von Stauungspapille, Netzhautblutungen und Exsudaten mehr vorhanden." Die Blutdruckwerte der Patientin waren: August 1952 (Beginn der Reisdiät) 250/137, Dezember 1952 184/97, Juni 1953 179/87.

In einer Gruppe von 860 Patienten, die 90 Tage oder länger (durchschnittlich 146 Tage) auf der Reisdiät waren, kam es bei 709 Patienten

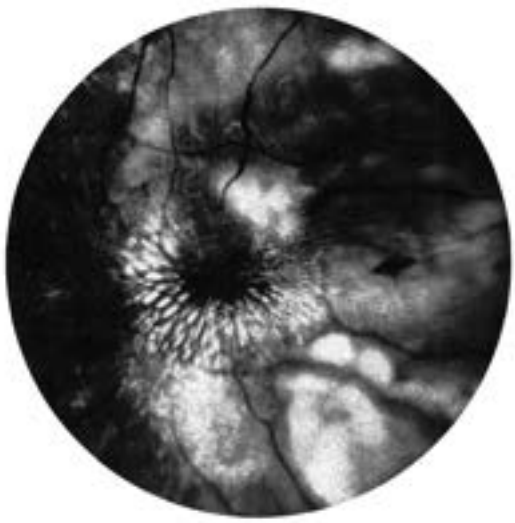


Abb. 17. August 1948.

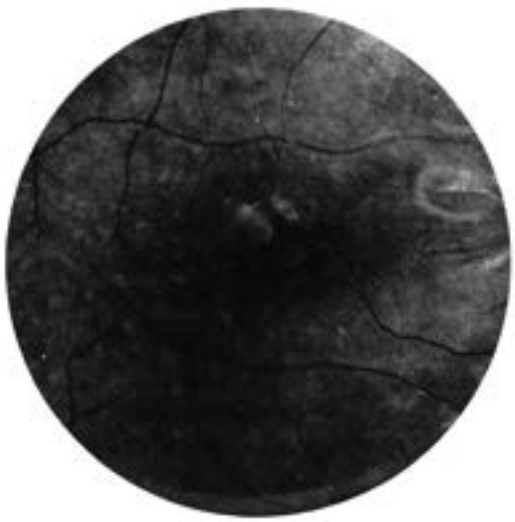


Abb. 18. Januar 1951.

Abb. 17. u. 18. Wirkung der Reisdiät bei maligner Hochdruckkrankheit: Verschwinden massiver Macula-Exsudate. D. T. (♀, 20 Jahre). Erste Untersuchung in Duke Hospital August 1948: Stauungspapille, Netzhautblutungen und Exsudate. Blutdruck 205/151. Nach 4 Monaten Reisdiät Blutdruck 105/78. Augenhintergrundsveränderungen verschwunden und nicht wieder aufgetreten, obgleich Patientin die Diät nur noch 1 Monat länger befolgte. Januar 1951, 2 Jahre nachdem die Diät aufgegeben war: Blutdruck 120/80; Augenhintergrund normal.

(82,4%) zu einem wesentlichen Absinken des Blutdrucks: von durchschnittlich 195/114 mm Hg auf durchschnittlich 145/91. Bei 291 Patienten (33,8%) sank der Blutdruck zur Norm: von 180/106 auf 127/81 (Durchschnitte). Je länger die Patienten die Reisdiät befolgten, desto höher war der Prozentsatz an positiven Resultaten.

In einer Gruppe von 420 Hochdruckkranken liegen Vergleichselektrokardiogramme nach mindestens einem Monat Behandlungsdauer vor. Bei 120 dieser Patienten war bei Beginn der Reisdiät die T_1-Zacke negativ (ohne Digitalis oder Anzeichen von Infarkt). Sie blieb negativ bei 68 (nach einer Behandlungsdauer von durchschnittlich 7 Monaten); bei 52 wurde sie positiv (nach durchschnittlich 10 Monaten). Bei keinem der 300 Patienten dieser Gruppe, deren T_1-Zacke bei Beginn der Behandlung positiv gewesen war, wurde sie (im Laufe von durchschnittlich 11 Monaten Reisdiät) negativ.

In einer Gruppe von 500 Patienten mit Hochdruckkrankheit, die mindestens 1 Monat, durchschnittlich 5 Monate, auf der Reisdiät waren, kam es bei 20 Patienten (4%) zu einer Vergrößerung des Herzens mit einer Zunahme des Querdurchmessers von 2%. Bei 480 Patienten (96%) wurde das Herz kleiner; die durchschnittliche Abnahme des Querdurchmessers betrug 11,8% (6% bei 218, 14% bei 207, 25% bei 55 Patienten).

Von 388 unserer Patienten mit vorgeschrittener vasculärer Netzhauterkrankung (Stauungspapille, Blutungen, Exsudaten, oft in Kombination) liegen Augenhintergrundsphotographien bei Beginn und nach mindestens einem Monat Reisdiät vor. 44 dieser Patienten hatten chronische Nephritis, 344 Hochdruckkrankheit. 125 wiesen Stauungspapille auf. Bei 4 zeigte sich keine Änderung; bei 2 verschwand die Stauungspapille teilweise, bei 119 vollständig. 296 der 388 Patienten hatten Augenhintergrundsblutungen. Bei 7 nahmen die Blutungen zu; bei 12 zeigte sich keine Veränderung; bei 46 verschwanden die Blutungen teilweise, bei 231 vollständig. 328 hatten Exsudate. Diese nahmen bei 5 Patienten zu; bei 18 zeigte sich keine Veränderung; bei 79 verschwanden die Exsudate teilweise, bei 226 vollständig.

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Effect of Diet on Experimental Hypertension and on the Development of Polyarteritis Nodosa in Rats

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By WALTER KEMPNER, M.D., ERNST PESCHEL, M.D., AND BERNARD BLACK-SCHAFFER, M.D.

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Rats with experimental renal hypertension were fed various diets differing in sodium and protein content. Marked prolongation of life was achieved by rice diet. Polyarteritis nodosa developed, as a result of the experimental procedures, in 23.5 per cent of the animals. Its incidence was closely correlated to sodium ingestion: 4 per cent in rats on low sodium intake, 36 per cent in rats on normal or slightly higher sodium intake. Protein intake showed no effect on incidence of polyarteritis but distinct effect on survival time. Except for one rat where a sarcoma destroyed almost all kidney tissue, no animal on rice diet developed polyarteritis nodosa.

THE present investigation grew out of a study of the influence of diet on hypertension and vascular disease. It had been established in man that a strictly enforced rice diet tends to restore normal tension and to cause regression of visible vascular lesions in the retina[1]. In order to obtain quantitative data on the effects of various dietary components, experimental hypertension was produced in rats.

It was noted in the course of the experiments, an observation frequently made by other investigators, that severe hypertension in rats was often accompanied by polyarteritis nodosa. This has been considered analogous to the arteriolonecrosis of malignant hypertension in man[2].

METHODS

Female rats of Osborne-Mendel strain were operated on when they attained a body weight of 75 grams; fascia and adrenal gland were stripped from one kidney but not removed, and the kidney enclosed in a latex capsule slightly greater in capacity than the kidney. The mouth of the capsule was drawn about the renal hilus by a thread, care being taken to avoid constricting the renal vessels or the ureter. One week later, the contralateral kidney was removed after stripping but retaining the fascia with the adrenal gland; the ureter and the blood vessels were ligated. The animals by this time were 40 to 50 days old.

Systolic blood pressure was measured in the unanesthetized animal once or twice a week by an apparatus similar to the Chittum, Hill and Grimson[3] modification of the Skeggs and Leonards[4] apparatus. The values listed in Table 2 are based on averages of the last four blood pressure figures before the death of the animal (excessively high or low values occurring only within the last two days before death were not included). Each figure represents the average of five successive measurements, which usually did not differ by more than 5 mm. Hg.

The rats were maintained, until one week after unilateral nephrectomy, on dog chow and tap water. By this time hypertension was established, and the animals could be separated into groups with comparable ranges of blood pressure.

Five diets represented decreasing sodium intake in the order given: dog chow, bread, meat, peas, and rice (table 1). These comprised the major groups. All five groups were divided into four sub-groups, receiving a) no salt addition; b) potassium chloride (50 mg. daily); c) sodium chloride (100 mg. daily); and d) sodium chloride + potassium chloride (100 and 50 mg., respectively, daily). The salt solutions were given in special 5 cc. containers which had to be emptied before tap water was permitted ad libitum. All diets were supplemented with vitamins: per day and per rat thiamine 40 γ; riboflavin 100 γ; niacin 500 γ; pyridoxin 40 γ; calcium pantothenate 150 γ; choline 7 mg.; ascorbic acid 2.5 mg.; β-carotene 200 γ; vitamin D 5 USP units; α-tocopherol 500 γ. Control, unoperated rats kept on the same diets and salt solutions showed that the vitamin supplements were adequate to insure normal growth and health.

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TABLE 1.—*Sodium and Protein Consumption in Five Diet Groups of Rats with Experimental Hypertension (Average daily intake)*

Diet	Sodium (mg.)	Protein (gm.)
1. Dog chow	80	5.2
2. Bread	67	1.5
3. Meat	12.4	7.9
4. Peas	7.6	2.4
5. Rice	0.8	0.7

TABLE 2.—*Blood Pressure and Survival Time of Hypertensive Rats on Various Diets without and with Addition of Sodium Chloride*

Averages With Standard Deviations

Number of Animals Shown in ( )

Diet	Without Additional NaCl	With Additional NaCl
(a) Systolic Blood Pressure (mm. Hg.)		
1. Dog chow	216 ± 35 (8)	226 ± 24 (5)
2. Bread	220 ± 28 (9)	194 ± 32 (9)
3. Meat	197 ± 29 (15)	189 ± 21 (17)
4. Peas	199 ± 24 (13)	204 ± 33 (10)
5. Rice	170 ± 52 (24)	194 ± 29 (22)
(b) Survival Time (Days After Nephrectomy)		
1. Dog chow	40 ± 25 (8)	37 ± 18 (5)
2. Bread	36 ± 13 (9)	35 ± 27 (9)
3. Meat	45 ± 31 (15)	27 ± 20 (17)
4. Peas	110 ± 98 (13)	39 ± 27 (10)
5. Rice	218 ± 153 (24)	71 ± 43 (22)

RESULTS

Hypertension developed in all animals with kidney encapsulation and contralateral nephrectomy. The systolic blood pressures of the unoperated rats varied between 90 and 120 mm. Hg. and were independent of food and salt intake. Among the operated rats, pressure rose in 4 to 7 days after nephrectomy to 160 to 200 mm. Hg. The hypertension was associated with rather severe renal damage. Some animals showed not only infarction of large areas of the kidney but suppurative perinephritis as well. At best, when infarction was absent, there was always a marked thickening of the renal capsule, which was associated with atrophy of subjacent nephrons, particularly at the poles. All these changes were the result of chronic perinephritis due to the presence of the latex capsule. The degree of impairment of renal function is not known. However, blood urea nitrogen determinations carried out on a number of rats indicate that, in the last weeks before death, renal insufficiency with rising urea concentrations was a frequent occurrence. Urea nitrogen values were most elevated in hypertensive rats on high-protein diets, and were only rarely increased in hypertensive rats on rice.

No difference was found between the subgroups to which potassium chloride alone was administered and those receiving no salt supplement; nor between the subgroups receiving potassium chloride and sodium chloride and those receiving sodium chloride alone. Therefore, subgroups a and b, and c and d, respectively, were combined, thus reducing the subgroups to two, one without and one with NaCl supplementation.

Table 2 (a) shows the blood pressures (averages) of the rats on the various diets without and with additional sodium chloride. Only the animals without sodium chloride addition in group 5 (rice) have a blood pressure average which differs significantly from that of the other groups. The average, 170 mm. Hg., includes the blood pressures of 10 rats which were the only ones in the entire series showing a return to normotensive levels. Fig. 1 illustrates the distribution of the individual blood pressures in the various diet groups. Statistical analysis showed that the differences of the averages are without significance ($p > 0.05$) for all groups except for group 5 without sodium chloride (p between 0.05 and 0.02) and for group 3 with sodium chloride ($p < 0.01$). The slightly lower blood pressure average for this latter group is most likely due to the very short survival time.

Table 2 (b) shows the survival times (averages) of the rats on the various diets. Even those animals in the rice group without additional salt which remained hypertensive, lived longer than those in the other groups; this is evident from the survival average of 218 days which, on statistical analysis, is

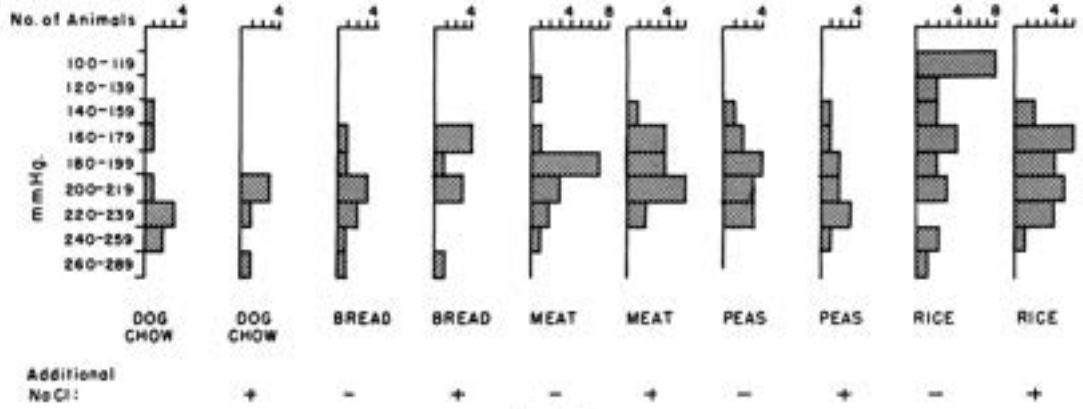

FIG. 1.

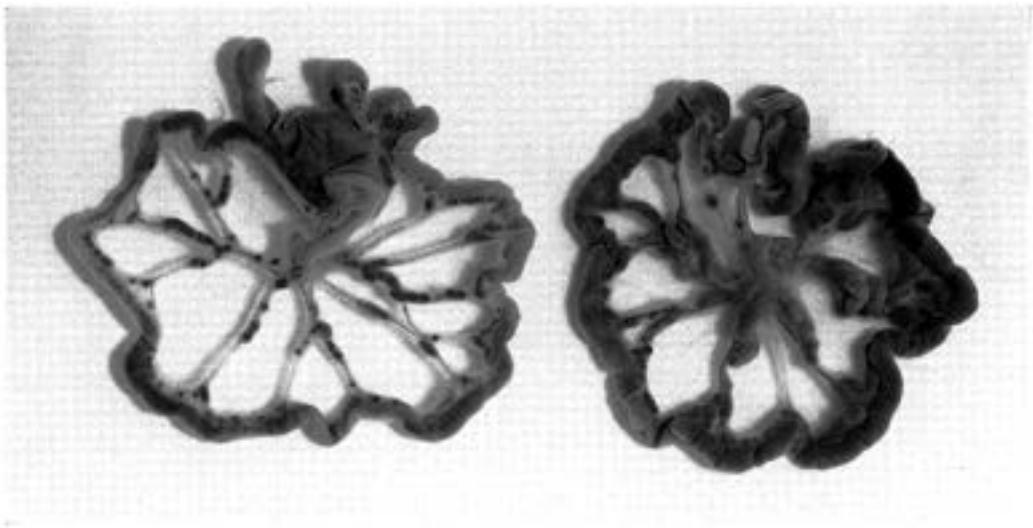

FIG. 2. Two loops of small intestine showing aneuryamal beading of the mesenteric arteries.

highly significant ($p < 0.01$). In addition to this group, rats on peas without additional salt showed a survival time average which differs significantly from that on normal rat food (dog chow), p being between 0.05 and 0.02. The differences between the other averages are without statistical significance ($p > 0.05$).

The animals fed rice without additional sodium chloride lived approximately six times as long as the animals on the two unsupplemented diets with high original NaCl content. The addition of sodium chloride to these diets (dog chow and bread) did not alter blood pressure and survival time. The influence of the addition of salt to the diets originally low in salt, i.e. meat, peas, and rice, on the survival time was not statistically significant in the meat group (p greater than 0.05); it was significant in the peas group (p between 0.05 and 0.02), and highly significant in the rice group (p less than 0.01). Rats on meat, even without additional salt, had a short survival time, comparable to that of rats on diets high in salt.

Of the 132 rats which were examined microscopically, 31 (23.5 per cent) showed the typical panarteritis of polyarteritis nodosa. The lesions were recognized grossly in the mesentery of some of the animals (Figure 2) and were histologically identical with those repeatedly described in the literature. Morphologic details and pathogenesis are discussed in a preceding paper[5]. The frequency of involvement of various arteries was as follows:

TABLE 3.—*Incidence of Polyarteritis Nodosa in Hypertensive Rats, in Relation to Diet Groups*

Diet	Without Additional NaCl		With Additional NaCl	
	Rats without Polyarteritis	Rats with Polyarteritis	Rats without Polyarteritis	Rats with Polyarteritis
Original salt content high:				
1. Dog Chow	1	7	3	2
2. Bread	6	3	6	3
Original salt content low:				
3. Meat	15	0	13	4
4. Peas	12	1	6	4
5. Rice	23	1	16	6

mesenteric, 17; coronary, 13; peripheral (axillary or femoral), 9; pancreatic, 6; renal, 2; lung, 2; root of aorta, 1; hepatic, 1; adrenal, 1; mesovarium, 1.

Table 3 shows the distribution of the cases of polyarteritis among the diet groups. Food groups 1 and 2 contain about one per cent of sodium chloride; this represents the usual salt intake of rats. Group 1 diet is also high in protein. The sodium chloride supplement increased the daily sodium chloride consumption in both groups by 50 to 70%; the additional NaCl intake did not seem to have any effect on the incidence of polyarteritis, but the number of animals is too small to be of statistical significance. Among the 31 animals on these two diets, either with or without sodium chloride addition, 15 (48 per cent) showed polyarteritis nodosa. Of the 52 animals on the naturally low NaCl diets, groups 3, 4 and 5, only 2 (4 per cent) developed polyarteritis nodosa. In contrast, 14 of 49 rats (29 per cent) on the same diets with additional NaCl developed the lesion.

In the two single animals on low-salt diet (Table 3, groups 4 and 5), in which polyarteritis nodosa occurred, it apparently began very much later than in the rats on a high salt intake; their survival time was 364 and 344 days, respectively, after nephrectomy.

The one animal on a rice and tap water diet who died with polyarteritis nodosa 344 days after nephrectomy developed a sarcoma, presumably arising from the latex-enclosed, thickened fibrous capsule of the remaining kidney. Almost all of the kidney was replaced by the sarcoma, and the rat was practically arenal. The kidneys of all other members of groups 4 and 5 showed the changes already described and attributed to the manipulations and the latex capsule.

DISCUSSION

The etiology of polyarteritis nodosa is still uncertain in spite of intensified interest during the past 15 years which has led to the reporting of numerous instances of the lesion in man and its discovery and/or production in several genera of animals. Since the lesion was first described by von Rokitansky in 1852[6] and by Kussmaul and Maier in 1866[7], etiologic importance has been attributed to various factors. Several reviews dealing with this subject have appeared recently[8, 9, 10, 11].

As is well known, polyarteritis nodosa, in older rats, is a spontaneously occurring disease. Thus, Wilens and Sproul[12] found it in 9.7 per cent of 487 animals. In no instance was the rat younger than 500 days. The authors state that 32 of their 47 polyarteritis animals showed renal lesions.

The rats of the present experiment, at the time of death, varied in age from 57 to 737, averaging 131 days. Only 3 animals among those which developed polyarteritis were older than 200 days, the age of the oldest being 414 days and the average age of the affected animals being 111 days. This age speaks against any significant incidence of spontaneously occurring renal lesions or of spontaneously occurring polyarteritis nodosa as reported by Wilens and Sproul. Furthermore, the overall incidence of 23.5 per cent polyarteritis nodosa in the animals of this report is significantly higher than the 9.7 per cent of Wilens and Sproul in old rats. Both facts indicate that the lesions found in the present series are a result of the experimental procedures.

Various factors may have been responsible for the development of polyarteritis nodosa in our rats: infection, high salt intake, hypertension, and renal dysfunction. Infection may have been present in many of the animals since no attempt at complete asepsis was made during the operations. Table 3 shows that sodium

chloride intake was a decisive factor in the development of polyarteritis in the present series. To our knowledge, no observations have been reported on the occurrence of polyarteritis in animals on a restricted sodium intake; in all instances mentioned, the salt intake was at least normal. In a recent study[13] on vascular lesions in alloxan-poisoned rats, Chute, Orr, O'Brien and Jones frequently found polyarteritic lesions when the diet contained 5 to 10 per cent sodium chloride. This represents a daily intake of approximately 750 to 1500 mg. of sodium chloride. The lesions developed more slowly and were less severe on the 5 per cent sodium chloride intake. In our series, the daily sodium chloride consumption considered a high salt intake was between 100 and 300 mg.; no distinct difference was noted within this range in the incidence and the period of time required for the development or the severity of the lesions. Hypertension was present in all of our animals. Its severity was not necessarily correlated with the development of polyarteritis nodosa. As was previously stated the blood urea determinations in a number of rats showed the existence of uremia in many of them. At death, severe injury of the kidney was histologically present in every case.

In their interesting work, Chute, Orr, O'Brien and Jones[13] make the following Statement: "The vascular lesions (periarteritis nodosa and fibrinoid degeneration) are produced by the action of sodium chloride in those cases in which the kidneys had been damaged by alloxan." The rats with the highest incidence of vascular lesions and the highest blood pressure average (177 mm. Hg.) are found in their experiment 10 in which 10 per cent sodium chloride was given and where the most severe renal damage occurred.

It would seem from this as well as from our work that renal damage and hypertension in the presence of normal or higher sodium chloride intake are decisive factors in the pathogenesis of fibrinoid degeneration and polyarteritis nodosa of the rat.

Rats with renal hypertension had a short survival time on a diet of meat. Control rats tolerated this diet rather well, although they too had an elevated blood urea. The natural salt intake is low on this diet (see Table 1); therefore, the short survival time of the hypertensive rats on meats must be attributed to a factor other than sodium.

The hypertension in our experimental animals was due to renal dysfunction but was not necessarily associated with azotemia. From our data it is hardly possible to separate the role of hypertension from that of other manifestations of renal dysfunction in the pathogenesis of the polyarteritis nodosa.

A certain degree of correlation between hypertension and polyarteritis was present only in group 5 of our animals. In the other groups on the low salt diets (groups 3 and 4), the incidence of polyarteritis nodosa was much lower than in those on the high-salt diets even though the average blood pressure figures were comparable. Apparently, then, hypertension cannot be the only cause of the vascular lesion. It may be argued that the rat like man has no critical blood pressure level separating the benign from the malignant forms of hypertension.

The results of these experiments are compatible with the concept of polyarteritis nodosa as the rat analogue of arteriolonecrosis in malignant hypertension and demonstrate the effectiveness of the rice diet in the control of the vascular sequelae of renal hypertension which cause the death of the animal.

One animal listed in Table 3, second column, deserves further mention. This rat, on rice and tap water diet, surviving 344 days, with the hypertension reversed to normotension for many months, developed a sarcoma, presumably arising from the latex-enclosed, thickened fibrous capsule of the remaining kidney. As a consequence of invasion, almost all of the kidney was destroyed. The long survival of this animal is an additional indication of the effectiveness of the rice diet in the treatment of chronic renal disease and the prevention of uremia.

SUMMARY AND CONCLUSIONS

Marked prolongation of life in rats with experimental hypertension may be achieved by the rice diet.

Polyarteritis nodosa develops in many

animals with experimental renal hypertension. The results of the present experiments are compatible with the concept of polyarteritis nodosa as the rat analogue of arteriolonecrosis in malignant hypertension in man.

The incidence of polyarteritis nodosa in rats with experimental renal hypertension is closely correlated to sodium ingestion. Of 52 rats on a low sodium intake, 4 per cent had polyarteritis; of 80 rats on a high sodium intake (though only moderately high: 40 to 120 mg. daily), 36 per cent had polyarteritic lesions.

Among the groups on low sodium diets without salt addition, the incidence of polyarteritis nodosa was negligible, no matter whether a diet high in protein of animal or vegetable origin (meat, peas), or low in protein (rice) was given. However, there was a great difference with regard to survival time: on meat, the average was 45 days, on peas 110 days, on rice 218 days.

No animal on the strict rice diet showed polyarteritis nodosa except one which, after a survival time much longer than the average, developed a sarcoma, arising from the experimentally damaged fibrous capsule of the kidney. Only after destruction of almost all of the kidney did recurrence of hypertension and polyarteritis nodosa develop.

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Analysis of 177 Cases of Hypertensive Vascular Disease with Papilledema

Analysis of 177 Cases of Hypertensive Vascular Disease with Papilledema*

One Hundred Twenty-six Patients Treated with Rice Diet

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THE prognosis in patients with hypertensive vascular disease and papilledema has always been grave. Until 1944[1,2] there was no medical treatment for this condition; since then a number of cases of malignant hypertension treated successfully with the rice diet have been reported.[3–15]

The purpose of this paper is to describe the clinical course of this disease as seen in 177 patients (treated and untreated) examined between October, 1942, and October, 1953, on our service. This series includes every patient with hypertensive vascular disease admitted during this period in whom the presence of neuroretinopathy was confirmed by fundus photographs. (Patients with chronic nephritis, i.e., history of albuminuria preceding hypertension, and polycystic kidney disease are not included.)

An attempt was made to treat all these patients with the rice diet. However, of these patients eighteen never actually took the rice diet. Sixteen of the eighteen are known to have died; in one no follow-up information is available. Only one of these eighteen patients, E. B., who was treated intermittently over a five and one-half months' period, is still living, nine years after she was first seen here. The clinical course in these patients was similar to that described by Wagener and Keith.[16] In their series of 146 patients with malignant hypertension without any special therapy only one survived five years and 79 per cent died within the first year after examination.

Thirty-three patients were willing to take the rice diet but this treatment had to be discontinued because they were unable to retain sodium or, in some cases, chloride in the serum when subjected to severe dietary restriction (less than 150 mg. sodium, less than 200 mg. chloride daily).

The rice diet was given for varying lengths of time to 126 patients. In three of these patients the follow-up information is incomplete and in three the follow-up period is too short, since treatment was started within the past year (these three are doing well). This leaves a total of 120 patients with malignant hypertension who were treated with the rice diet and in whom the effect of the rice diet on malignant hypertension can be studied. Fifty-two of these 120 patients are living.

Most of these patients, after an initial period usually of two to four months on the "basic" rice diet, received a "modified" rice diet which included small amounts of potato, cereals, nonleguminous and leguminous vegetables, meat, et cetera. In patients who continued under supervision the diet was increasingly liberalized as improvement permitted. Other patients discontinued the diet at various stages of treatment, but most of them continued to follow a salt-poor, fat-poor diet.

The urinary excretion of chloride, calculated as NaCl, on the basic rice diet, except in patients who are losing edema or who are acute or chronic salt losers) should be 5 to 15 mg. per 100 cc. urine (determined in a twenty-four-hour urine collection) if properly adhered to; on the "modified" rice diet, if correctly followed, it should be 15 to 25 mg. The chloride excretion in the urine therefore is a guide to whether or not the diet is being followed correctly.

Three of the 120 patients were between twenty and twenty-nine years of age, seventeen be-

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tween thirty and thirty-nine, fifty between forty and forty-nine, thirty-eight between fifty and fifty-nine, twelve between sixty and sixty-nine when the treatment was started. Of the fifty-two patients who are living two were between twenty and twenty-nine when the rice diet was started, five between thirty and thirty-nine, twenty-three between forty and forty-nine, sixteen between fifty and fifty-nine and six between sixty and sixty-nine. In our series age was not a significant factor in prognosis.

TABLE I

TOTAL PSP EXCRETION IN TWO HOURS AND SURVIVAL*

Total PSP Excretion in 2 Hours (%)	Number of Patients	Number Dead	Survived	
			Over 6 Months	Over 1 Year
Not done	1	1	0	0
0–15	15	15	1	0
16–25	7	7	0	0
26–35	8	8	0	0
36–45	1	1	0	0
Above 46	1	1	0	0
	33	33	1	0

* 33 patients: NaCl or Cl added to diet.

RENAL AND ELECTROLYTE STATUS

The two most important factors influencing the effectiveness of the rice diet in the treatment of malignant hypertension are the renal status (especially since salt-losing often precludes the use of the diet in patients with advanced renal involvement) and the length of time the patient is willing to adhere rigidly to treatment.

In Tables I to IV the survival times of the 120 patients treated with the rice diet and of the thirty-three patients to whom supplementary NaCl or Cl was given are correlated with the renal function and ability to conserve electrolytes: (1) Total PSP excretion in two hours (Tables I and II); (2) blood non-protein nitrogen concentration (Tables III and IV); (3) inability to maintain adequate sodium and/or chloride levels in the serum on the rice diet. (Tables I and III.)

Tables I and III list the thirty-three patients in whom drastic salt restriction was not carried out because of inability to conserve sodium and/or chloride in the serum. Tables II and IV list the 120 patients who were treated with the rice diet.

In Tables I and II the patients in both groups are listed according to the PSP excretion at the beginning of treatment. There were five patients who were critically ill in whom the PSP was not determined; all died in less than one year. There were twenty-eight patients with a total PSP excretion, in two hours, between 0 and 15 per cent. Twenty-six of the twenty-eight died in less than one year and none survived twenty-five months. Fifteen were salt losers receiving salt and thirteen were not, but with a total PSP excretion below 15 per cent in two hours the prognosis is nearly as bad in patients who do not lose salt as in those who do.

There were forty-seven patients in whom the total PSP excretion was between 16 and 35 per

TABLE II

TOTAL PSP EXCRETION IN TWO HOURS AND SURVIVAL*

Total PSP Excretion in 2 Hours (%)	Number of Patients	Number Dead	Survived One Year		Patients Living		
			Number	(%)	Number	(%)	Years (average)
Not done	4	4	0	0	0	0	...
0–15	13	13	2	15	0	0	...
16–35	32	21	19	59	11	34	3
36–55	34	19	26	76	15	44	4½
Above 56	37	11	34	92	26	70	5
	120	68	81	67	52	43	4

* 120 patients treated with rice diet.

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cent in two hours. Nineteen (40 per cent) of the forty-seven patients survived one year; eleven (23 per cent) are still living with an average survival time, so far, of three years. Fifteen of the patients in this group were salt losers and received salt; all of them died.

There were thirty-five patients with a total PSP excretion between 36 and 55 per cent in two hours. Only one patient was a salt loser and received salt. Twenty-six (74 per cent) of the thirty-five patients survived one year; fifteen (43 per cent) are still living with an average survival time, so far, of four and one-half years.

There were thirty-eight patients with a total PSP excretion in two hours of 56 per cent or more. Only one patient was a salt loser and received salt. Thirty-four (89 per cent) survived one year; twenty-six (68 per cent) are still living with an average survival time, so far, of five years.

In Tables III and IV the patients in both groups are listed according to the initial non-protein nitrogen concentration in the blood. The non-protein nitrogen was over 60 mg. per 100 cc. of blood in thirty-seven patients. Twenty of the thirty-seven patients were salt losers and received salt; all twenty died. Of the seventeen who were treated with the rice diet, only three survived one year and only one (initial non-protein nitrogen 75 mg. per 100 cc. of blood; total PSP excretion in two hours 20 per cent) is still living four and one-half years after the start of treatment.

In eighty-seven patients the non-protein nitrogen was between 35 and 59 mg. per 100 cc. of blood. Twelve of these patients were salt losers and received salt; all twelve died. Seventy-five were treated with the rice diet. Fifty-five (63 per cent) of the eighty-seven patients survived one year; thirty-seven (43 per cent) are still living with an average survival time of four years.

TABLE III

INITIAL BLOOD NPN LEVEL AND SURVIVAL*

NPN (mg. per 100 cc. of blood) (Range)	Number of Patients	Number Dead	Survived	
			Over 6 Months	Over 1 Year
Over 100	6	6	0	0
75 to 99	6	6	0	0
60 to 74	8	8	0	0
50 to 59	3	3	0	0
35 to 49	9	9	1	0
Below 35	1	1	0	0
	33	33	1	0

* 33 patients: NaCl or Cl added to diet.

In twenty-nine patients the non-protein nitrogen was below 35 mg. per 100 cc. of blood. One patient was a salt loser and received salt. Twenty-three (79 per cent) of the twenty-nine patients survived one year; fourteen (48 per cent) are still living with an average survival time so far of four years.

The thirty-three patients who developed severe electrolyte imbalance are listed in Tables

TABLE IV

INITIAL BLOOD NPN LEVEL AND SURVIVAL*

NPN (mg. per 100 cc. of blood) (Range)	Number of Patients	Number Dead	Survived One Year		Patients Living		
			Number	(%)	Number	(%)	Years (average)
Over 100	4	4	0	0	0	0	...
75–100	5	4	1	20	1	20	4½
60–74	8	8	2	25	0	0	...
50–59	12	6	8	67	6	50	4½
35–49	63	32	47	76	31	49	4
Below 35	28	14	23	82	14	50	4
	120	68	81	67	52	43	4

* 120 patients treated with rice diet.

I and III; in these patients the rice diet treatment was discontinued. Development of marked electrolyte disturbance during drastic sodium and chloride restriction is a most ominous sign. Sodium chloride was given to fourteen during the first month of treatment, to seven during the second month and to seven during the third month. Five received chloride as NH_4Cl, KCl or HCl during the second to seventh week. All thirty-three patients died; twenty-seven died in Duke Hospital after an average of seventy-one days, and the other six died shortly after returning home (one to four months after first being seen in our clinic). In general, the likelihood of electrolyte loss on the rice diet is greater in patients with a low PSP excretion and/or marked azotemia. However, the inability to conserve electrolytes may, in some instances, be the chief manifestation of renal dysfunction and may occur in the absence of severe impairment of PSP excretion or of marked azotemia.

In contrast to surgical measures,[17–20] which are contraindicated when there is nitrogen retention or even moderate renal impairment (PSP excretion in the first fifteen minutes below 15 to 20 per cent), advanced renal impairment does not preclude an attempt at treatment with the rice diet and such treatment is not dangerous if the electrolyte balance can be controlled. The criteria for selection of patients for drug therapy have not yet been worked out; renal impairment, advanced age, cerebral and coronary artery involvement may under certain circumstances[21,22] contraindicate the use of hypotensive drugs; they do not contraindicate the use of the rice diet. However, Tables I to IV indicate that far advanced renal impairment seriously diminishes the chances of successful treatment with the rice diet, as with other forms of treatment of malignant hypertension.

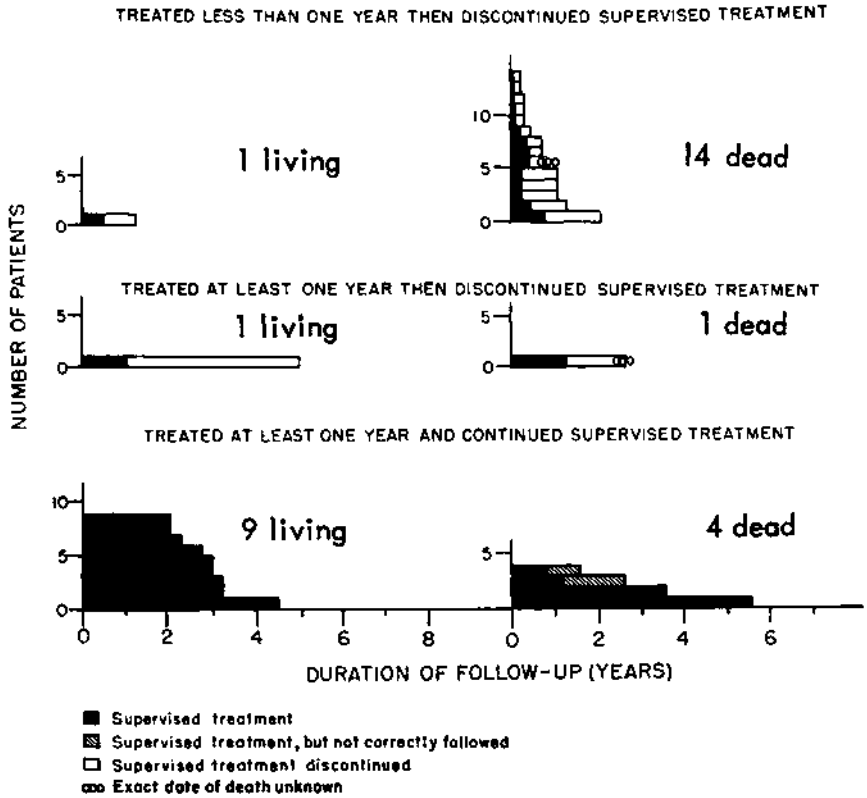


FIG. 1. Survival time and period of treatment (thirty patients, total PSP excretion in two hours, 35 per cent or less). Living, eleven patients; dead, nineteen patients.

TIME FACTOR

Since 1944[1] it has been known that the malignant phase of hypertensive vascular disease can be reversed by the rice diet; occasionally we have seen papilledema disappear within as short a time as one month, and six months of treatment with the rice diet is usually enough to cause

malignant hypertension either to revert to "benign" essential hypertension or to disappear completely.

However, the period of treatment required for modification of the underlying vascular disease and the degree to which it can be modified are more variable. In patients with the most severe involvement, uninterrupted maximal dietary treatment (as checked by a chloride excretion below 15 mg., expressed as NaCl, per 100 cc. of urine) may be necessary for years or in some cases perhaps indefinitely to maintain improvement. On the other hand, one patient, age twenty, had a normal blood pressure after two months on the rice diet, and her blood pressure is still normal five and one-half years after she had had malignant hypertension, although for the past three years she has been on a normal diet.

In Table v and Figures 1 and 2 the survival times are given according to the duration of treatment. With one exception (a patient who followed the diet poorly and died within eighteen months after first being seen in our clinic), the malignant phase of the disease had disappeared within one year in all patients treated for that length of time. The subsequent course of these patients was influenced by the severity of the underlying cardiovascular renal disease and the intensity and duration of treatment. In some patients improvement has been continuous; in others the vascular disease has remained stationary; in others it has progressed and cardiac or renal failure, coronary or cerebral artery disease or other complications have caused death. The data on the present status of the patients are given here but it is not within the scope of this paper to discuss the effect of rice diet therapy on the course of hypertensive vascular disease except when it is in the malignant phase.

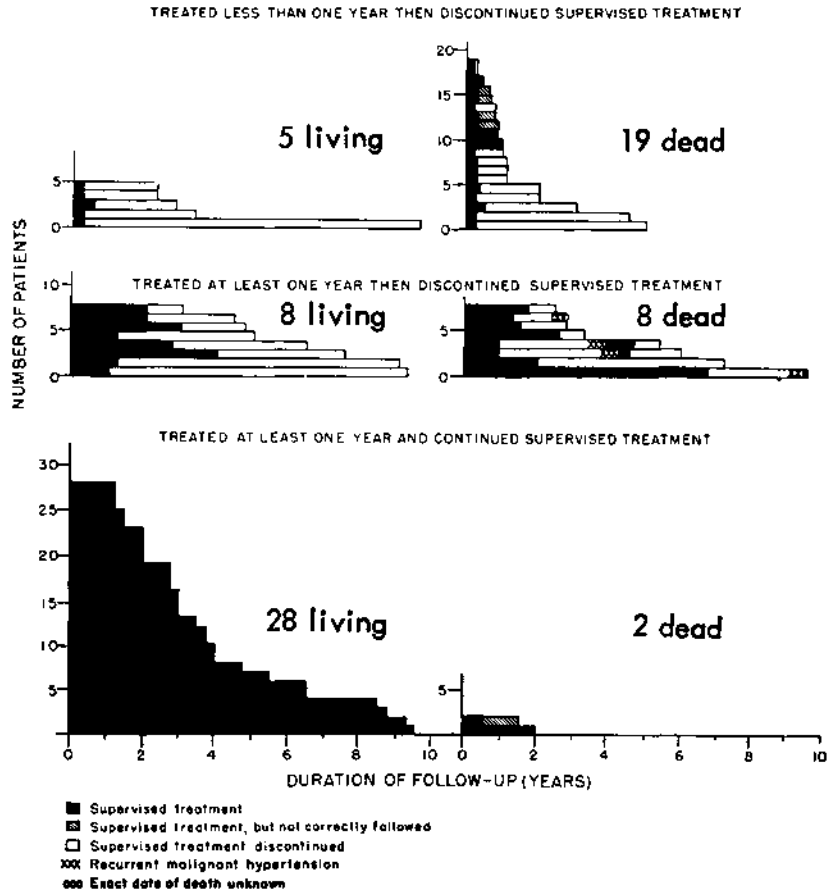


FIG. 2. Survival time and period of treatment (seventy patients, total PSP excretion in two hours, 36 per cent or more). Living, forty-one patients; dead, twenty-nine patients.

There were one hundred patients (Table v)

who were treated with the rice diet and were followed after the initial period of treatment; in these patients the relation of the length of time of supervised treatment to the survival time could be studied. (The eighteen patients who died in Duke Hospital during the initial period of treatment and two patients in whom the PSP was not determined are omitted.)

In thirty-nine of the one hundred patients, the period of supervised treatment was two to twelve months. Seven of the thirty-nine died during this period while supposedly still following the diet; only three of the seven were following it correctly. Thirty-two of the thirty-nine were treated for two to twelve months, and then to a greater or lesser extent discontinued the treatment; only six (19 per cent) of the thirty-two are still living.

Eighteen of the one hundred patients were treated one to seven and one-half, average three, years and then to a greater or lesser extent discontinued the treatment. Nine of these (50 per cent) are still living. In three instances malignant hypertension recurred two and one-half to three and one-half years after discontinuing treatment, and in two of the three papilledema again disappeared during a second period of treatment with the rice diet, which was again discontinued; in one the malignant phase could not be reversed a second time; all three died. The nine who are living had been treated with the rice diet, strict and modified, for an average of three years before discontinuing it; they have survived an average of four years since they discontinued the diet. Two are being treated elsewhere for heart failure, five have continued on a "salt-poor, fat-poor" diet; two have resumed a general diet.

Forty-three of the one hundred patients continued treatment with the rice diet; they have been treated one to nine and one-half, average four years. Thirty-seven (86 per cent) of these are still living; of the six who died, only three were following the diet correctly.

TABLE V

RELATION OF LENGTH OF TIME OF SUPERVISED TREATMENT WITH RICE DIET TO SURVIVAL*

Time of Supervised Treatment	Number of Patients	Survived One Year		Patients Living		
		Number	%	Number	%	Years (average)
Less than 1 year	39†	20	51	6	15	3
Over one year:						
Supervised treatment discontinued (after 1 to 7½, average 3 years)	18	18	100	9	50	4
Supervised treatment continued (1 to 9½, average 4 years)	43‡	43	100	37	83	4

* 100 patients treated with rice diet.

† Seven of these patients died while supposedly following the rice diet; only three of the seven were following the diet correctly.

‡ Of the six patients who died after the first year of treatment, only three were following the diet correctly.

Since, as has already been indicated, there is a marked difference in survival of patients with a total PSP excretion below 35 per cent in two hours as compared to those with a total PSP excretion of 36 per cent or more in two hours, the effect of the time factor was studied in these two groups of patients separately.

Thirty (Figure 1) of the one hundred patients had a PSP excretion (in two hours) below 35 per cent. Fifteen of these patients were treated six months or less. Eight died within the first year; six died after one to two, average one and one-half years; one is still living one year after treatment was started.

Two patients discontinued treatment after one and one-half and two and one-half years, respectively; the first one died shortly thereafter; the other is still living two and one-half years after discontinuing supervised treatment. Thirteen have continued treatment from one to five and one-half, average three years; nine (69 per cent) are still living. Of the four who died while supposedly still following the diet, two were following it well as shown by a chloride

excretion, expressed as NaCl, usually below 25 mg. per 100 cc. of urine (as compared to 5 to 15 mg. on the basic and 15 to 25 mg. on the correctly followed "modified" rice diet); two adhered to the diet poorly, chloride excretion 44 mg. per 100 cc. of urine, average of the last five determinations in each of the patients. The nine who are still alive do not at all times follow the diet correctly; the average chloride excretion in the urine has been 25 to 40, average 32 mg. per 100 cc. (average of the last five to fifteen determinations in each instance). These patients continue to return here for examination and, if indicated, for short periods of strict treatment several times a year.

Seventy patients (Figure 2) had a total PSP excretion of 36 per cent or more in two hours. In twenty-four the period of controlled treatment under our supervision was less than one year. Seven of the twenty-four died while supposedly still on the diet after six to nine, average seven and one-half months of dietary treatment; three were following the diet well (chloride excretion usually below 25 mg. per 100 cc. of urine); two were following the diet moderately well (chloride excretion 36 mg. per 100 cc. of urine, average of the last three determinations in each instance); one was not adhering well to the diet (chloride excretion 53 mg. per 100 cc. of urine, average of the last five determinations); one had been given small amounts of toast and other additions to increase the salt content of the diet during the fourth month of treatment when electrolyte imbalance developed. The other seventeen patients in this group were treated less than six months; thirteen survived one year and five are still living (three years average after first being seen at our clinic).

In forty-six patients the period of controlled treatment under our supervision was at least one year. Sixteen discontinued the diet after one to seven and one-half years: eight have died; eight are still living.

Thirty continued to follow the rice diet, strict and modified: twenty-eight (93 per cent) are still living, one to nine and one-half, average four, years after first being seen here. Two died while supposedly still on the diet: one was following the diet well (chloride excretion usually below 20 mg. per 100 cc. of urine), the other was following the diet only moderately well (chloride excretion 35 mg., average of ten determinations).

TABLE VI
RETINOPATHY IN 100 PATIENTS TREATED WITH RICE DIET*

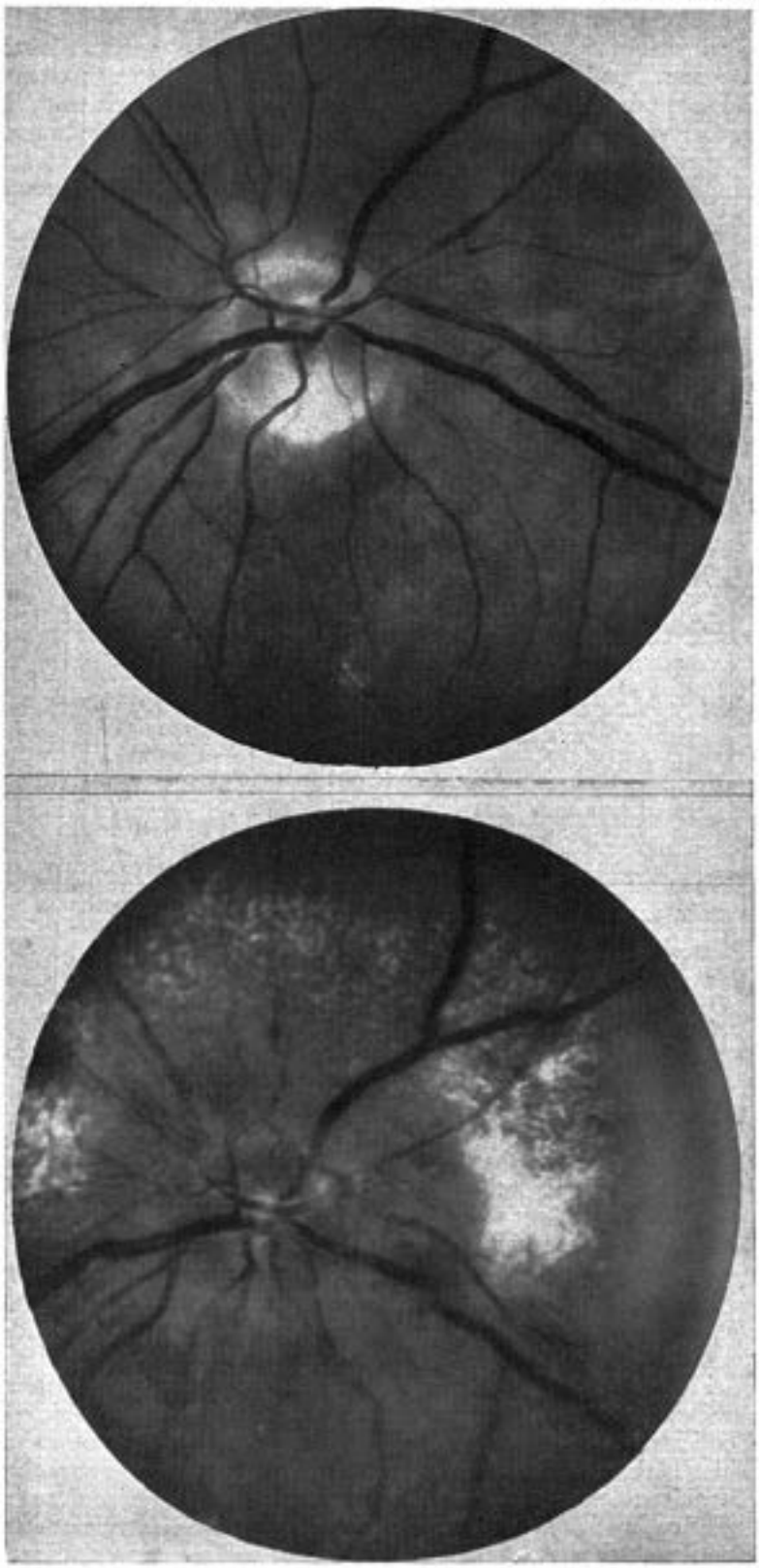
	Disappeared Completely		Disappeared Partially		No Change	
	Number of Patients	Time in Months (averages)	Number of Patients	Time in Months (averages)	Number of Patients	Time in Months (averages)
Papilledema (100 patients)	92	5	3	2	5	4
Hemorrhages (90 patients)	69	8	16	8	5	4
Exudates (94 patients)	56	15	30	7	8	5

* Eyeground photographs available before and 1 to 121 months after treatment with the rice diet was started.

EFFECT OF RICE DIET ON RETINOPATHY

In 100 of the 126 patients with malignant hypertension in whom treatment with the rice diet was used, eyeground photographs are available before and after 1 to 121 months of treatment. (Table VI, Figure 3.) All the 100 patients had papilledema before treatment and in ninety-two it disappeared completely with treatment. The eight in whom papilledema was not affected or did not completely disappear died.

Ninety patients had hemorrhages before treatment. In sixty-nine the hemorrhages disappeared completely after two to thirty-one months. In sixteen they disappeared partially



July, 1954

June, 1944

FIG. 3. Ten year follow-up in malignant hypertension (A. A. H., man, age 47 to 57).

after two to thirty-one months. In five there was no change after two to eight months. In two patients hemorrhages developed during treatment but were not present at the most recent examination. In three patients in whom hemorrhages had disappeared, they recurred and were present at the most recent examination.

2 to 6 mg. (two patients), apresoline® 50 to 150 mg. (twelve patients; one patient has taken as much as 400 mg. of apresoline at times), hexamethonium chloride 250 to 1500 mg. (eleven patients), and raudixin 50 to 150 mg. (nine patients).

Table VII shows the length of treatment with

TABLE VII

FIFTEEN PATIENTS GIVEN HYPOTENSIVE DRUGS

Initials	Fundi before Diet P H E†	Length of Dietary Treatment before Drugs Were Started (mo.)	Chloride Excretion before Drugs (as NaCl mg. per 100 cc. of urine)*	Fundi before Drugs Added P H E†	Medication at Most Recent Examination (mg. daily)			Fundi at Most Recent Examination P H E†
					C_6	Apresoline	Raudixin	
E. N.	+++	30	30	0 0 0		none‖		0 0 0
J. N.	+0+	30	40	0 0 0	1000	100		0 0 0
H. G.	+++	24	28	0 0 0			100	0 0 0
H. L.	+++	21	37	0 0 0		100		0 0 0
L. M.	+++	20	21	0 ++			100	0+0
J. M.	+++	18	105	0 ++		75	100‡	0 0 0
W. L.	+++	17	63	0 0 0		none‖		0 0 +
W. R.	+++	14	36	0 0 +		none‖		0 0 +
B. T.	+++	14	23	0 0 0			150	0 0 0
L. R.	+++	9	36	0 ++		200–400		0 0 0
P. C.	+++	9	26	0 ++	750	75		0++
J. C.	+++	8	40	0 ++	750	100	150	0 0 0
J. W.	+0+	6	34	0 ++	750		150	0 0 0
J. K.	+++	½		+++		none‖		0 0 +
M. B.§	+++	0		+++		100	150	0 0 0

* Should be 5 to 15 mg. per 100 cc. of urine on the basic rice diet and 15 to 25 mg. on the correctly followed "modified" diet.

† PHE stands for papilledema, hemorrhages, exudates.

‡ 3 mg. veraloid plus medication as listed.

§ Had received 25 mg. veraloid before she came to us, dose cut to 6 mg. during first four months, then all drugs stopped and resumed twenty-eight months later. (Chloride excretion 33 mg. per 100 cc. of urine before drugs restarted.)

‖ Had received 50–100 mg. apresoline, 500–1000 mg. hexamethonium, or 100 mg. raudixin singly or in combination for two to ten months, but were not receiving medication at most recent examination.

Ninety-four patients had exudates before treatment. In fifty-six the exudates disappeared completely after two to thirty-four months. In thirty they disappeared partially after one to twenty-two months; in eight there was no change after one to eleven months. In five patients in whom the exudates had disappeared, they were again present at the most recent examination.

After zero to thirty-six, average fifteen, months of treatment by diet alone, fifteen of the one hundred patients were given hypotensive drugs in addition to the strict or modified rice diet for three to thirty, average fourteen, months. The drugs were used singly or in combination. The doses per day were: veraloid

the rice diet before drugs were added, the funduscopic findings before treatment with the rice diet, before the drugs were given and at the most recent examination, and the present medication.

These drugs in the doses in which we have used them have caused a further lowering of the blood pressure in some instances but did not alter the course of the retinopathy nor was there any improvement of hypertensive heart or kidney disease noted which could be attributed to them. Treatment with the drugs was started in only two instances before the disappearance of papilledema and these fifteen patients, therefore, have been included with the other patients.

EFFECTS OF RICE DIET ON PATIENTS FOLLOWED FOR AT LEAST ONE YEAR

There are sixty-one patients who were re-examined here at least one year after treatment with the rice diet had been started. These sixty-one patients include fifty-seven of the sixty-one patients listed as treated for over one year in Table v, three patients who are listed as treated for less than one year but who were re-examined here one year after treatment with the rice diet had been started, and one patient who was followed here for thirteen months but whose present condition is not known. Of the sixty-one patients eighteen had a total PSP excretion of 16 to 35 per cent in two hours; twenty-three had a total PSP excretion of 36 to 55 per cent in two hours; 20 had a total PSP excretion of 56 to 88 per cent in two hours. The effects of the rice diet on blood pressure, serum cholesterol, blood non-protein nitrogen, T_1 in the electrocardiogram, cardiothoracic ratio and renal function are shown in Tables VIII to XIV. A comparison is made of the findings during the period of "strictest adherence to the rice diet" with those at the most recent examination.

TABLE VIII

BLOOD PRESSURE IN SIXTY-ONE PATIENTS TREATED WITH RICE DIET*

Before Treatment (average)	During Period of Strictest Adherence to Rice Diet (average†)	At Most Recent Examination (average‡)
219/134	168/105	184/109

* Followed for at least one year.
† After 2 to 13, average 4, months.
‡ After 1 to 9½, average 4, years.

Even during the period of "strictest adherence to the rice diet" determinations of the chloride excretion in the urine showed that some patients were deviating from the prescribed diet; the chloride excretion of these sixty-one patients during the period of "strictest adherence to the rice diet" was 5 to 52, average 18, mg. per 100 cc, expressed as sodium chloride.

Table VIII lists the average blood pressures before treatment, during the period of "strictest adherence to the rice diet," and at the most recent examination. The average blood pressure of these sixty-one patients decreased from 219/134 to 168/105 during the period of "strictest adherence to the rice diet." In eighteen (30 per cent) of the sixty-one patients the blood pressure decreased to 149/99 or below; in eight (13 per cent) of the sixty-one to 125/89 or below during the period of "strictest adherence to the rice diet."

TABLE IX

BLOOD NPN IN FORTY PATIENTS TREATED WITH RICE DIET*

Range before Treatment (NPN mg. per 100 cc. of blood)	Number of Patients	Before Treatment (averages)	During Period of Strictest Adherence to Rice Diet (averages†)	At Most Recent Examination (averages‡)
36–45	22	39	33	32
46–75	18	53	36	45

* Followed for at least one year. Initial NPN 36 mg. or more per 100 cc. of blood.
† After 2 to 9, average 4, months.
‡ After 1 to 9½, average 3, years.

Thirty-two of the sixty-one patients were following the rice diet well or moderately well at the most recent examination (chloride excretion, as NaCl, 24 mg. per 100 cc. of urine, average of the most recent determinations, one to eight and one-half, average five, years after the rice diet had been started). The average blood pressure of these thirty-two patients at the most recent examination was 175/105 as compared to 217/132 before treatment and 165/104 after the first two to six, average four, months on the rice diet.

The other twenty-nine patients followed the diet moderately well to poorly most of the time since the initial period of strict treatment here (chloride excretion, as NaCl, 65 mg. per 100 cc. of urine, average of most recent determinations, 1 to nine and one-half, average three, years after the rice diet was started). The average blood pressure of these twenty-nine patients at the most recent examination was 193/114 as compared to 220/136 before treatment and 170/106 after the first two to thirteen, average five, months on the rice diet.

In fifty-nine of the sixty-one patients blood NPN determinations are available before treatment, during the period of "strictest adherence to the rice diet," and at least one year after treatment was started. The NPN was elevated in forty of these patients and Table IX shows the changes during treatment. In thirty-three (82 per cent) it was lower at the most recent examination than it had been initially. Three patients, who had had a normal NPN before

the rice diet was started, developed azotemia. All three had followed the diet poorly, chloride excretion 92 mg. per 100 cc. of urine, average of four to seven determinations each; the NPN, average, was 32 mg. per 100 cc. of blood before treatment, 31 mg. after the first four months, average, on the rice diet and 51 mg., two to five, average three, years after treatment with the rice diet had been started.

TABLE X
SERUM CHOLESTEROL IN FORTY-SIX PATIENTS TREATED WITH RICE DIET*

Serum Cholesterol Level	Number of Patients	Serum Cholesterol (mg./100 cc.) Before Treatment (averages)	During Period of Strictest Adherence to Rice Diet (averages†)	At Most Recent Examination (averages‡)
Increased	6	259	233	330
Decreased:	40	288	199	200
to 219 or below	32	282	192	183
to 220 or above	8	312	230	266

* Followed for at least one year. Initial cholesterol concentration in serum 220 mg. per 100 cc. or above.
† After 2 to 9, average 4, months.
‡ After 1 to 7, average 3, years.

In fifty-five of the sixty-one patients the cholesterol concentration in the serum was determined before treatment, during the period of "strictest adherence to the rice diet" and one to seven years after the treatment had been started.

Forty-six (84 per cent) of these fifty-five patients had a serum cholesterol concentration of 220 mg. per cent or more when first seen here, and the data on these patients are shown in Table x. Only two of these forty-six patients had an increase in the serum cholesterol concentration during treatment with the strict rice diet; the average cholesterol concentration in these two patients was 257 mg. per 100 cc. of serum before treatment and 290 mg. after the first four months, average, on the rice diet.

In six patients (13 per cent) the serum cholesterol was higher at the most recent examination three to six, average four, years after treatment with the rice diet was started than before. In forty (87 per cent) of the forty-six patients with an initial cholesterol concentration in the serum above 220 mg. the cholesterol concentration in the serum decreased; in thirty-two (70 per cent) of the forty-six it decreased to 219 mg. per 100 cc. or below. In two of the nine patients who had had a cholesterol concentration in the serum of 219 mg. or below per 100 cc. before treatment, the cholesterol concentration in the serum increased to 220 mg. or above. In these two patients the cholesterol concentration in the serum, average, was 215 mg. per 100 cc. before treatment, 212 mg. after the first three months, average, on the rice diet and 252 mg. two and one-half years, average, after treatment had been started.

TABLE XI
T_1 IN THE ELECTROCARDIOGRAM IN FORTY-NINE PATIENTS TREATED WITH RICE DIET*

	Before Treatment (Number of Patients)	During Period of Strictest Adherence to Rice Diet (Number of Patients)	At Most Recent Examination (Number of Patients)
T_1 upright	14	38	28
T_1 diphasic	10	4	5
T_1 inverted	25	7	15†

* Followed for at least one year.
† One patient who was following the diet poorly developed a left bundle branch block.

In forty-nine of the sixty-one patients electrocardiograms are available for comparison (no digitalis, no infarction, etc.) before treatment, during the period of "strictest adherence to the rice diet" and one to nine and one-half years after treatment had been started. (Table XI.) In thirty-five (71 per cent) T_1 was abnormal before treatment; in ten it was diphasic; in twenty-five it was inverted.

In fourteen patients T_1 was upright before the rice diet was started; in none of the fourteen was there a change in the direction from upright to inverted after one and one-half to eight and one-half, average four, years. In nine of the ten patients in whom T_1 was diphasic before treatment it became normally upright after three to thirty-two, average eight, months of adequately followed dietary treatment. In one patient, it remained diphasic. In seven of the twenty-five patients in whom T_1 was inverted before treatment it remained inverted after one to three, average two, years. In eighteen (72 per cent) of the twenty-five patients there was a change in the direction from inverted to upright; in three T_1 became diphasic after seven to ten, average eight, months; in fifteen it

became normally upright after three to seventeen, average eight, months.

In twelve of the twenty-seven in whom the electrocardiogram had initially shown improvement it again became more abnormal. Nine of the twelve were following the diet poorly. In one of the nine patients a left bundle branch block developed.

In forty-nine of the sixty-one patients comparable chest films (no digitalis) are available before treatment, during the period of "strictest adherence to the rice diet" and at the most recent examination one to nine and one-half, average three, years after treatment had been started. (Table XII.) Before treatment the cardiothoracic ratio was 0.42 or below in only three patients (6 per cent); during the period of "strictest adherence to the rice diet" it was 0.42 or below in twenty-four (49 per cent). The cardiothoracic ratio before treatment was over 0.48 in twenty-nine (59 per cent); in nineteen it was 0.48 to 0.52 and in ten it was 0.53 to 0.59. During the period of "strictest adherence to the rice diet," the cardiothoracic ratio was over 0.48 in only seven (14 per cent). In these seven patients the average cardiothoracic ratio had decreased from 0.54 to 0.49 after the first five months, average, on the rice diet.

In thirty-six (73 per cent) of the forty-nine patients the decrease in cardiothoracic ratio during the period of "strictest adherence to the rice diet" was more than 10 per cent. In twenty-one of these thirty-six patients the cardiothoracic ratio at the most recent examination had again increased by 10 per cent or more. Fourteen of the twenty-one patients in whom cardiomegaly recurred were following the diet poorly; the cardiothoracic ratio, average, in these fourteen patients increased from 0.43 after the first four months, average, on the rice diet to 0.50 at the most recent examination. In the seven patients who were following the diet "satisfactorily" and in whom cardiomegaly recurred, the cardiothoracic ratio increased from average figures of 0.40 to 0.46.

TABLE XII

CARDIOTHORACIC RATIO IN FORTY-NINE PATIENTS TREATED WITH RICE DIET*

Initial Cardiothoracic Ratio (range)	Before Treatment		During Period of Strictest Adherence to Rice Diet		At Most Recent Examination	
	Number of Patients	CT Ratio (averages)	Number of Patients	CT Ratio (averages †)	Number of Patients	CT Ratio (averages ‡)
0.36 to 0.42	3	0.41	24	0.40	12	0.41
0.43 to 0.47	17	0.45	18	0.45	16	0.46
0.48 to 0.52	19	0.50	6	0.49	16	0.50
0.53 to 0.59	10	0.56	1	0.53	5	0.55
0.36 to 0.59	49	0.49	49	0.43	49	0.46

* Followed for at least one year.
† After 1 to 22, average 6, months.
‡ After 1 to 9½, average 3, years.

TABLE XIII

KIDNEY FUNCTION (PSP EXCRETION) IN FORTY PATIENTS TREATED WITH RICE DIET*

	Number of Patients	Total PSP Excretion in 2 Hours (%)		Length of Time in Months (averages)
		Before Treatment (averages)	At Most Recent Examination (averages)	
Diet poorly followed (after initial period):	14	49	43	48
Increased or unchanged	5	52	59	45
Decreased	9	47	35	50
Diet well followed:	26	44	47	46
Increased or unchanged	17	43	54	51
Decreased	9	44	37	38

* Followed for at least two years.

Table XIII shows the change in total PSP excretion in two hours in forty patients treated with the rice diet, strict and modified, for two years or longer. In nine (64 per cent) of

the fourteen who followed the diet poorly after the initial period of treatment, the PSP excretion decreased; in five (36 per cent) it increased. In nine (35 per cent) of the twenty-six who followed the diet well it decreased; in seventeen (65 per cent) it increased.

TABLE XIV
KIDNEY FUNCTION (PSP EXCRETION) IN TWELVE PATIENTS TREATED WITH RICE DIET*

	Number of Patients	Total PSP Excretion in 2 Hours (%)	
		Before Treatment (averages)	At Most Recent Examination (averages)
Diet poorly followed (after initial period)	5	53	44
Followed diet well	7	52	60

* Followed for at least five years.

There are twelve patients in whom repeated determinations of the total PSP excretion in two hours are available after five years or more of observation. (Table XIV.) Five followed the diet poorly; the average PSP excretion in two hours of these five patients decreased from 53 to 44 per cent. Seven have adhered to the diet well; in these seven the average PSP excretion in two hours has increased from 52 to 60 per cent.

It usually takes at least three to four months of intensive dietary treatment to produce a significant decrease in the heart size and blood pressure and it frequently takes over one year for the inverted T_1 in the electrocardiogram to become normally upright. For improvement in kidney function at least two to three years are needed.

COMMENT

When treatment with the rice diet was started in 1939 it was thought that extreme dietary restriction would have to be continued indefinitely to compensate for an underlying renal metabolic dysfunction. At present we have quite a few patients who have been able to resume a salt-poor, fat-poor diet and some who, after an adequate period of intensive treatment first with a strict and then with a modified rice diet, have been able to tolerate a general diet without recurrence of vascular disease.

In patients with malignant hypertension treated with the rice diet before the PSP excretion in two hours has decreased to less than 35 per cent, the prognosis is no longer as unfavorable as it was. Sixty (84 per cent) of the seventy-one patients with a total PSP excretion of 36 per cent or more in two hours survived one year (Table II) and had overcome the malignant phase of the hypertensive vascular disease. Of these sixty patients, thirty (Fig. 2) continued to follow the rice diet; twenty-eight (93 per cent) of the thirty are still living four years after initiation of treatment. However, since most cases of malignant hypertension are preceded by known "benign" hypertensive vascular disease, malignant hypertension can now be regarded as a preventable condition. Hypertensive vascular disease, no matter how mild the symptoms, should be treated immediately and vigorously as soon as the diagnosis has been established, and in those patients who have already developed the malignant phase and have been successfully treated intensive dietary treatment should not be discontinued before the underlying disease has disappeared.

SUMMARY

One hundred seventy-seven patients with hypertensive vascular disease with papilledema (confirmed by eyeground photographs) were seen between October, 1942, and October, 1953. In six patients follow-up information is inadequate or the treatment period too short for evaluation.

In thirty-three patients with hypertensive neuroretinopathy who were willing to be treated with the rice diet, electrolyte imbalance developed within the first three months on the rice diet. Treatment with drastic salt restriction therefore could not be carried out, but additional NaCl or other chloride was given. In thirty-one of these thirty-three patients the total PSP excretion in two hours was below 36 per cent. All thirty-three patients died.

In eighteen patients treatment with the rice diet was not carried out at any time; only one of these is still living.

In 120 patients with hypertensive neuroretinopathy treatment with the rice diet was carried out. The period of treatment was from 1 to 117 months. In 83 of the 120 patients the

total PSP excretion in two hours was below 55 per cent. (This includes four patients in the terminal stage of the disease, in whom the PSP was not measured.) Forty-seven (57 per cent) of these patients survived one year; twenty-six (31 per cent) are still living four and one-fourth years (average) after treatment was started. In thirty-seven patients the total PSP excretion was 56 per cent or more in two hours; thirty-four (92 per cent) survived one year; twenty-six (70 per cent) are still living five years (average) after treatment was started.

One hundred of the 120 patients were followed after the initial period of the treatment with the rice diet, and in these patients the relation of the length of time of supervised treatment to the survival time could be studied. In 39 of the 100 patients the period of supervised treatment was two to twelve months. Seven of the thirty-nine died during this period while presumably still following the diet; only three of the seven were following it correctly. Thirty-two of the thirty-nine were treated for two to twelve months, and then to a greater or lesser extent discontinued the treatment; only six (19 per cent) of the thirty-two are still living.

Eighteen of the 100 patients were treated one to seven and one-half, average three, years and then to a greater or lesser extent discontinued the treatment. Nine of these (50 per cent) are still living.

Forty-three of the 100 patients were treated over one year with the rice diet and continued treatment. Thirty-seven (86 per cent) of these are still living; of the six who died, only three were following the diet correctly.

The effect of the rice diet on retinopathy was studied in 100 patients in whom eyeground photographs were available. In ninety-two of the 100 patients, papilledema disappeared completely.

The effects of the rice diet on blood pressure, serum cholesterol, blood non-protein nitrogen, T_1 in the electrocardiogram, cardiothoracic ratio and renal function were studied in sixty-one patients who were re-examined here at least one year after treatment had been started. A comparison of the findings before treatment, during the period of "strictest adherence to the rice diet" and at the most recent examination shows that the "strictest adherence to the rice diet" produces the most favorable results. Dietary modifications therefore should be made gradually and with careful observations of blood pressure readings, blood chemical findings, electrocardiograms, chest films, eyeground photographs, etc.

The results are interpreted as indicating that intensive dietary treatment should be started as early as possible and continued until all signs of the vascular disease have disappeared.

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Effect of Rice Diet on Diabetes Mellitus Associated with Vascular Disease

Postgraduate Medicine

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Effect of Rice Diet on Diabetes Mellitus Associated With Vascular Disease

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BECAUSE of a high incidence of advanced vascular disease among our patients with diabetes mellitus, we have for the past 15 years treated numerous diabetic patients with the rice diet. Since more than 90 per cent of the calories in this diet are derived from carbohydrates, it was anticipated that increased amounts of insulin would be necessary to keep the blood sugar at its previous level. However, the opposite proved to be true. As previously reported,[1-5] not only is the rice diet well tolerated but in many instances the blood sugar and the insulin requirements decrease.

This paper deals with the effect of the rice diet on some vascular complications, particularly diabetic retinopathy, as well as with its effect on blood and urine chemical findings, especially blood sugar and insulin levels. Findings are given for 100 consecutive patients who were first examined by us between May 1944 and September 1955 and who followed the rice diet more or less strictly for at least three months. The period of observation in these 100 cases ranged from three months to 11 years and averaged 22 months. Nine patients died during the period reported here.

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This paper was written for Dr. Otto Warburg in honor of his seventy-fifth birthday.

Clinical and Laboratory Data

Table 1 gives the average figures before and after treatment for blood sugar, urine sugar, insulin dosage, serum cholesterol, weight, blood pressure, heart size, blood nonprotein nitrogen, phenolsulfonphthalein excretion and urine protein, as well as averages for duration of diabetes, period of observation, age and sex, and incidence of vascular calcifications on x-rays.

Blood sugar—In 22 cases the fasting blood sugar remained relatively unchanged. In 78 cases a change of 20 mg. or more per 100 cc. was found. In 15 the blood sugar increased, the average levels being 140 mg. before treatment and 241 mg. after treatment. In the remaining 63 of the 78 cases the blood sugar level decreased, with averages of 236 mg. before treatment and 135 mg. after treatment.

TABLE 1

EFFECT OF RICE DIET ON 100 PATIENTS WITH DIABETES MELLITUS; CLINICAL AND LABORATORY DATA (AVERAGES)

Average age of patients, 51 years (19 to 71)
Sex distribution, 46 men and 54 women
Average known duration of diabetes, nine years (0 to 33)
Average period of observation, 22 months (3 to 137)

	Before diet	*After diet*
Fasting blood sugar (mg. per 100 cc.)	202	155
Insulin (units)	25	17
Urine sugar (gm. in 24 hours)	21.1	4.2
Cholesterol (mg. per 100 cc. of serum)	297	239
Weight (kg.)	71.3	64.0
Blood pressure (mm. Hg)	179/97	151/85
Heart size (heart-chest ratio)	0.48	0.45
Incidence of arteriosclerosis (x-rays) (per cent)	66	
Nonprotein nitrogen (mg. per 100 cc. of blood)	42	37
Phenolsulfonphthalein excretion (per cent in two hours)	55	49
Proteinuria (gm. per 1000 cc. of urine)	0.36	0.19

Insulin—Twenty-eight patients did not take insulin either at the beginning or at the end of treatment. In 21 of the 72 cases in which the patients did take insulin the dosage was not changed; in 51 it was changed. Insulin dosage was increased in nine cases, including four in which the patients started without insulin (averages, 22 units before and 44 units after treatment). It was decreased in 42 cases. The average dosages in these cases were 39 units before treatment and 16 units after treatment; in 18 cases with an average initial insulin requirement of 26 units, insulin could be completely discontinued.

Glycosuria—Sixty-six of the 100 patients did not have glycosuria either at the beginning or at the end of treatment. In three of the 34 cases in which the patients had glycosuria, there was an increase in the amount excreted; in two of these three cases the average increase was from zero to 11.2 gm. in 24 hours, and in the third case the amount increased from 4 to 14.6 gm. in 24 hours. In 31 of the 34 cases in which the patients had glycosuria, there was a decrease in the amount excreted: from 28.1 to 8.1 gm. in 24 hours (averages), nine cases; from 4 plus to 3 plus, three cases; from 4 plus to 1 plus, one case; from 22.1 gm. in 24 hours (average) to zero, eight cases; from 4 plus to zero, four cases; from 2 plus to zero, three cases; and from 1 plus to zero, three cases.

Serum cholesterol—Twenty of the 100 patients had a serum cholesterol concentration of 220 mg. or less per 100 cc. at the beginning of treatment. In 13 of these cases the concentration increased, the averages being 191 mg. before treatment and 232 mg. after treatment. In two cases the cholesterol concentration remained unchanged. In five it decreased (average, 201 mg. to 174 mg.).

Eighty patients had a serum cholesterol concentration of 221 mg. or more per 100 cc. at the beginning of treatment. The concentration increased in 12 of these cases (averages, 303 mg. before treatment and 352 mg. after treatment). In the other 68 cases the cholesterol concentration decreased, the average values being 325 mg. before treatment and 227 mg. after treatment.

Blood pressure—Ten patients had blood pressures of 129/88 or less at the beginning of treatment; the average readings in these 10 cases were 122/77 before treatment and 129/82 after treatment.

Ninety patients had blood pressure readings of 135/82 or more (average, 185/99) at the beginning of treatment. Their average blood pressure after treatment was 153/85. In 19 cases the blood pressure returned to normal (118/75, average).

Heart size—Chest films of 87 patients are available for comparison before and after treatment (no digitalis after beginning of rice diet). In 59 cases the heart-chest ratio was less than 0.50 before treatment; it decreased from 0.44 to 0.43 (averages). In 28 cases the heart-chest ratio was 0.50 or more before treatment. It decreased from 0.56 to 0.50 (averages). In no case did the heart become larger in size.

Electrocardiogram—Electrocardiograms of 86 patients are available for comparison before and after treatment (no digitalis). Fifty of the 86 patients had a normal electrocardiogram at the beginning of treatment. In 46 cases it remained normal, and in four cases

abnormal findings were observed: infarct, one case; T_1 inverted, two cases; and diphasic T_1, one case.

Thirty-six of the 86 patients had an abnormal electrocardiogram at the beginning of treatment; four had previous infarction, five had bundle-branch block, and 27 abnormal T_1. In 15 of these cases the abnormal findings persisted (four previous infarction, five bundle-branch block, six inverted or diphasic T_1). In five cases the electrocardiographic findings became worse; in three the diphasic T_1 became inverted, and in two with inverted T_1 a bundle-branch block and an infarction developed, respectively. In 16 cases the electrocardiogram improved; the T_1, which had been inverted in six, diphasic in five, and flat in five, became upright.

Nonprotein nitrogen—Sixty of the 100 patients had a nonprotein nitrogen level of 40 mg. or less per 100 cc. of blood at the beginning of treatment. In 20 of these cases the nonprotein nitrogen increased, the averages being 31.1 mg. before treatment and 39.6 mg. after treatment. In three cases the level remained unchanged. In 37 there was a decrease in the nonprotein nitrogen, from 35.2 mg. before to 30 mg. after treatment (averages).

Forty patients had a nonprotein nitrogen level of more than 40 mg. per 100 cc. of blood at the beginning of treatment. In six of these cases the level increased from an average of 52 mg. before treatment to an average of 64 mg. after treatment. In two the level remained unchanged, and in 32 there was a decrease, from an average of 83 mg. before treatment to an average of 38 mg. after treatment.

Phenolsulfonphthalein excretion—Data on phenolsulfonphthalein excretion before and after treatment are available for 77 of the 100 patients. In only 11 cases was the initial phenolsulfonphthalein excretion 75 per cent or more in two hours. Including these, in 59 cases there was an initial phenolsulfonphthalein excretion of 40 per cent or more in two hours. In 39 of these 59 cases the percentage of phenolsulfonphthalein excreted decreased from an average of 64.7 before treatment to 50.7 after treatment. In two cases the excretion remained unchanged. In 18 it increased, the averages being 60.9 per cent before treatment and 70.1 per cent after treatment.

Eighteen patients had an initial phenolsulfonphthalein excretion of less than 40 per cent in two hours (range, zero to 39 per cent). Of these, nine showed a decrease, from an average of 33 per cent before to an average of 25 per cent after treatment. In one case the excretion remained unchanged. In eight cases it increased, the average before treatment being 20 per cent and the average after treatment 35 per cent.

Proteinuria—Thirty-three patients did not have proteinuria either at the beginning or at the end of treatment. In 10 of the 67 cases with proteinuria, the amount increased from an average of 0.20 gm. per 1000 cc. before treatment to an average of 0.40 gm. per 1000 cc. after treatment. In four cases the amount of protein in the urine did not change, and in 53 it decreased (in 32 from an average of 0.88 gm. before to an average of 0.41 gm. after treatment; in 21 from an average initial level of 0.24 gm. to zero).

Retinopathy—Tables 2 and 3 show the incidence and course of retinopathy, the frequency of renal disease, and duration of diabetes. Of the 100 patients, 68 had advanced retinal involvement.

In 48 cases (44 with comparable photographs) there was specific diabetic retinopathy manifested by capillary aneurysms, punctate, preretinal or vitreous hemorrhages, waxy exudates, neovascularization and retinitis proliferans, with or without other changes in the retina (renal, hypertensive, arteriosclerotic). Thirty of the 48 patients had the most severe form of diabetic retinopathy, retinitis proliferans. Diabetic retinopathy was considered improved if the eyeground photographs after treatment showed marked regression of "diabetic" hemorrhages, exudates, aneurysms or retinitis proliferans.

In 13 of the 44 cases in which photographs are available for comparison, these showed marked improvement. In one case "diabetic" hemorrhages and aneurysms disappeared completely and have not recurred during three years of observation. In eight cases these changes disappeared to a large extent. In four

TABLE 2

INCIDENCE OF RETINOPATHY IN 100 DIABETIC PATIENTS TREATED WITH RICE DIET, AND ITS RELATION TO RENAL DISEASE

	NUMBER OF PATIENTS	AGE* (Years)	KNOWN DURATION OF DIABETES* (Years)	PERIOD OF OBSERVATION* (Months)
Specific diabetic retinopathy	48	48	14	19
(Without renal disease)	(19)	(53)	(15)	(19)
(With renal disease)	(29)	(44)	(14)	(19)
Nonspecific vascular retinopathy	20	53	5	33
(Without renal disease)	(13)	(53)	(5)	(41)
(With renal disease)	(7)	(54)	(5)	(18)
No retinopathy	32	55	4	19
(Without renal disease)	(29)	(54)	(3)	(19)
(With renal disease)	(3)	(61)	(11)	(23)

*Averages.

cases, in addition to improvement of hemorrhages, there was a considerable clearing of retinitis proliferans; the patients in these four cases have been observed for periods of four months, 10 months, five years and five years, respectively.

Twenty patients (19 with comparable photographs) did not have specific diabetic retinopathy as defined in the foregoing discussion but had other forms of retinopathy (renal, hypertensive, arteriosclerotic) manifested by vascular thromboses, hemorrhages, exudates, and papilledema. This retinopathy was considered improved if the eyeground photographs after treatment showed either complete disappearance or considerable clearing of the hemorrhages or exudates or complete disappearance of the papilledema. Eleven of the 19 patients of whom comparable photographs are available showed marked improvement.

In only one of the 32 cases in this series in which the patients did not have retinopathy at the beginning of treatment did it develop during the period of observation (exudates).

TABLE 3

EFFECT OF RICE DIET ON RETINOPATHY IN 63 PATIENTS WITH DIABETES

	NUMBER OF PATIENTS	PERIOD OF OBSERVATION (Months) (Average and Range)
*Specific diabetic retinopathy**		
Eyeground photographs available for comparison	44	19 (4-102)
Progression of lesions	9	28 (4-102)
Lesion improved in one eye, progressed in other	7	19 (4-76)
No change	15	8 (4-48)
Improved	13	25 (4-60)
*Nonspecific vascular retinopathy**		
Eyeground photographs available for comparison	19	33 (4-137)
Progression of lesions	3	8 (5-13)
No change	5	10 (4-21)
Improved	11	52 (8-137)

*Comparable photographs are not available of four patients with specific diabetic retinopathy and one with nonspecific vascular retinopathy.

Representative Case Histories

Figures 1 through 6 are eyeground photographs taken before treatment and after 3½ to 60 months of treatment with the rice diet.

Case 1—The patient in figure 1, a 54 year old woman, was first seen in March 1949. She had had known diabetes mellitus for 10 years. For the first few years there was good control of the disease by diet, and she did not take insulin. Since 1947 she had taken 25 units of insulin daily. Three months before we saw her, she noted the beginning of impairment of vision. One month before we saw her, she suddenly was unable to read headlines with her left eye. At the time we examined her, her vision was somewhat improved, and she could

pick out a few words of smaller headlines with her left eye. Blood pressure had increased for the past 10 years.

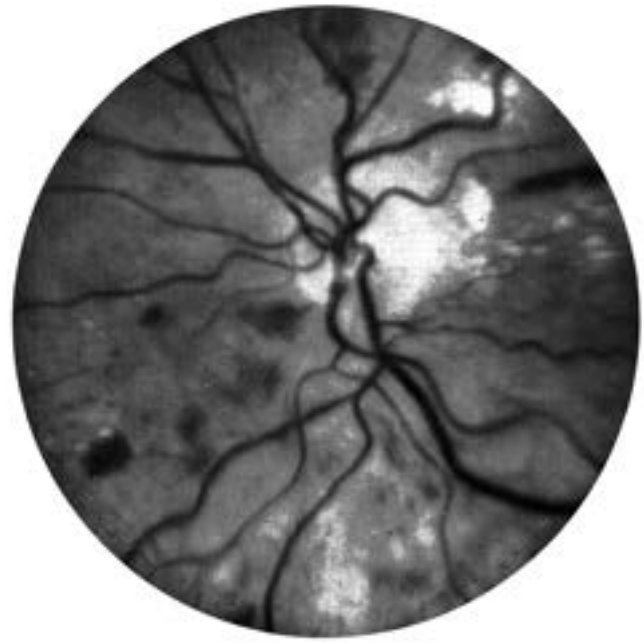
The rice diet was started in March 1949.

Laboratory data—Findings at the first examination in March 1949 and in September 1952 were as follows:

	1949	*1952*
Blood pressure (average)	234/108	180/90
Insulin (units)	25	18
Blood sugar, fasting (mg. per 100 cc.)	189	166
Urine sugar	0	0
Cholesterol (mg. per 100 cc. of serum)	225	224
Phenolsulfonphthalein excretion (per cent in two hours)	52	
Albuminuria (gm. per 1000 cc.)	0	0.16
Nonprotein nitrogen (mg. per 100 cc. of blood)	44	50

Vision—In 1949 the patient could see well with the right eye, and with the left she could read small headlines with difficulty. There were hemorrhages (large and pinpoint), aneurysms and numerous cottony and hard exudates throughout both fundi, the left macula being more involved than the right. In 1952 vision was normal. Both fundi showed a few sprinkles of exudates, without hemorrhages or aneurysms.

Case 2—The patient represented in figure 2 was a 24 year old man first seen in August 1950. He had a nine year history of diabetes mellitus. There was good control with diet and insulin; he had not had coma, but acidosis had occurred at the ages of 14, 17 and 21 years. He was asymptomatic until January 1949, when the glare of the sun caused difficulty in vision. There were carbuncles on both arms at the sites of insulin injections. Insulin dosage had increased to 85 units. Hemorrhages were found in the eyes. In February 1950 he experienced difficulty in reading because the lines blurred. When driving, the lights were out of focus. His vision was dim,



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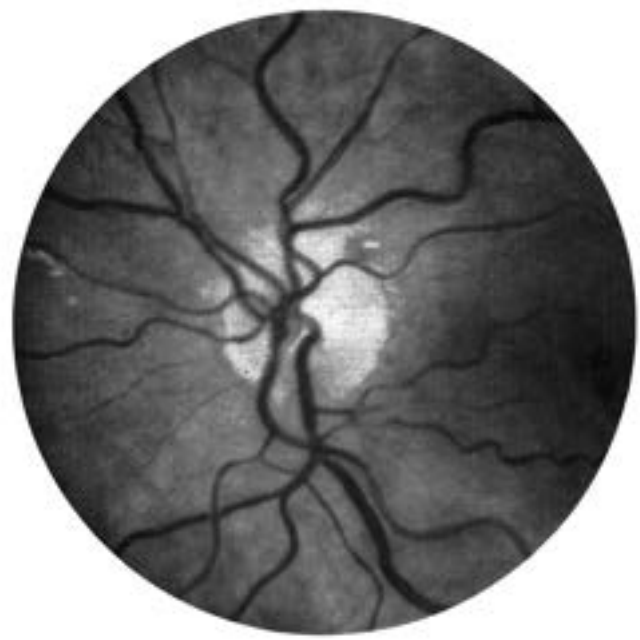
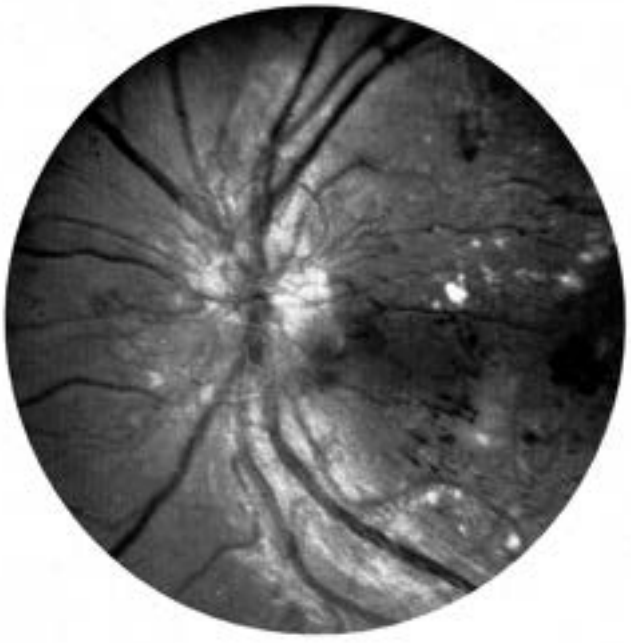
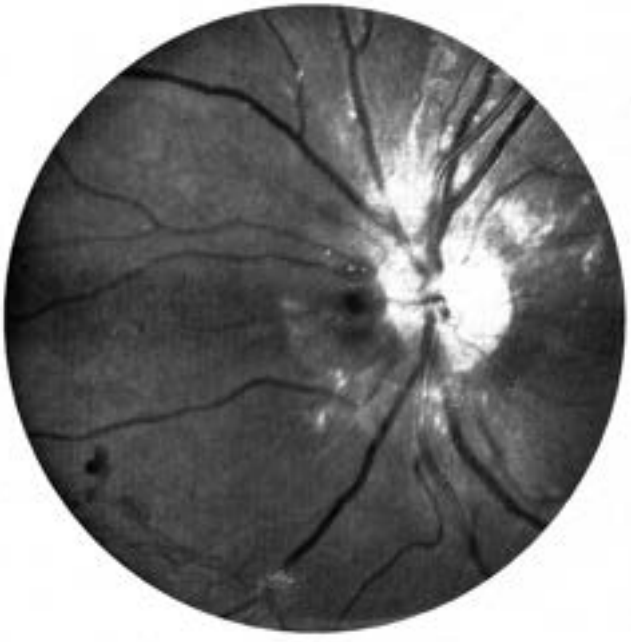


9-25-52

FIGURE 1. Case 1.



8-18-50



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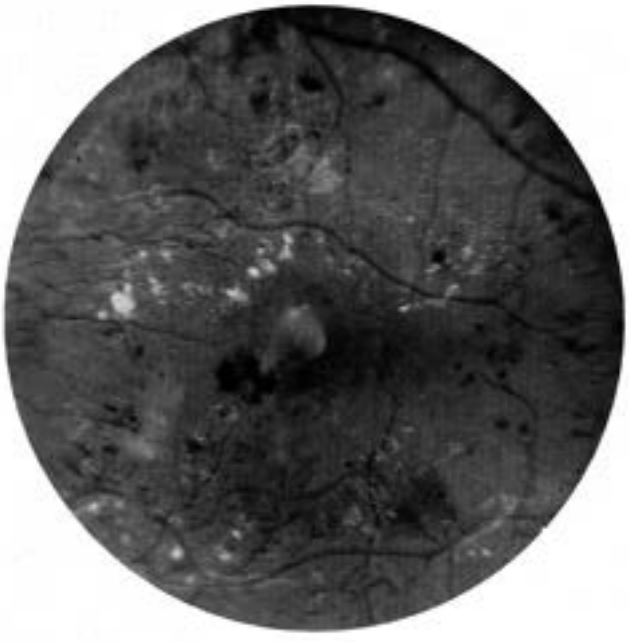

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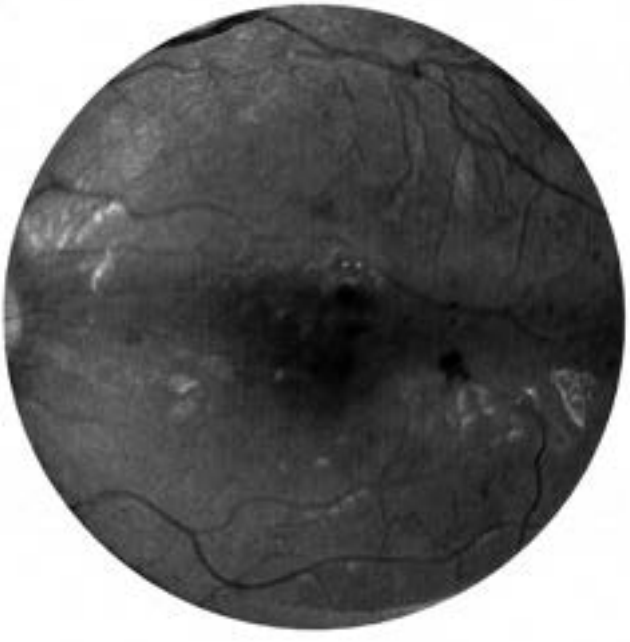

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FIGURE 2. Case 2.

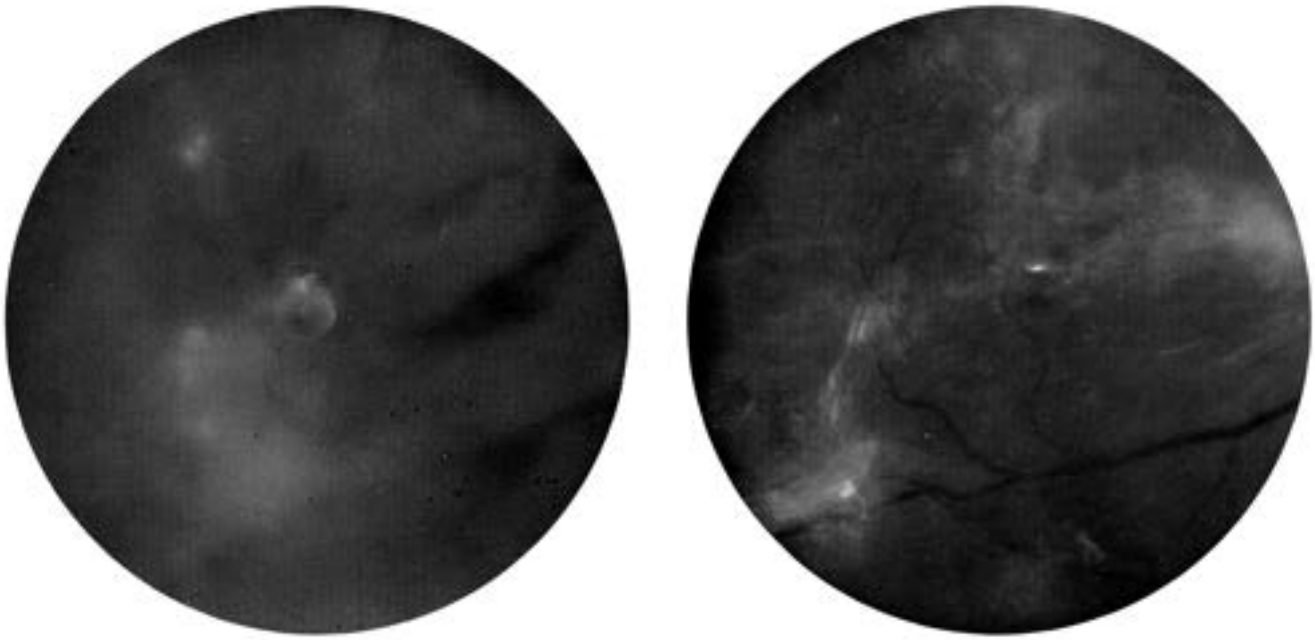


FIGURE 3. Case 3.

and he could not read the signs on buses.

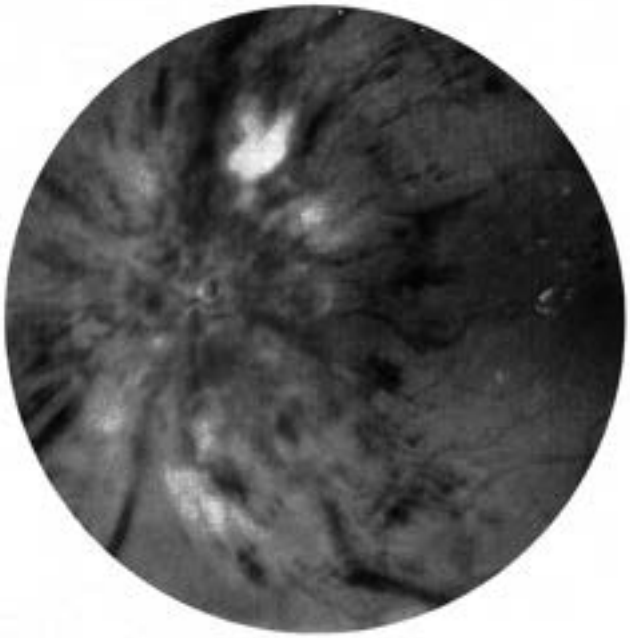
The rice diet was started in August 1950.

Laboratory data—Findings at the first examination in August 1950 and in August 1955 were as follows.

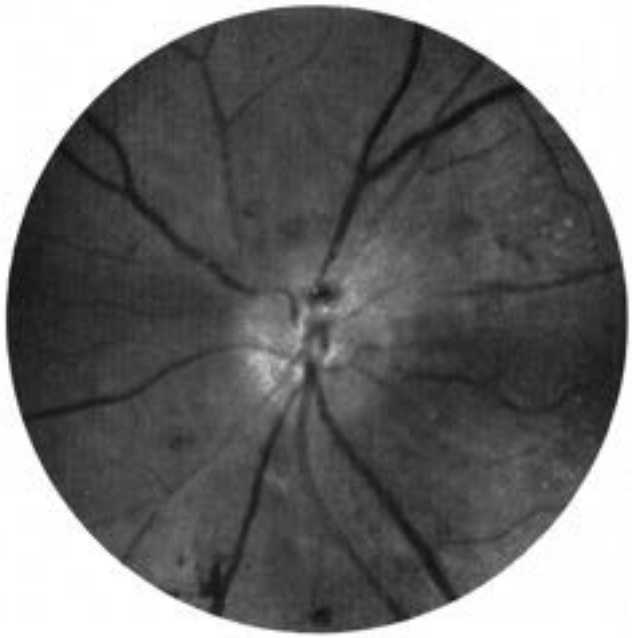
	1950	*1955*
Blood pressure (average)	126/80	135/90
Insulin (units)	75	42
Blood sugar, fasting (mg. per 100 cc.)	91	272
Urine sugar (gm. in 24 hours)	0	1 plus
Cholesterol (mg. per 100 cc. of serum)	165	156
Phenolsulfonphthalein excretion (per cent in two hours)	73	65
Albuminuria (gm. per 1000 cc.)	0.32	0.28
Nonprotein nitrogen (mg. per 100 cc. of blood)	33	43

Vision—In 1950 the patient could read ⅜ in. print. The disks were obscured by marked neovascularization and beginning retinitis proliferans. There were numerous round and flame-shaped hemorrhages, capillary aneurysms, and hard and cottony exudates bilaterally. In 1955 the patient could read small print with his left eye and ½ in. print with the right eye. The right disk was obscured by a hazy veil, but the largest part of the retina, especially the macular region, was almost clear. There were no hemorrhages or exudates. The disk on the left was well outlined. Neovascularization had disappeared, and hemorrhages, exudates and aneurysms had almost completely disappeared.

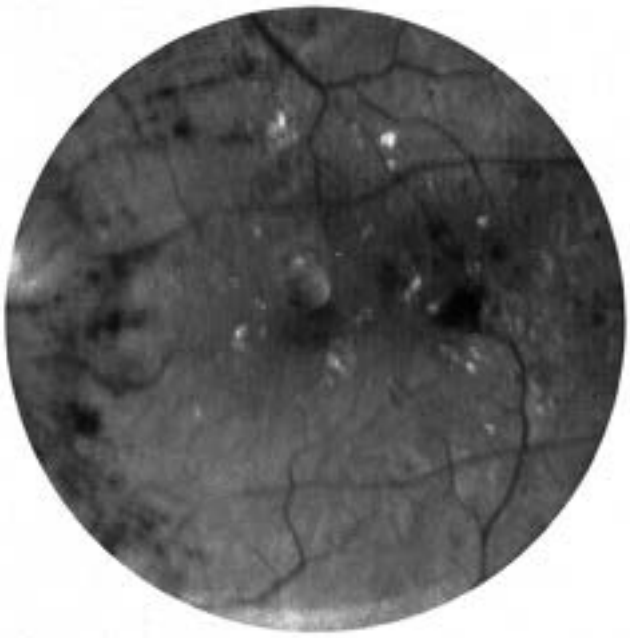
Case 3—A 60 year old woman was first seen in October 1950 (figure 3). Her past history included diabetes mellitus for two years, and weight loss for 16 years although she ate well. In 1948 urinalysis showed 2 plus sugar. A diabetic diet was prescribed but she did not take insulin. One and a half years before we saw her she had visual difficulty. Hemorrhages were found in the right eye. Treatment consisted of RUTORBIN® and 10 units of insulin.



4-12-51



7-25-51



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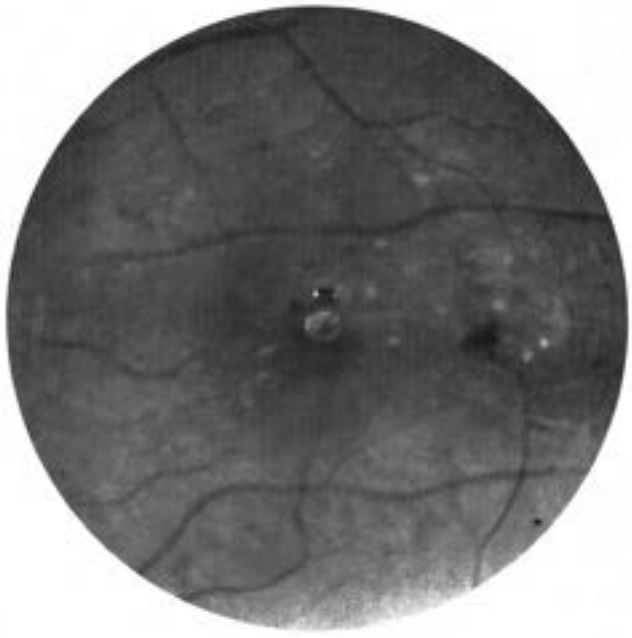

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FIGURE 4. Case 4.

Visual impairment in the right eye persisted. Five weeks before we saw the patient she had sudden impairment of vision in the left eye.

The rice diet was started in October 1950.

Laboratory data—The findings in October 1950 compared with those in October 1955 were as follows.

	1950	*1955*
Blood pressure (average)	186/90	170/80
Insulin (units)	14	0
Blood sugar, fasting (mg. per 100 cc.)	161	95
Urine sugar	0	0
Cholesterol (mg. per 100 cc. of serum)	335	228
Phenolsulfonphthalein excretion (per cent in two hours)	64	40
Albuminuria (gm. per 1000 cc.)	0	0.16
Nonprotein nitrogen (mg. per 100 cc. of blood)	39	37

Vision—In 1950 the patient could see contours of large objects with the right eye. With the left eye there was light perception only. There were fundal hemorrhages bilaterally, especially extensive in the left macular region. Marked proliferative changes were noted in both fundi. In 1955 the vision in the right eye had improved. The patient could make out faces and read signs and large newspaper print. With the left eye there was light perception only. There were no fundal hemorrhages or exudates in the right eye; except for proliferative changes around the disk, the retina, especially the macular region, was considerably clearer. Examination of the left eye showed extensive retinitis proliferans, with no hemorrhages.

Case 4—The patient whose eyeground photographs are shown in figure 4 was a 42 year old man first seen in April 1951. Diabetes mellitus had been diagnosed three and a half years previously. He had lost 30 lb., and the blood sugar level at that time was 157 mg. per 100 cc. Treatment consisted of restriction of sweets, and 15 units of insulin. Blood pressure was elevated. Two months before we saw the patient he had blurred vision in his right eye. Blood pressure was 230 systolic, albuminuria was noted, and a hemorrhage was found in the right eye. He was given a salt-poor diet. The vision in the right eye cleared; however, that in the left became cloudy.

The rice diet was started in April 1951.

Laboratory data—Comparative findings in April 1951 and in July 1951 were as follows.

	April	*July*
Blood pressure (average)	220/120	143/80
Insulin (units)	15	0
Blood sugar, fasting (mg. per 100 cc.)	85	142
Urine sugar	0	0
Cholesterol (mg. per 100 cc. of serum)	289	183
Phenolsulfonphthalein excretion (per cent in two hours)	26	
Albuminuria (gm. per 1000 cc.)	2.8	0.22
Nonprotein nitrogen (mg. per 100 cc. of blood)	81	70

Vision—In April the patient could see well with the right eye, but had blurred vision with the left. Bilateral papilledema was noted, and numerous hemorrhages and exudates in both eyes. There were capillary aneurysms. In July the patient's vision was normal. The left disk was clearly outlined. The right disk was still slightly hazy but greatly improved. There were a few hemorrhages and small hard exudates, and fewer aneurysms.

Case 5—A 29 year old man (figure 5) first seen in May 1952 had had known diabetes mellitus for 19 years. The diabetes was under good control with 60 to 80 units of insulin daily, and later the dosage was 48 units. There was no history of coma or acidosis, and the urine was almost always sugar-free. For five years before we saw him the patient had albuminuria and hypertension. Blood pressure at a recent examination prior to May 1952 was 180/110. In November 1951 he had an episode of blurring of vision and spots before the eyes. Small hemorrhages were found, and

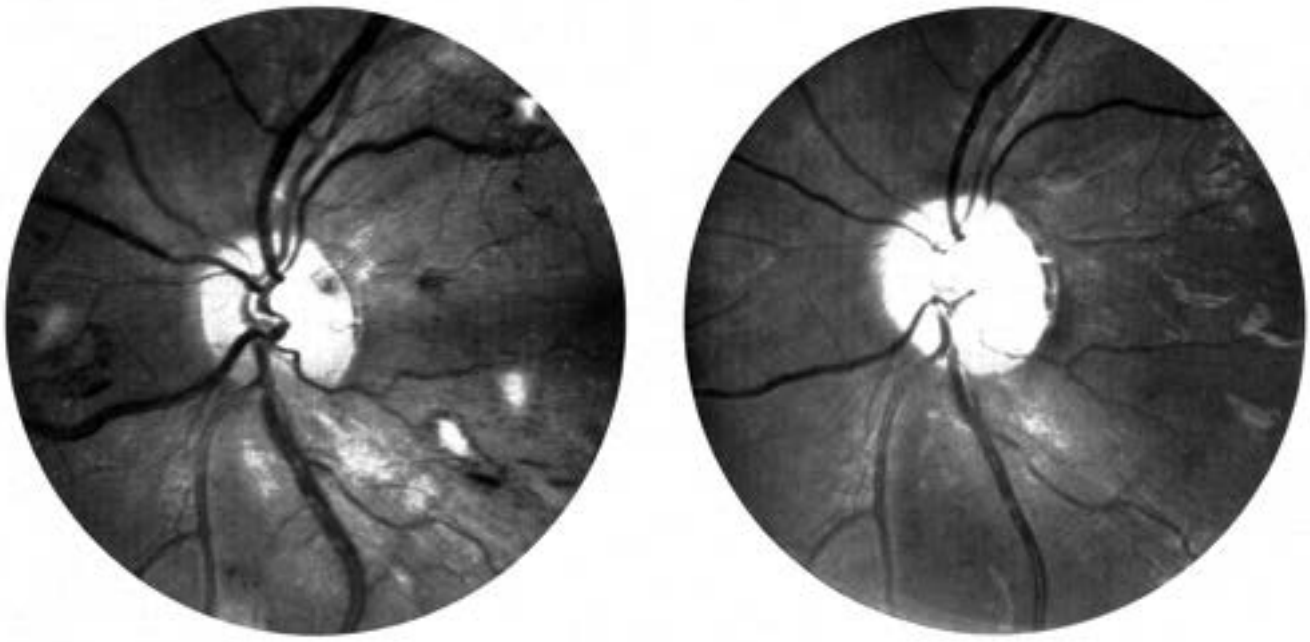

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FIGURE 5. Case 5.

subsequently he had repeated episodes of blurred vision.

The rice diet was started in May 1952.

Laboratory data—Examinations in May 1952 and in November 1955 gave the following findings.

	1952	*1955*
Blood pressure (average)	214/130	141/89
Insulin (units)	62	42
Blood sugar, fasting (mg. per 100 cc.)	58	78
Before lunch	225	177
Before dinner	78	61
Urine sugar (gm. in 24 hours)	8	0
Cholesterol (mg. per 100 cc. of serum)	346	209
Phenolsulfonphthalein excretion (per cent in two hours)	34	25
Albuminuria (gm. per 1000 cc.)	1.3	0.62
Nonprotein nitrogen (mg. per 100 cc. of blood)	38	45

Vision—In May 1952 vision was blurred. There were numerous hemorrhages and cottony exudates scattered throughout both fundi. Capillary aneurysms were noted. In November 1952 there was improvement of vision and regression of hemorrhages and exudates. In March 1953, examination showed complete disappearance of hemorrhages, exudates and aneurysms. Between March 1953 and November 1955, the patient had seven checkups, each including eyeground photographs. There was no recurrence of diabetic or other retinopathy. In November 1955 visual acuity was normal; disks were well outlined, and there were no hemorrhages, exudates or aneurysms.

Case 6—The patient represented in figure 6 was a 65 year old woman first seen in August 1955 with a 15 year history of diabetes mellitus. When the disease was diagnosed, the blood sugar was 200 mg. per 100 cc., and the blood pressure was elevated. A general diet was prescribed, restricting carbohydrates, and 40 units of insulin was given daily. The diabetes was fairly well controlled. Over a period of 10 to 15 years before we saw her, the patient had failing vision in the left eye, and had

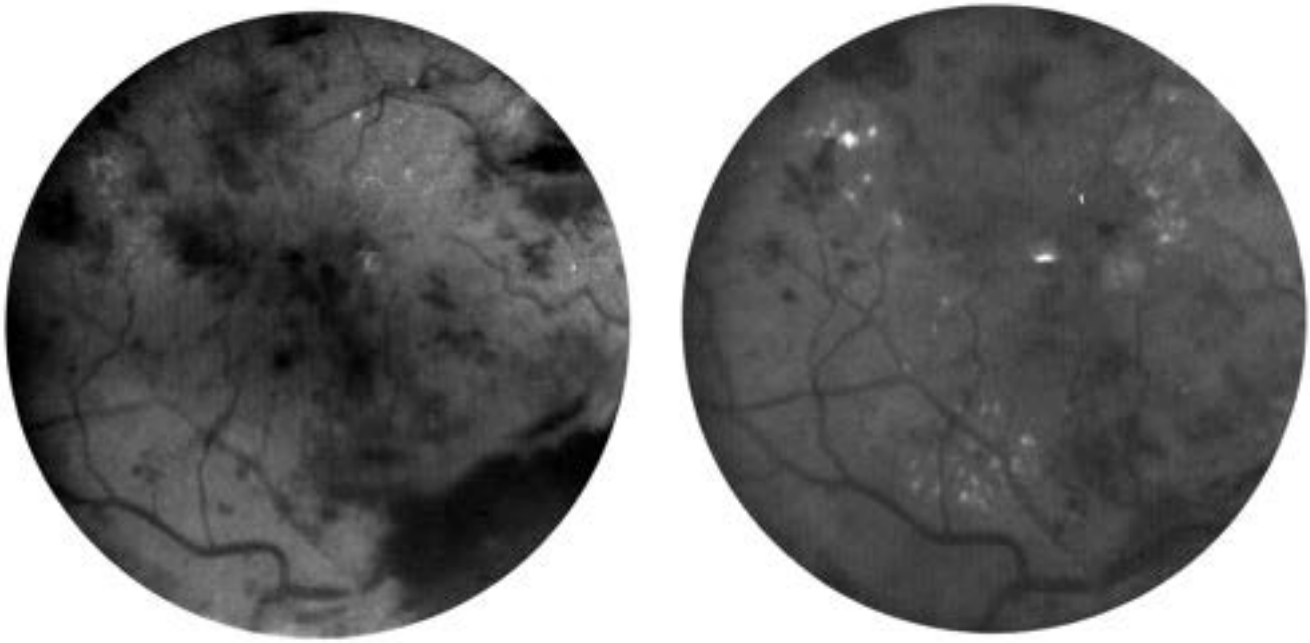

FIGURE 6. Case 6.

noticed failing vision in the right eye for one and a half years. The patient was said to have "bleedings and scars" in the eyes. Rapid impairment of vision occurred in the two month period before we saw her. She could still see objects and read big headlines.

The rice diet was started in August 1955.

Laboratory data—Findings in August 1955 and in December 1955 were as follows.

	Aug.	*Dec.*
Blood pressure (average)	190/100	146/74
Insulin (units)	40	20
Blood sugar, fasting (mg. per 100 cc.)	161	136
Urine sugar	0	0
Cholesterol (mg. per 100 cc. serum)	226	191
Phenolsulfonphthalein excretion (per cent in two hours)	68	
Albuminuria (gm. per 1000 cc.)	0.1	0
Nonprotein nitrogen (mg. per 100 cc. of blood)	40	30

Vision—In August 1955 the patient could read large print with either eye. The disks were well outlined, and there were numerous hemorrhages and hard exudates in both fundi. In the right eye there was inferior temporal vein thrombosis with massive hemorrhage. Capillary aneurysms were noted. In December 1955 the patient could read newspaper print. Disks were well outlined, and marked regression of hemorrhages and exudates was noted. Capillary aneurysms were still present.

Discussion

It has been known since 1943[1-5] that patients with diabetes mellitus not only tolerate the rice diet well but also are often benefited by it. (The rice diet contains 565 to 570 gm. carbohydrate, 20 to 25 gm. protein, less than 5 gm. fat, and 70 to 120 mg. sodium per 2400 calories.) The present survey of 100 patients shows again that the average blood sugar levels and average insulin requirements decrease. Although this group included many patients with severe diabetes, ketosis occurred only once. Acidosis did not occur; on the contrary, the plasma carbon dioxide-combining power

increased in the majority of cases and moved away from the acid toward the alkaline side.

Patients who were obese were urged to reduce. However, changes in blood sugar levels, insulin requirements, cholesterol levels, blood pressure, and so on occurred both in patients who lost weight and in those who did not have a significant weight change.

In view of the frequency of the development of arteriosclerosis in diabetic patients, the decrease in the serum cholesterol level may be of importance.

The reduction in blood pressure and heart size and the improvement in abnormal electrocardiographic patterns in diabetic patients treated by the rice diet are the same as those found in nondiabetic patients with cardiovascular disease who are treated with the rice diet. This is also true for the decrease in azotemia in cases in which there is renal involvement. An increase in the average phenolsulfonphthalein excretion was not found, and we cannot yet state whether this is because a much longer treatment period may be necessary for this change to occur.[6]

Of particular interest was the effect of the rice diet on diabetic retinopathy. The ophthalmoscopic picture of "specific" diabetic retinopathy differs from that of renal, arteriosclerotic or hypertensive vascular retinopathy. All forms of vascular retinopathy may occur together with the "specific" diabetic retinopathy, as was also found in this series.

Table 2 shows again that diabetic retinopathy develops more commonly in patients who have had diabetes for a long time. In the 52 cases without evidence of diabetic retinopathy the known duration of diabetes prior to the first examination at our institution averaged 4.4 years; the known duration of diabetes in the 48 patients with "specific" diabetic retinopathy averaged 14 years. The table confirms further the frequent coincidence of renal disease and diabetic retinopathy (60 per cent). Table 3 indicates that at least during the period of observation covered by this study the renal, arteriosclerotic and hypertensive changes improved in a significantly higher percentage of cases than did the "specific" retinal changes; the percentages were 55 and 27 per cent, respectively. Hemorrhages, exudates and papilledema heal as well in diabetic patients as they do in nondiabetic patients treated with the rice diet.

Diabetic retinopathy has been considered a sign of irreversible destruction. "The retinal complications of long-standing diabetes are grave and have an unfavorable prognostic significance. Any observation, therefore, is valuable which indicates a favorable influence in at least some patients."[7]

In our group of 48 patients with diabetic retinopathy the incidence of retinitis proliferans, the severest form of diabetic retinopathy, was very high, 63 per cent. Thirteen patients with diabetic retinopathy, four of them with retinitis proliferans, showed marked improvement. In the 26 of the 30 cases of retinitis proliferans in which this lesion did not improve the patients were observed for 3 to 102 months (average, 17 months), compared with observation periods of 4 to 60 months (average, 34 months) in the four cases in which the lesion did improve.

The effect of the rice diet on diabetes mellitus with or without retinopathy has been explained as "due to a reversible inactivation of the pituitary and/or adrenal gland achieving in a conservative and unbloody way what has been tried by hypophysectomy and adrenalectomy."[8] In this connection the report[9] of a case of improvement in diabetic retinopathy after pituitary necrosis might be interesting. This is one of the few instances reported in the literature in which severe diabetic retinopathy disappeared.

The observations of Handler and Georgiade[10] of our department of biochemistry are also interesting along these lines. They studied the effect of proteins on blood sugar in two groups of rats, the first of which received a low protein diet and the second a high protein diet. They found that the rats receiving a low protein diet were much more sensitive to insulin than were the rats receiving a high protein diet, and also that their fasting blood sugar concentrations were lower. This difference in the blood sugar concentrations disappeared when the animals who were on a low protein diet were treated with ACTH. The in-

vestigators concluded from these results that prolonged low protein diet causes the pituitary to secrete less ACTH.

No matter which single factor may cause the effects of the rice diet on diabetes mellitus and its vascular complications, the rice diet contains less sodium, protein and fat than any other diet for treating diabetes mellitus.

Summary

A report is given on 100 consecutive patients with diabetes mellitus associated with vascular disease who were treated with the rice diet. They were followed for from three months to 11 years, and the average period of observation was 22 months. Nine patients died.

The rice diet, which is a high carbohydrate, low protein, low fat, low sodium diet containing 565 to 570 gm. carbohydrate, 20 to 25 gm. protein, less than 5 gm. fat, and 70 to 120 mg. sodium per 2400 calories, was well tolerated. Average insulin requirements as well as average blood sugar levels decreased.

Manifestations of cardiovascular and renal disease such as hypertension, enlargement of the heart, electrocardiographic abnormalities, azotemia and proteinuria improved significantly in the majority of cases. Hypercholesteremia, present in 80 of the 100 cases, decreased in 85 per cent from an average level of 325 mg. to an average level of 227 mg. per 100 cc.

The effect of the rice diet on "specific" diabetic retinopathy (aneurysms; punctate, preretinal, vitreous hemorrhages; waxy exudates; retinitis proliferans) in 44 patients was as follows: progression of lesions, nine cases; improvement in one eye but progression of lesion in other eye, seven; no change, 15; improved, 13. In 19 cases in which the patients had hypertensive, arteriosclerotic or renal retinopathy (papilledema, hemorrhages, exudates, venous thrombosis), the lesions progressed in three, did not change in five, and improved in 11 cases.

Our experience leads us to conclude that an attitude of resignation with regard to the prognosis in diabetes mellitus with vascular complications including diabetic retinopathy is no longer necessary. The course of the disease can be favorably changed by intensive treatment with the rice diet.

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Effect of Salt Restriction on Experimental Nephrosis

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January 4, 1965, Vol. 191, Page 51

Effect of Salt Restriction on Experimental Nephrosis

Walter Kempner, MD

AN EFFICIENT and dependable method to produce a nephrotic syndrome experimentally has been developed, in which young rats are subcutaneously injected with aminonucleoside of puromycin. The animals have proteinuria, hypercholesterolemia, and edema, largely as free fluid in the peritoneal cavity and as gel in the skin. The disease can easily be made so severe that most of the animals die within one to three weeks after the injections.[1-3]

Steroids did not modify the disease once it had appeared nor did they prevent it from appearing.[4] Adenine (6-aminopurine), but not adenosine, temporarily delayed the onset of proteinuria, but by the second week the nephrotic syndrome was fully developed.[5]

Our report deals with the death rate in this experimental nephrosis in the presence and absence of sodium chloride.

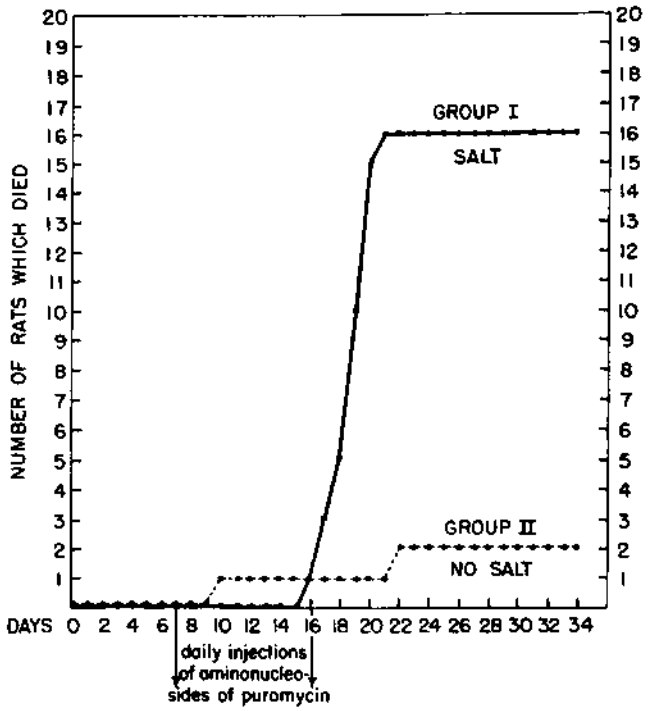
In a typical experiment which may serve as an example, two groups of twenty rats each were used; they were female rats of the Wistar strain. When the rat's average weight was 80 gm, subcutaneous injections of 1.75 mg of aminonucleoside of puromycin in 0.2 cc H_2O were given on ten successive days.

The diet of all the rats was limited to rice and vitamins.

The drinking fluid of the animals in group 1 was tap water to which sodium chloride had been added to make a concentration of 181 mEq of sodium per liter; the drinking fluid of the animals in group 2 was plain tap water. The average fluid intake was 20 cc in group 1 and 17 cc in group 2.

Two control groups of ten rats each on the same diet were given the same drinking fluids as groups 1 and 2, but did not receive the injections. The average fluid intake was 26 cc and 21 cc, respectively. None of the rats without nephrosis in the two control groups whether on water-plus-salt or on plain water died.

The Figure shows the death rate in each group of the 20 nephrotic rats.



Death rate in two groups of 20 nephrotic rats each.

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Reprint requests to Department of Medicine, Duke University School of Medicine, Durham, NC 27706 (Dr. Kempner).

Summary

The death rate in experimental nephrosis was found to be eight times higher in rats which received salt than in rats when salt was excluded from the diet.

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Sodium-Restricted Diet: Sodium Content of Various Wines and Other Alcoholic Beverages

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June 1969, Vol. 123

Sodium-Restricted Diet

Sodium Content of Various Wines and Other Alcoholic Beverages

Barbara Newborg, MD, Durham, NC

Wine and water might be unexpected sources of error in the dietary treatment of heart or kidney disease or hypertensive vascular disease.

If the daily intake of sodium is to be restricted, for instance, to 8.5 mEq (the amount in 0.5 gm of table salt) or even to less than 4 mEq (as in the basic rice diet) a daily intake of 1 qt of "unsatisfactory" water containing more than 13 mEq of sodium per quart (which is the case in many places in this country) would already exceed the total permissible allowance even though the patient might not eat or drink anything else. Proponents of rigid sodium restrictions, therefore, have stated: "If the sodium concentration of the plain water available is greater than 20 mg/liter (0.87 mEq/liter), distilled water should be used." [1]

We have recently analyzed the sodium contents of 68 different kinds of domestic and foreign wines and of 24 different brands of beer and other alcoholic beverages. The results given in the Table show that customary and not excessive amounts of some of them are not compatible with even moderate sodium restriction.

Comment

The Table shows that the sodium concentration per quart of the 32 domestic (red, white, and rosé) still and sparkling table wines analyzed was 1.4 to 52.6 mEq (average, 20.1 mEq); of the 11 French wines, 0.4 to 3.1 mEq (average, 1.9 mEq); and of the 7 German wines, 0.6 to 2.1 mEq (average, 1.2 mEq). The sodium content of the 19 liqueurs and hard liquors analyzed was 0.2 to 2.5 mEq/qt (average, 0.7 mEq). An Italian sweet vermouth contained 1.9 mEq/qt; a domestic sweet vermouth, 22.2 mEq/qt.

It is obvious that a patient who drinks a quart of a table wine with a sodium content of 52.6 mEq (corresponding to more than 3 gm of table salt) exceeds at least sixfold the maximum amount of sodium allowed in a liberal sodium-restricted diet, even if he has no additional sodium intake from any other drink or food. On the other hand, moderate amounts of alcoholic beverages with sodium concentrations of less than 2.0 mEq/qt are compatible with most sodium-restricted diets.

It is recommended that patients who have to follow sodium-restricted diets should have their favorite alcoholic beverages tested for sodium content just as they do with the other foodstuffs which they consume.

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From the Department of Medicine, Duke University Medical Center, Durham, NC.
Reprint requests to Duke University Medical Center, Durham, NC 27706 (Dr. Newborg).

Sodium Content of Various Domestic and Imported Wines and Other Alcoholic Beverages

	Country of Origin	Sodium, mEq/qt
	White Wines	
1	Germany	0.6
2	France	0.7
3	Germany	0.9
4	Austria	1.0
5	Germany	1.0
6	Germany	1.1
7	Germany	1.2
8	Germany	1.4
9	United States	1.4
10	Germany	2.1
11	United States	2.3
12	France	2.5
13	Spain	2.6
14	France	2.8
15	France	3.1
16	United States	3.5
17	United States	3.5
18	United States	4.1
19	United States	10.3
20	United States	14.1
21	United States	14.2
22	United States	20.4
23	United States	23.0
24	Spain	28.3
25	United States	30.7
26	Spain	30.9
27	United States	34.5
28	United States	37.1
29	United States	40.4
30	United States	41.0
31	United States	51.1
	Red Wines	
32	France	0.4
33	Spain	0.8
34	France	1.5
35	United States	2.1
36	Italy	2.3
37	France	2.3
38	France	2.4
39	France	2.4
40	United States	4.0
41	United States	12.6
42	United States	12.7
43	United States	13.5
44	United States	28.5
45	United States	38.1
46	United States	52.6

	Country of Origin	Sodium, mEq/qt
	Rose Wines	
47	Portugal	1.1
48	France	1.9
49	United States	5.0
50	Portugal	5.4
51	United States	10.8
52	United States	19.5
53	United States	46.1
54	United States	47.7
	Dessert Wines	
55	England	1.1
56	Italy	1.9
57	Greece	2.1
58	United States	3.3
59	United States	4.3
60	Spain	4.7
61	Spain	5.1
62	United States	7.7
63	United States	12.6
64	United States	22.2
	Champagne	
65	France	0.5
66	United States	2.6
67	United States	4.3
68	United States	12.2
	Beer	
69	United States	0.5
70	United States	0.5
71	United States	0.5-2.8
72	United States	0.5-2.8
73	United States	4.2

	Type	Country of Origin	Sodium, mEq/qt
	Liqueurs and Hard Liquors		
74	Gin	United States	0.2
75	Bourbon	United States	0.2
76	Bourbon	United States	0.2
77	Vodka	United States	0.2
78	Cognac	France	0.3
79	Rum	Puerto Rico	0.3
80	Kirsch	Germany	0.3
81	Cognac	France	0.4
82	Cognac	France	0.4
83	Bourbon	United States	0.4
84	Campari	Italy	0.5
85	Blended whiskey	United States	0.5
86	Scotch whiskey	Scotland	0.8
87	Drambuie	Scotland	0.8
88	Ouzo	Greece	0.9
89	Creme d'Allash	Holland	1.0
90	Cherry brandy	Denmark	1.3
91	Creme de menthe	United States	1.7
92	Brandy	Greece	2.5

The Walter Kempner Symposium

Archives of Internal Medicine

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May 1974, Volume 133

THE WALTER KEMPNER SYMPOSIUM

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The Walter Kempner Symposium
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Walter Kempner: Editor's Note

So radically has the medical view of hypertension changed in the past 30 years that the recent series of national task force programs sponsored by the National Heart and Lung Institute gave but little mention of the dietary treatment program for hypertension that the ARCHIVES has chosen to review in some detail in this issue. The sharp contrast between the impact of the rice diet treatment for hypertension that occurred in the late 1940s and the almost forgotten status of that regimen in the 1970s merits comment. It is clear that the drug treatment of hypertension and the specific surgical treatment of modifiable or removable causes of hypertension have provided less cumbersome and less discommodious types of therapy. When the rice diet treatment was enunciated, it demonstrated that malignant hypertension was a reversible illness, and it surely gave new heart to investigators and clinicians to pursue diligently other avenues of therapy. Though the Columbia University group among others was able to replicate the effectiveness of the Duke University work, few physicians were actually able to sustain the intensity of interest and the scope of commitment that the rice diet program demands. Thus, the continued effort in Durham became not so much an institutional preference as it was the singular dedication and totality of effort of a remarkable physician, Walter Kempner, MD. As other forms of treatment became available, Kempner sustained his commitment and extended his efforts to other entities. His retirement from "active" status as Professor of Medicine at Duke University, although he remains a quite active consultant, is the event that has occasioned this special section of the ARCHIVES.

Jay Skyler, MD, has sketched Kempner's personal history and Eugene A. Stead, Jr., MD, has offered an assessment of Kempner's role as physician-educator-investigator. During the years that Duke's Department of Medicine was building its broad base of strength, Kempner provided a model of clinical excellence that significantly complemented the bench science distinction of that campus. It takes a rich mix of varied talents to educate well the demanding aspirants of a university medical center; Kempner's contribution was extremely important. Dr. Skyler, J. Caulie Gunnells, MD, and Jonathan Dranov, MD, have reviewed the current status of the management of malignant hypertension, and Barbara Newborg, MD, a long-time associate of Kempner, has summarized her observations of the efficacy of the rice diet in pseudotumor cerebri.

The Kempner article that had such a wide impact on the practice of medicine is also reprinted. M.D.B.

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Walter Kempner

A Biographical Note

Jay S. Skyler, MD, Durham, NC

Considering Walter Kempner's family background, it is not surprising that he chose medical research as a career. By the time of his birth, Jan 25, 1903, both of his parents were active medical investigators. His father made the first antitoxin against the poison of *Bacillus botulinus*. His mother established the pathogenicity in humans of the bovine strain of *Mycobacterium tuberculosis*. Both had begun as assistants to Robert Koch, discoverer of the tubercle bacillus. Koch was the godfather of Dr. Kempner's brother who made a name for himself as the American deputy chief counsel in the war crime trials in Nuremberg.

Walter Kempner graduated from the Medical School of the University of Heidelberg in Germany in 1926. After internship in Heidelberg, where his first paper, on diabetes, was published, he worked in 1927 to 1928 and again in 1933 to 1934 at the Kaiser Wilhelm Institute for Cellular Physiology in Berlin-Dahlem, in the laboratory of Dr. Otto Warburg, the 1931 Nobel laureate in biochemistry. From 1928 to 1933 he was Assistant Physician at the School of Medicine of the University of Berlin, under Professor Gustav von Bergmann. During these years his laboratory investigations centered on respiration and fermentation of isolated cells, on the chemical nature of butyric acid fermentation (the "red ferment"), and on chemical changes associated with tissue damage and inflammation.

Meanwhile, in the United States, Frederic M. Hanes, chairman of medicine at the fledgling Duke University School of Medicine, was recruiting faculty. Eager to add a full-time medical investigator of outstanding competence to his department, he visited Dr. Kempner in Germany and offered him an appointment. Kempner accepted and became the first salaried member of the Department of Medicine whose major responsibilities were teaching and medical research. Kempner studied oxidative and fermentative metabolism in a variety of tissues and bacteria and became especially interested in biological oxidations. This interest led him to work on the effect of oxygen concentration on metabolic function and dysfunction of the kidney. Kempner's work in renal metabolism led him in turn, at first reluctantly, into the clinical arena, where he made his revolutionary contributions to dietary therapy.

In 1939, Kempner originated the rice-fruit-sugar diet for treatment of chronic glomerulonephritis with uremia. The basic "rice diet," consisting of nothing but rice, sugar, fruit, and fruit juices, contains in 2,400 calories *less* than 150 mg of sodium, *less* than 200 mg of chloride, *less* than 5 gm of fat, no cholesterol, and about 25 gm of protein derived from rice and fruit. He used the diet with some success to treat under close supervision patients with acute and chronic glomerulonephritis for a few days or

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weeks.

A major breakthrough occurred by accident in 1942. One of Dr. Kempner's patients, a 33-year-old North Carolina farmer's widow with chronic glomerulonephritis and papilledema, apparently was baffled by Kempner's German accent. She understood on discharge from the hospital that she was to eat rice, but misunderstood his instructions to return in two weeks. After two months, she returned to the medical ward with dramatic reduction of blood pressure from 190/120 to 124/84 mm Hg, resolution of retinal hemorrhage and papilledema, and a noticeable decrease in heart size. Her success with more long-term adherence to the rice diet regimen led Kempner to expand his studies and to apply long-term dietary therapy to patients with severe renal disease. Some of them did surprisingly well, surpassing his most optimistic expectations. One of the more striking features was the improvement of blood pressure. This led Kempner to try his diet in patients with essential hypertension, both benign and malignant. The majority of these patients also responded to the dietary treatment. The remarkable observations were made that not only could the disease progress be arrested, but that there could be a reversal to normal of cardiomegaly; of electrocardiographic abnormalities; and of hemorrhagic, exudative neuroretinopathy. Failing kidney function could be restored if the treatment was continued for a long period of time.

Later, struck by the beneficial results achieved in glomerulonephritis and hypertensive cardiovascular disease, Kempner applied his dietary therapy to patients with diabetes mellitus, especially those with vascular complications. Despite the high carbohydrate content of the diet, insulin requirements fell and vascular complications, including advanced diabetic retinopathy, were ameliorated. This improvement occurred in diabetic patients both with and without accompanying weight loss. However, the successful loss of large amounts of weight in some diabetic and hypertensive patients led to the referral to Kempner of a large group of patients with severe obesity and related metabolic and psychological problems.

As Kempner's early work in the successful treatment of severe renal and hypertensive vascular disease was contrary to existing dogma, it was met with considerable skepticism. With little else to offer patients with these problems, several groups in this country and abroad launched intense investigations in the late 1940s and early 1950s—investigations that confirmed Kempner's observations.

The rice diet is a regimen difficult to administer and difficult to tolerate. Therefore, as the years have gone by and newer drug therapies have become available, the direct applicability of the rice diet for the treatment of hypertension has diminished. These subsequent discoveries have somewhat obscured the impact of Kempner's observations on medical history. Therefore, for the sake of clarification, it is important to note those areas where Kempner's contributions became the basis for modern therapy. First, the restriction of sodium in the treatment of hypertension and cardiovascular renal disease is today, as a consequence of Kempner's research, standard practice, whether achieved by "low salt" diets or pharmacologically through the use of diuretics. Second, one of the mainstays in the treatment of renal dysfunction is the "low protein" diet. Third, the use of low-cholesterol and low-fat diets is now widely proclaimed as an important measure in attempting to prevent atherosclerosis and coronary artery disease. Fourth, current recommendations state that "every effort should be made by the physician to control the symptomatic, maturity-onset diabetic with diet alone."[1] And recently, much attention has been given to the use of "high-carbohydrate" diets for treatment of diabetes, even leading to the revision of the American Diabetes Association's recommendations about dietary therapy.[2] Fifth, the associated mortality and morbidity (in terms of hypertension, cardiovascular disease, carbohydrate intolerance, and cholesterol and triglyceride alterations) of obesity have become well-recognized. In all of these conditions, the rice diet has proven efficacious. It uniquely combines a low-salt, low-protein, low-fat, and low cholesterol regimen and it allows for a degree of restriction of these substances greater than ordinarily achievable. The principles established with this diet by Kempner's work, in extreme, now have been applied, in moderation, to all these med-

ical problems. His pioneering efforts have borne much fruit.

It is also worth noting that Kempner, impressed by the severe complications he saw, was one of the first to stress early treatment of even moderate hypertension. That this approach was justified is evidenced by its adoption by most physicians, with the resulting sharp decrease in recent years of the incidence of malignant hypertension and of hypertensive complications. The Veterans Administration Cooperative Study clearly documents the benefits of this course of action.[3,4]

In addition, Kempner also was one of the first to stress exercise as an adjuvant in the treatment of cardiovascular disease, an approach now widely used. His careful records of the clinical course of his patients have been detailed prospectively on flow sheets since 1940. This is interesting to me in view of the current interest in problem-oriented records and flow sheets. In this regard, it is intriguing that Kempner was not satisfied with "diagnoses" but rather approached "problems." Finally, Dr. Eugene Stead has noted that observing Kempner's use of nonprofessionals in the detailed care of his many patients contributed to his initiation of the concept of Physician's Assistants.

Walter Kempner has had a profound influence on all those who passed through Duke Medical Center, be they faculty or student. His unique contributions to the Medical Center, to his many patients, and to medicine in general have earned him a position of great esteem among his colleagues and they have brought international recognition to Duke University Medical Center. In August of 1972 after 38 years on the active faculty, Walter Kempner became professor emeritus of medicine and now serves in a consultant capacity. To recognize in small part the contributions he has made to his patients, to medicine, and to Duke University Medical Center, the Department of Medicine has established an endowed professorship to be known as the Walter Kempner Professorship of Medicine. Dr. Andrew G. Wallace, professor of medicine and chief of the cardiology section at Duke, has been named the first incumbent.

Walter Kempner

Curriculum Vitae

Birth date: Jan 25, 1903

Education: MD, University of Heidelberg Medical School, 1926

Appointments: University of Heidelberg Medical School: Intern, 1926. Kaiser Wilhelm Institute for Cellular Physiology: Fellow, 1927-1928 and 1933-1934 School of Medicine, University of Berlin: Assistant Physician, 1928-1933. Duke University School of Medicine: Associate in Medicine, 1934-1941 Assistant Professor of Medicine, 1941-1947 Associate Professor of Medicine, 1947-1952 Professor of Medicine, 1952-1972 Professor Emeritus of Medicine, 1972-Present

Societies:
American Physiological Society
American Medical Association
American College of Physicians (Fellow)
American Society of Internal Medicine
World Medical Association

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Walter Kempner: A Perspective

Eugene A. Stead, Jr., MD, Durham, NC

In January 1947, I came to Duke Medical School as professor of medicine, chairman of the Department of Medicine, and physician-in-chief of Duke Hospital. I was directly responsible for the care of staff patients and for any private patients who came to me for medical services. The medical students, interns, and residents supervised the care of the staff patients under guidance from the senior staff and me. They also helped with the care of private patients, both those of my own and of other members of the staff. From the beginning, the students and house staff pointed out to me that edematous patients and patients with malignant hypertension treated by Kempner with his rice diet did better than the patients treated by me with digitalis, diuretics, and moderate sodium restriction. My own observations supported theirs and, with the aid of the Durham-Orange County Heart Association, Bernard C. Holland, MD and I opened a Heart House to provide rice diet therapy for the staff patients of Duke Hospital. We made no new advances. We did have the satisfaction of seeing many of our previously difficult patients do remarkably well.

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Kempner did not try to minimize the problems of vascular disease. He did not try to gloss over the illness with symptomatic treatment. The patients knew that the treatment was long and difficult but that, all along the way, they would have a good chance of seeing objective improvement in edema, heart size, electrocardiographic abnormalities, blood pressure, optic fundi, cholesterol levels, and urea levels. Kempner initiated a form of protection from the demands of daily living that was reminiscent of that provided by a tuberculosis sanatorium.

Kempner realized that all dieters are liars and, therefore, substituted the analysis of the 24-hour urine collection for a dietary history. Any break in the rice diet would cause a rise in chloride, sodium and nitrogen levels. Kempner's patients believed that he had second sight, because he always spotted breaks in diet.

The rice diet was low in calories, protein, and sodium chloride. It was relatively high in potassium and adequately supplemented by vitamins. Kempner demonstrated that, with a complete protein, such as rice, and an adequate supply of carbohydrate, nitrogen balance could be achieved after a few weeks on as little as 4 gm of nitrogen per day. The amounts of solids excreted in the urine were tremendously reduced.

The reduction in protein was essential if the sodium and chloride con-

tent of the diet was to be maintained at the levels demanded by Kempner. Any increase in other proteins invariably ended up with a larger excretion of electrolytes. The sharp reduction in sodium and chloride intake resulted in a fall in glomerular filtration and a reduction in blood flow. Nevertheless, the total effect on nitrogen values in the blood was favorable. Less wise doctors than Kempner, restricting sodium and chloride with less attention to nitrogen, have reduced filtration rates and blood flow with an increase in blood urea nitrogen.

Kempner restricted fluids because patients with kidney disease on this low intake of salt were very susceptible to water intoxication. This danger was increased if the kidney could not conserve sodium and potassium normally. Of course, patients who followed the diet were rarely thirsty. Intense thirst usually accompanied breaks in the diet.

Kempner showed that his patients became insulin-sensitive and that the dose of insulin required by diabetic patients was decreased. It was interesting to watch the diabetic patient adapt to this high carbohydrate diet. The patient would watch himself for impending signs of ketosis. The physicians, knowing that his insulin requirements would fall, watched him for signs of hypoglycemia. In 1945, Dr. Kempner published his first eyegrounds pictures showing the disappearance of exudates and hemorrhages in a diabetic patient.

Kempner demonstrated that his diet would lower serum cholesterol levels and that this lowering could be maintained. He showed the disappearance of xanthoma.

Kempner treated many patients with renal disease. The edema, hypercholesterolemia, hypoproteinemia, and hypertension responded well. He believed that he improved the underlying pathologic findings, but he never had an untreated group of his own for comparison. He demonstrated that nephrotic children wasting large amounts of protein did well on the rice diet. The proteinuria decreased dramatically and the children showed good growth.

Kempner's greatest triumphs came in the treatment of malignant hypertension. Here was a dramatic disease of short duration in which he could demonstrate reversibility. The outcome of the disease was well enough known so that the favorable effects could be reasonably attributed to diet. Patients who at that time would have died in all other hospitals had a reasonable chance for survival if they came under Kempner's care. The closing sentence of a talk which he gave 25 years ago to the 30th Annual Session of the American College of Physicians was as follows: "The important result is not that the change in the course of the disease has been achieved by the rice diet but that the course of the disease can be changed."

It is of interest to consider why Kempner has received in this country little recognition for his tremendous achievements.

He did not appeal to the scientific community. It wanted him to set up various kinds of control studies. He contended that each patient was his own control and that there were already enough studies of patients treated by other forms of therapy. He was unwilling to deny any of his patients the full benefit of what he thought was best. Moreover, he pointed to his unequivocal results on rats with experimental hypertension, nephrosis and polyarteritis.

He has made many enemies because he has been honest and uncompromising and has never spent a single hour of his life, except for some scientific talks on rare occasions, in any society or even in a committee meeting.

He treated all forms of vascular disease—mild, intermediate, and severe. He was not concerned about the patient's symptoms. The patient's physician at home knew that the vascular disease was in many instances not the cause of the complaining. When the patient returned home after three months of rigid therapy directed at an asymptomatic disease, the physician saw red. But in Kempner's defense, for many years he saw more destructive vascular disease than any other physician. In many instances, the disease destroyed the patient in spite of everybody's best efforts. It is little wonder that Kempner treated mild disease seriously.

He believed in maximal therapy, with the rice diet being the most radical dietary restriction that he could apply. He used this diet for all patients with hypertension, heart failure, renal failure, diabetes, and obesity. He took moderate obesity as seriously as advanced diabetic retinopathy. Things are more black or white in Kempner's mind than in the minds of most other physicians.

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Treatment of Hypertensive Vascular Disease with Rice Diet*†

WALTER KEMPNER, M.D.
Durham, North Carolina

THE treatment of hypertensive vascular disease with the rice diet[1–5] was suggested by observations made on the protein, fat and carbohydrate metabolism of isolated kidney cells under various pathologic conditions (cell injury and/or changes in pH, sodium bicarbonate concentration, oxygen tension and metabolizable substrate[6–11]).

Until 1944 the consensus was that dietary treatment was useful in kidney disease but of no value in hypertensive vascular disease. "The diet in uncomplicated hypertension requires no essential change from the normal. There is no justification for restriction of protein intake, indeed, such restriction may result in anemia and other evidences of malnutrition. Likewise, in the absence of edema or paroxysmal dyspnea, the restriction of salt is unwarranted; claims that such restriction may lower the blood pressure have not been substantiated. Obesity should be avoided for the same reasons that apply to normal individuals and not because of any demonstrated relationship to hypertensive disease."[12] "No dietary treatment is known which has a specifically favorable effect on essential hypertension."[13]

The rice-fruit-sugar diet is more rigid than any of the fat-poor, salt-poor or protein-poor "hypertension" diets. (The therapeutic possibilities and limitations of these will not be discussed here.) The rice diet contains in 2,000 calories not more than 5 Gm. of fat and about 20 Gm. of protein derived from rice and fruit and not more than 200 mg. of chloride and 150 mg. of sodium. A patient takes an average of 250 to 350 Gm. of rice (dry weight) daily; any kind of rice may be used provided no sodium, chloride, milk, etc. has been added during its processing. The rice is boiled or steamed in plain water or fruit juice, without salt, milk or fat. If the sodium concentration of the plain water available is greater than 20 mg. per liter, distilled water should be used. All fruit juices and fruits are allowed, with the exception of nuts, dates, avocados and any dried or canned fruit or fruit derivatives to which substances other than white sugar have been added. Not more than one banana a day should be taken. White sugar and dextrose may be used *ad libitum;* on an average a patient takes about 100 Gm. daily but, if necessary, as much as 500 Gm. daily should be used. Tomato and vegetable juices are not allowed. Usually no water is given and the fluid intake is limited to 700 to 1,000 cc. of fruit juice per day. Supplementary vitamins are added in the following amounts: vitamin A 5,000 units, vitamin D 1,000 units, thiamine chloride 5 mg., riboflavin 5 mg., niacinamide 25 mg., calcium pantothenate 2 mg. No other medication is given unless it is specifically indicated.

During the first period of "regulation" on the diet, the patient should be under constant medical supervision and blood

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† This work was supported by grants from the Anna H. Hanes Research Fund, The Life Insurance Medical Research Fund and The Herman Horneman Research Fund.

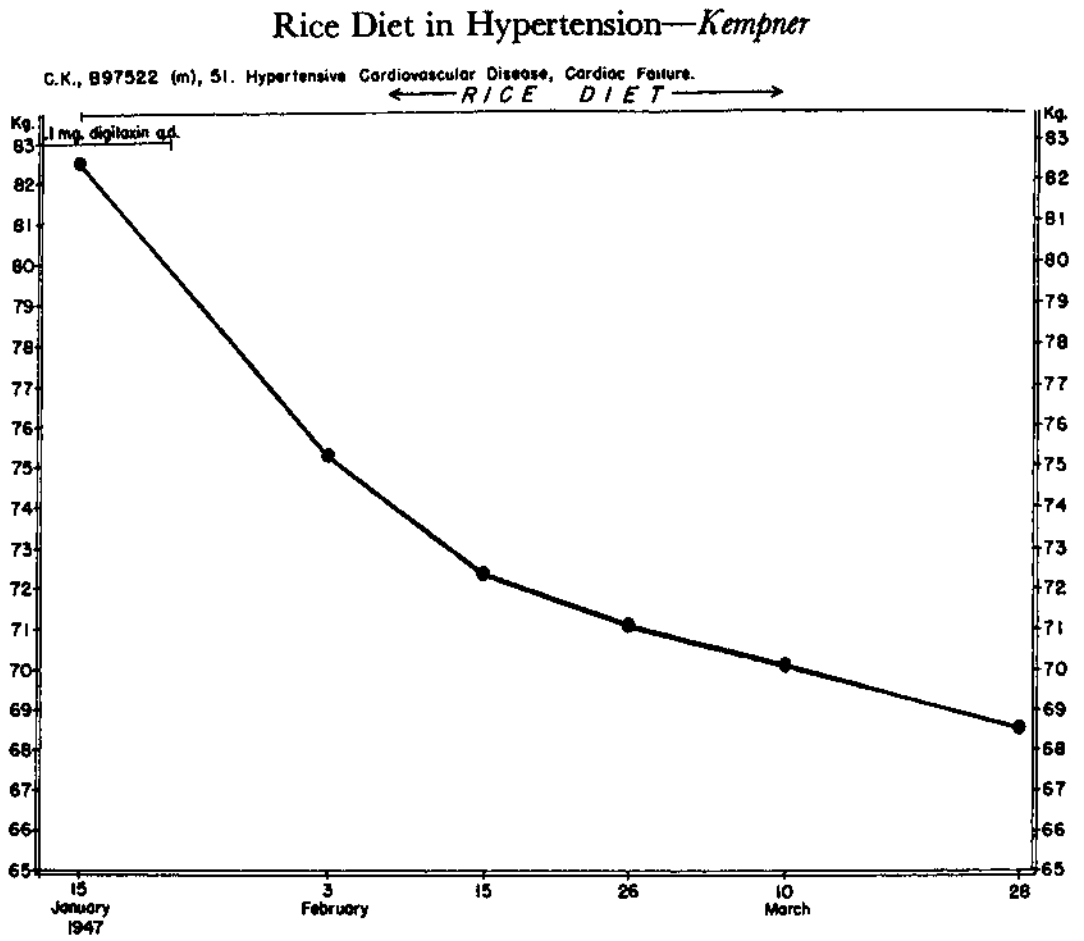

FIG. 1. C. K., male, fifty-one years of age. The patient had hypertensive vascular disease of seven years' duration, auricular fibrillation, cardiac failure of one year's duration, enlargement of liver and spleen and ascites. Previous treatment: digitalis, mercurials, ammonium chloride; codein; low salt, low fat, high protein diet; paracentesis 12 times in past year. January 15 to 21, 1947: Blood pressure, average, 174/97; NPN 44 mg. per 100 cc. blood; venous pressure 380 mm. of saline; total PSP excretion in two hours: 39 per cent. Rice diet started January 18, 1947, was strictly followed. All medication discontinued. On March 17, 1947, NPN 27 mg. per 100 cc. blood. March 24 to 30, 1947: Blood pressure, average, 137/82. Ascites and edema unchecked by digitalis, mercurials, ammonium chloride, low salt high protein diet disappeared on rice diet without medication. There was a 14 Kg. weight loss in sixty-eight days.

and urine chemistry should be checked frequently.

Rest in bed, unless the severity of the condition demands it, is neither necessary nor desirable.

It is not unusual for the weight to decrease more or less markedly during the first twenty days. The reason for this weight loss may be that the amount of food given does not cover the caloric requirements; in this case the amount of rice, fruit and sugar must be increased unless reduction of weight is indicated. Another reason may be that the patient does not eat the full amount of his diet during the first period of adjustment. The most frequent cause is the loss of visible or invisible edema; for example, one patient with marked edema lost 63 pounds in the first sixteen days on the diet (no digitalis, mercurials, etc., were given).[5] Figure 1 shows the weight chart of another patient, a fifty-one year old physician, with hypertensive heart disease and auricular fibrillation whose persistent liver enlargement, ascites and edema had not improved in spite of intensive treatment with digitalis, mercurials, ammonium chloride, salt-poor diet and frequent paracenteses.

As a rule the diet should be continued without modification until those conditions

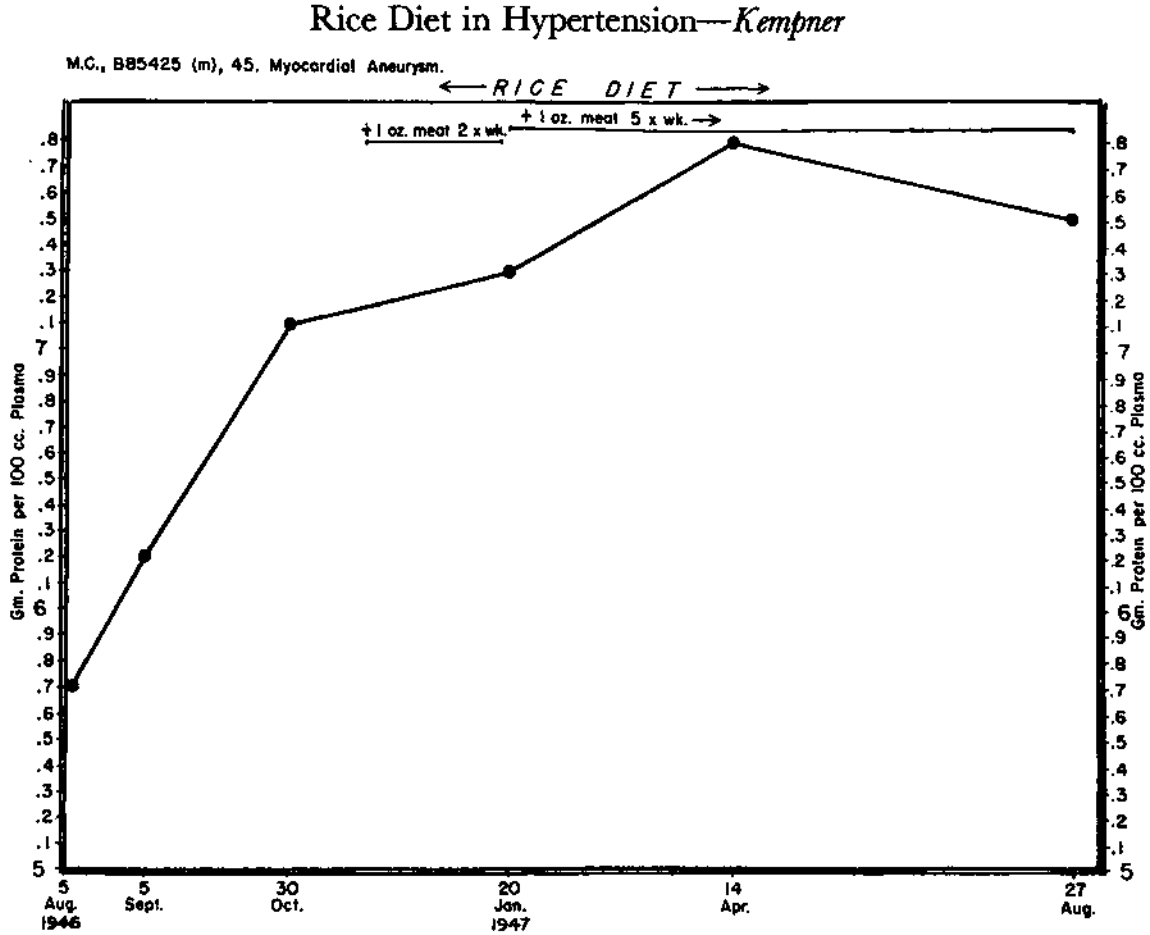

Fig. 2. Increase of plasma proteins on rice diet (for history see Figure 17).

which were the indication for its use have disappeared. Then small amounts of non-leguminous vegetables, potatoes, lean meat or fish (all prepared without salt or fat) may be added. But only so much additional food should be allowed as can be taken without producing undesirable changes in blood pressure, heart size, electrocardiogram, eyegrounds, non-protein nitrogen, etc. When a critical condition of heart, kidney or retina exists, the strict rice diet should be continued indefinitely provided that the equilibrium between intake and loss of those substances which are indispensable for the body is maintained.

CHEMICAL CHANGES PRODUCED BY THE RICE DIET

Nitrogen Metabolism. Because of the protein-sparing effect of carbohydrates, the protein equilibrium is maintained in spite of the low protein content of the rice diet.

A minimum of 50 Gm. of protein (type of protein not specified) has been postulated as the so-called "wear and tear quota" necessary to cover the daily protein requirements. However, since this figure is derived from the total nitrogen excretion of fasting individuals, which is about 7 Gm. in the urine and 0.9 Gm. in the stools, it indicates only the amount of the body protein broken down in fasting ($7.9 \times 6.25 = 49.4$). In patients who have followed the rice diet for two months or more the daily urinary total nitrogen excretion is less than one third of that in fasting. It averages 2.26 Gm.[5] If an allowance of 0.9 Gm. per twenty-four hours is made for the excretion of nitrogen other than that excreted in the urine, the total nitrogen loss in twenty-four hours is about 3.16 Gm. With a daily intake

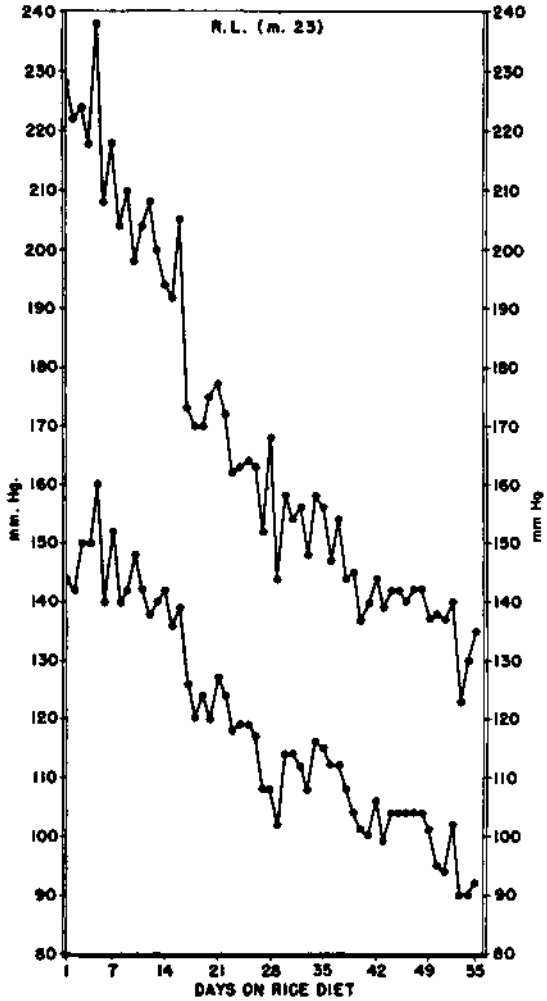

FIG. 3. R. L., male, twenty-three years of age. This patient had hypertensive vascular disease of three years' duration. He was previously treated with a "modified rice diet." EKG T_1 inverted. (Fig. 22.) Total PSP excretion in two hours: 2.5 per cent; NPN 79 mg. per 100 cc. blood; cholesterol 340 mg. per 100 cc. serum. There was advanced retinopathy. (Fig. 30.) Rice diet started December 18, 1945 and strictly followed for three months (8–21 mg. Cl per 100 cc. of urine). March 17, 1946: NPN 60 mg. per 100 cc. of blood; cholesterol 173 mg. per 100 cc. serum.——————Decrease in blood pressure started in first week of rice diet.

of $3.16 \times 6.25 = 19.8$ Gm. of protein, these patients are in nitrogen equilibrium.

In fasting the daily urea nitrogen excretion in the urine is about 5.5 Gm. In the urine of patients who have followed the rice diet for two months or more the average daily urea nitrogen excretion is 1.1 Gm.[5]

In fasting the blood non-protein nitrogen and the blood urea nitrogen concentrations

TABLE 1
AVERAGE NPN AND UREA-N OF 261 PATIENTS WITH HYPERTENSIVE VASCULAR DISEASE
(Initial NPN 20 to 45 mg. Per 100 cc. Blood)

No. of Patients	Average Period of Treatment (Days)	NPN		Urea-N	
		Average Before Rice Diet	Average After Rice Diet	Average Before Rice Diet	Average After Rice Diet
		Mg. Per 100 cc.	Mg. Per 100 cc.	Mg. Per 100 cc.	Mg. Per 100 cc.
NPN and Urea-N Increased					
13	62	31	35	12.5	16.0
NPN Increased, Urea-N Decreased					
10	74	30	32	11.4	7.5
NPN Decreased, Urea-N Increased					
3	83	32	31	8.9	12.8
NPN and Urea-N Decreased					
235	109	34	26	14.4	7.3
Total					
261	106	34	27	14.1	7.8

are higher than normal; on the rice diet they are lower than normal.[5] Table 1 shows the non-protein nitrogen and urea nitrogen in a series of 261 non-uremic patients with hypertensive vascular disease. The non-protein nitrogen before the diet ranged from 20 to 45 mg. per 100 cc. of blood; the average was 34 mg. After the diet it ranged from 18 to 45 mg.; the average was 27 mg. The urea nitrogen before the diet ranged from 4.8 to 30.3 mg. per 100 cc. of blood; the average was 14.1 mg. After the diet it ranged from 1.2 to 30.4 mg.; the average was 7.8 mg.

In starvation, hemoglobin and plasma protein concentrations decrease; on the rice

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TABLE II
EFFECT OF HIGH AND LOW PROTEIN DIETS ON URINARY TOTAL NITROGEN AND CREATININE OF NORMAL MAN (FOLIN[14])

	120 Gm. Protein Egg-Milk Diet (3rd Day)	6 Gm. Protein Cream-Starch Diet (7th Day)
Total nitrogen (mg. N per 24 hr.)	16,800	3,600
Creatinine (mg. N per 24 hr.)	580	600

TABLE III
EFFECT OF FASTING ON URINARY CREATININE AND CREATINE OF NORMAL MAN (BENEDICT[15])

	1st Day of Fasting (Weight 59.6 Kg.)	6th Day (Weight 55.9 Kg.)	12th Day (Weight 53.6 Kg.)
Creatinine (mg. N per 24 hr.)	480	390	370
Creatine (mg. N per 24 hr.)	0	130	120
Total creatine bodies (mg. N per 24 hr.)	480	520	490

diet hemoglobin and plasma protein levels are maintained.[5] (Fig. 2.)

The excretion of creatinine plus creatine (total creatine bodies) has been supposed to remain fairly constant in spite of variations in protein intake and nitrogen excretion. (Table II).

The excretion of the total creatine bodies does not decrease in one to twelve days of fasting. The creatine fraction increases. (Table III.)

The excretion of total creatine bodies decreases markedly on the rice diet; the excretion of creatine does not increase. (Table IV.)

The decrease in the excretion of total creatine bodies ranged from 7 to 48 per cent, averaging 29 per cent; the decrease in weight ranged from 0 to 11 per cent, with an average of 6 per cent.

TABLE IV
CREATININE AND CREATINE IN URINE OF TWENTY-TWO PATIENTS (FIFTEEN MEN, SEVEN WOMEN) WITH HYPERTENSIVE VASCULAR DISEASE

	Before Rice Diet	After 35 Days (av.) on Rice Diet
Creatinine (mg. N per 24 hr.)	480	346
Creatine (mg. N per 24 hr.)	40	19
Total creatine bodies (mg. N per 24 hr.)	520	365

TABLE V
TOTAL SERUM CHOLESTEROL OF 284 PATIENTS WITH HYPERTENSIVE VASCULAR DISEASE

Initial Concentration (Mg. Per 100 cc. of Serum)		No. of Patients	Average Period of Treatment (Days)	Mg. Cholesterol Per 100 cc. of Serum (average)		
				Before Treatment	After Treatment	Change
110–218	Increased	18	123	156	180	+24
	Increased to 220 or over	4	93	208	240	+32
	Decreased or constant	61	109	195	157	−38
		83	110	187	165	−22
220–585	Increased or constant	10	146	250	262	+12
	Decreased	59	76	320	253	−67
	Decreased below 220	132	81	273	177	−96
		201	82	286	204	−82
110–585		284	90	257	192	−65

As far as the metabolism of kidney cells is concerned rice protein cannot be indiscriminately replaced by other protein. Proteins differ from each other in regard both to the type and the relative proportion of the various amino acids of which they are composed. They also differ in regard to the rate and degree of assimilation; 30 Gm. of a protein of which 88 per cent is assimilated may be preferable to 50 Gm. of a protein of which only 40 per cent is assimilated.

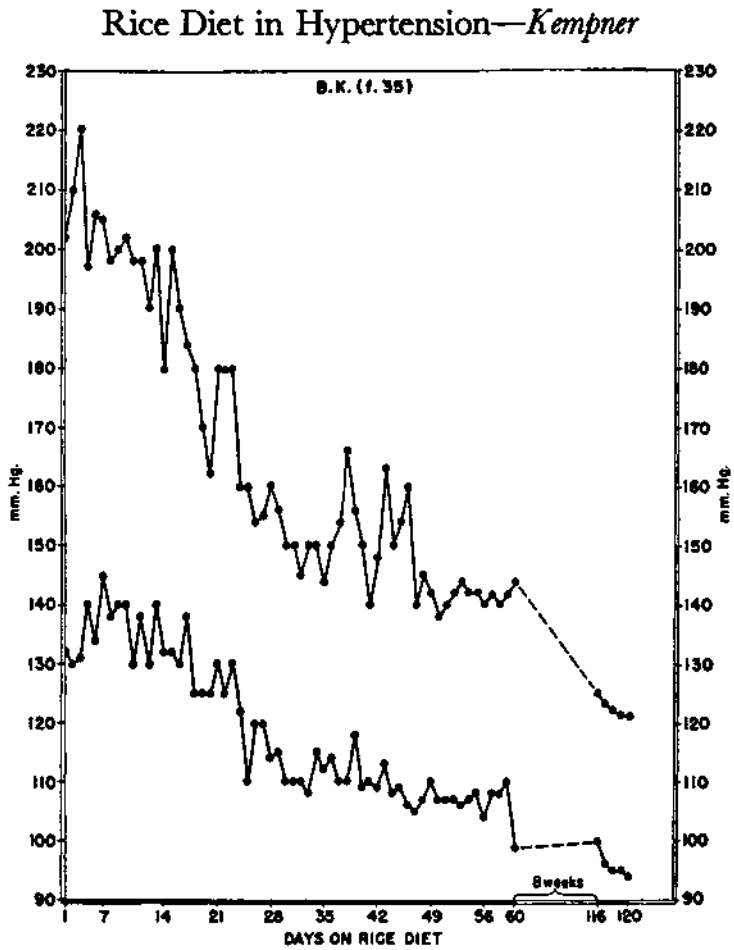

FIG. 4. B. K., female, thirty-five years of age. Patient had hypertensive vascular disease of eleven years' duration beginning during the eighth month of her second pregnancy. Of two brothers with hypertensive vascular disease, one had died at the age of thirty-seven (stroke). The patient had two retinal hemorrhages. Previous treatment: rutin, vitamin K, sedatives. Total PSP excretion in two hours 64 per cent; serum cholesterol 250 mg. per 100 cc. Rice diet was started April 23, 1947, and strictly followed (7–14 mg. Cl per 100 cc. of urine). No medication was given.———A decrease in blood pressure began in third week on rice diet.

The factor of assimilation may be important not only because of the amount of protein that can be utilized to meet the body requirements but also because of the amount of the non-utilized protein fraction, the fate and rôle of which have yet to be determined.

Cholesterol. The relation between serum cholesterol and vascular disease (arteriosclerosis, coronary disease, vascular retinopathy, hypertensive vascular disease) has been the subject of extensive study.

Hypercholesterolemia, regardless of its primary cause in a given case, is just as significant a metabolic disturbance as persistent hyperglycemia or hyperuricemia and should probably be considered as serious a disease, as far as potential consequences are concerned, as diabetes mellitus and gout.

Hypercholesterolemia decreases markedly with the rice diet.[1,6,11] Table v shows the effect of the diet on the total serum cholesterol concentration of 284 patients with hypertensive vascular disease. Two hundred one of these patients (i.e., 70 per cent) had hypercholesterolemia (cholesterol concen-

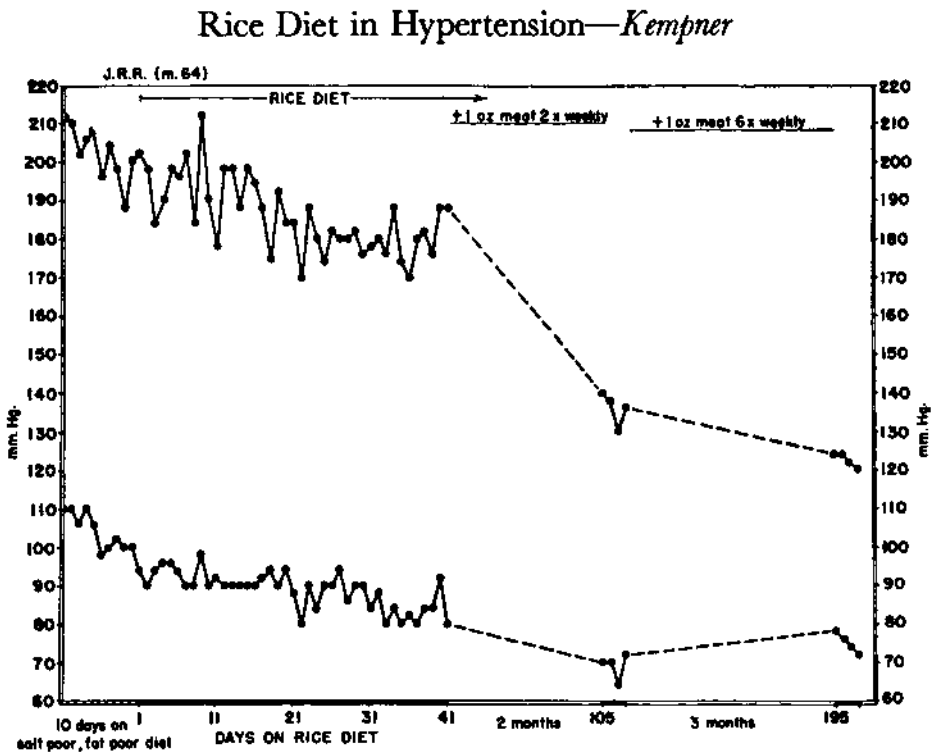

FIG. 5. J. R. R., a male, sixty-four years of age, had hypertensive vascular disease of six years' duration, four retinal hemorrhages and severe headache. He was treated previously with potassium thiocyanate. Total PSP excretion in two hours, 32 per cent. On October 7, 1946: Transverse diameter of heart, 15.2 cm; diameter of great vessels, 10.5 cm.; weight, 62.8 Kg. Rice diet was started October 17, 1946, and strictly followed (4–9 mg. Cl per 100 cc. of urine). No medication was given. The patient was working and was asymptomatic. May 2, 1947: Transverse diameter of heart, 11.9 cm.; diameter of great vessels, 8.6 cm.; weight, 64.4 Kg. No retinal hemorrhages were present. There was reduction in heart size and in size of great vessels. (Fig. 8.)——— Decrease in blood pressure was definite after 105 days.

tration of at least 220 mg. per 100 cc. serum) at the beginning of the diet.

Four patients whose serum cholesterol concentration was below the upper limits of normal had an increase to a hypercholesterolemic level (average before rice diet 208 mg. per 100 cc. serum, after rice diet 240 mg. per 100 cc. serum). One hundred thirty-two patients who had hypercholesterolemia had a decrease to a normal level (average before treatment 273, after treatment 177 mg. per 100 cc. serum). (Table v.)

Starke[16] examined the concentration of free and esterified cholesterol in the serum of seventy-nine patients with hypertensive vascular disease who had a total cholesterol concentration of 220 to 463 mg. per 100 cc. of serum at the beginning of the diet. Free cholesterol and esterified cholesterol esters decrease on the rice diet in about the same proportion. (Table vi.)

Chloride, Sodium, Potassium. Therapeutic results with sodium chloride restriction such as those obtained by Allen and Sherrill[17] and by Volhard[18] were explained by Fishberg[18] on the assumption that the unpalatability of the diet led to an inadequate caloric intake and thus to a reduction of the metabolic rate. According to Page[19] the results obtained were due not to salt restriction but to "rest in bed and the psychotherapy of constant attention."

The treatment with the rice diet, which includes rigid sodium and chloride restriction, made it possible to determine the effect of a prolonged minimal intake of sodium and chloride on the concentration of these ions in blood, serum and urine.

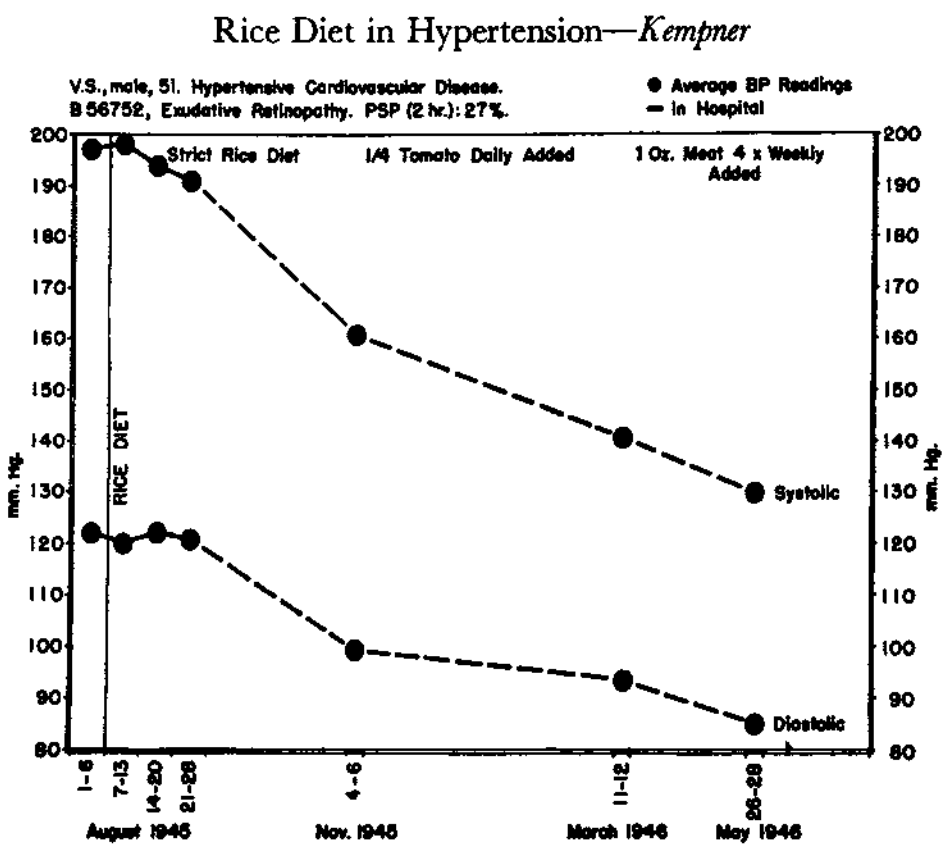

FIG. 6. V. S., a male, fifty-one years of age, had hypertensive vascular disease of eleven years' duration and retinal exudates. Previous treatment consisted of rest, sedatives and a "modified rice diet" for one month. Total PSP excretion in two hours: 21–33 per cent. Rice diet was started August 6, 1945, and strictly followed (5–20 mg. Cl per 100 cc. of urine). No medication was given. Working hours were restricted.———There was a gradual decrease of blood pressure after the third month of rice diet.

In a series of 213 patients treated with the rice diet the lowest urine chloride concentration found was 48 mg. Cl per liter with a total urinary excretion of 18 mg. Cl in twenty-four hours in a patient with hypertensive vascular disease who had been on the rice diet for seventy days. The plasma chlorides were 93.1 mEq. (as NaCl: 544 mg. per 100 cc.). The average values of 381 determinations of the plasma chlorides in ninety-one non-uremic patients with hypertensive vascular disease or primary kidney disease were: before rice diet, 97.0 mEq. per 1,000 cc. of plasma; after forty-four days (average) of rice diet, 91.7 mEq. per 1,000 cc. of plasma.[5]

Table VII gives a comparison of the concentrations of chloride, sodium and potassium in the urine of persons on a normal diet and of patients after two months on the rice diet.[11]

The average values of the chloride, sodium and potassium concentrations and their ratios in whole blood, serum and urine in thirty-seven patients with hypertensive vascular disease treated with the rice diet for an average of thirty-six days are shown in Tables VIII and IX.

In thirteen of the thirty-seven patients there was "secondary" renal involvement; in twenty-four patients there was no evidence of renal involvement. The sodium chloride content of the diet of many of these patients had been limited before they were started on the rice diet. None of these patients was in renal failure with sodium chloride leakage.

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The following average changes were found: In the urine there was a decrease in the sodium concentration of 99 per cent and in the chloride concentration of 96 per cent and an increase in the potassium concentration of 78 per cent. The sodium to potassium ratio decreased by 99 per cent and the chloride to potassium ratio by 97 per cent. There was a decrease of 79 per cent in the sodium to chloride ratio. All these changes are statistically significant.

In whole blood there was a statistically significant decrease of 4.3 per cent in the sodium concentration corresponding to an increase in hemoconcentration. There was a statistically significant decrease of 5.6 per cent in the chloride concentration. The sodium to chloride ratio remained constant. There was a statistically insignificant increase of 0.8 per cent in the potassium concentration and a statistically insignificant decrease of 3.4 per cent in the sodium to potassium ratio. The chloride to potassium ratio showed a decrease of 4.7 per cent (T value 2.1; probably statistically significant).

In the serum there was a statistically insignificant decrease of 0.7 per cent in the sodium concentration. Statistically significant changes in the serum were: a decrease of 6.2 per cent in the chloride concentration; an increase of 6.1 per cent in the sodium to chloride ratio; an increase of 11.3 per cent in the potassium concentration; a decrease of 8.6 per cent in the sodium to

TABLE VI
FREE AND ESTERIFIED CHOLESTEROL IN THE SERUM OF 79 PATIENTS WITH HYPERTENSIVE VASCULAR DISEASE

	Before Rice Diet	After 159 Days (Average) on Rice Diet
Free cholesterol (mg. per 100 cc. serum)	80	61
Esterified cholesterol (mg. per 100 cc. serum)	205	146
Total cholesterol (mg. per 100 cc. serum)	285	207

TABLE VII
URINE CHLORIDE, SODIUM, POTASSIUM ON "NORMAL" DIET AND ON RICE DIET

	Normal Diet	Rice Diet (after 2 Months)
Chloride (Gm. Cl per 1,000 cc.)	6	0.1
Sodium (Gm. Na per 1,000 cc.)	4	0.01
Potassium (Gm. K per 1,000 cc.)	2	3.0
Gm. Na/Gm. K Ratio	2	0.003

TABLE VIII
CHLORIDE, SODIUM AND POTASSIUM CONCENTRATIONS IN WHOLE BLOOD, SERUM AND URINE OF THIRTY-SEVEN PATIENTS WITH HYPERTENSIVE VASCULAR DISEASE BEFORE AND AFTER THIRTY-SIX DAYS (AVERAGE) ON RICE DIET
(Average Values)

	Whole Blood			Serum			Urine		
	Before Rice Diet	After Rice Diet	Change %	Before Rice Diet	After Rice Diet	Change %	Before Rice Diet	After Rice Diet	Change %
	mEq./1,000 cc.			mEq./1,000 cc.			mEq./1,000 cc.		
Chloride	80.2	75.7	−5.6	100.8	94.5	−6.2	86.2	2.50	−96.2
Sodium	82.0	78.2	−4.3	142.8	141.7	−0.7	81.7	0.43	−99.2
Potassium	49.5	49.5	+0.8	4.47	4.86	+11.3	64.4	88.6	+77.8

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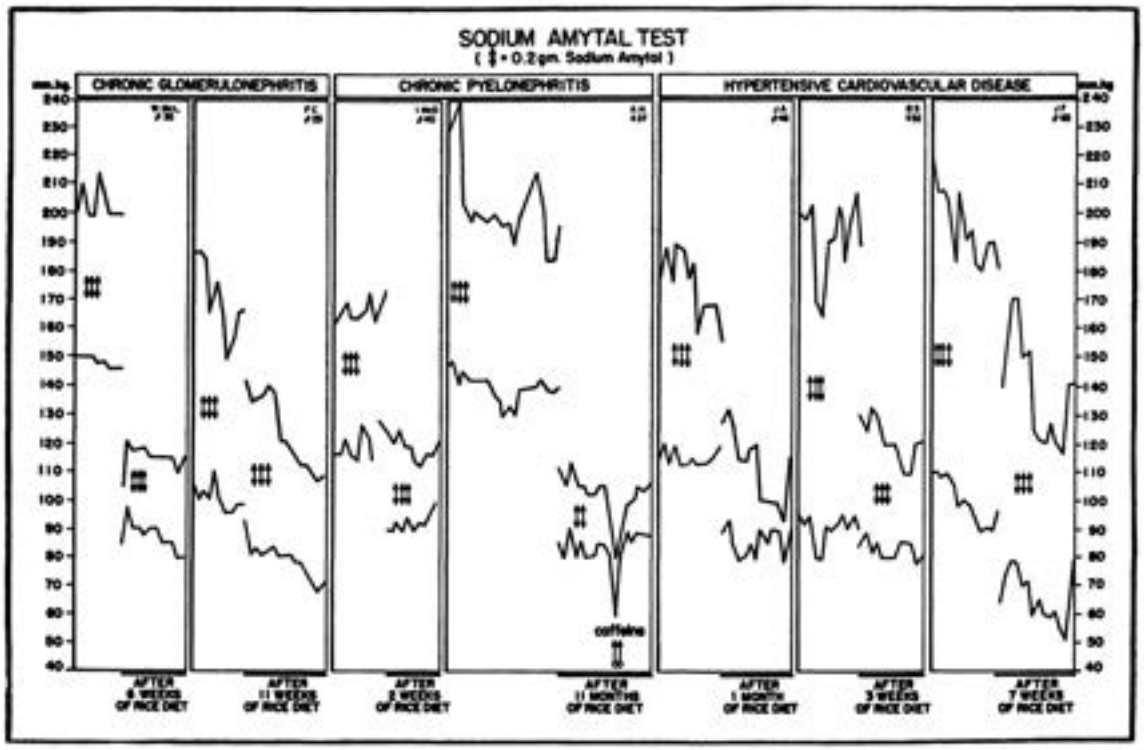

FIG. 7. Effect of 0.6 Gm. of sodium amytal on blood pressure before and after rice diet. (Reprinted from *North Carolina M. J.*, 6: 65, 1945).

TABLE IX

$\frac{\text{SODIUM}}{\text{POTASSIUM}}$, $\frac{\text{CHLORIDE}}{\text{POTASSIUM}}$ AND $\frac{\text{SODIUM}}{\text{CHLORIDE}}$ RATIOS

IN WHOLE BLOOD, SERUM AND URINE OF THIRTY-SEVEN PATIENTS WITH HYPERTENSIVE VASCULAR DISEASE BEFORE AND AFTER THIRTY-SIX DAYS (AVERAGE) ON RICE DIET

(Average Values)

	Whole Blood			Serum			Urine		
	Before Rice Diet	After Rice Diet	Change %	Before Rice Diet	After Rice Diet	Change %	Before Rice Diet	After Rice Diet	Change %
Na/K	1.67	1.61	−3.4	32.7	29.4	−8.6	1.66	0.006	−99.3
Cl/K	1.63	1.55	−4.7	23.1	19.6	−14.0	1.71	0.03	−96.9
Na/Cl	1.02	1.03	+1.6	1.42	1.50	+6.1	0.92	0.18	−79.4

potassium ratio; a decrease of 14.0 per cent in the chloride to potassium ratio.

Sulfate, Phosphate and Ammonia Excretion in Urine. Chloride, sulfate and phosphate account for about 85 per cent of the acid excreted in the urine on a normal diet.

As Tables X and XI show the inorganic sulfate excretion in patients on the rice diet decreases by 80 per cent; the inorganic phosphate excretion decreases by 60 per cent.[20]

Ammonia is formed in the kidney by oxidative deamination of amino acids; blood and tissue acids reaching the kidney

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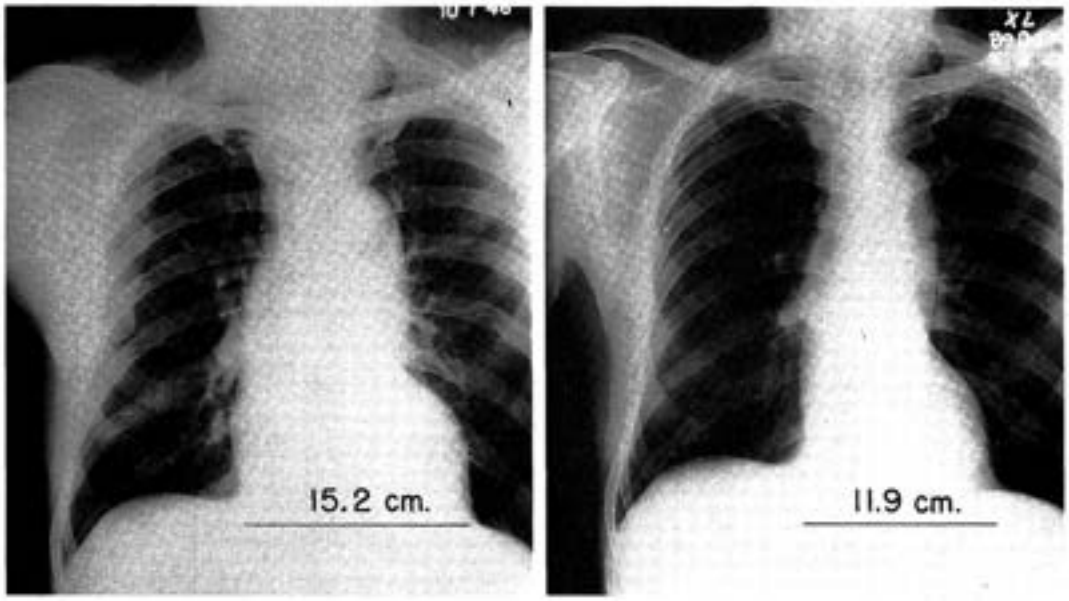

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FIG. 8. J. R. R., a male, sixty-four years of age, had hypertensive vascular disease of six years' duration, four retinal hemorrhages and severe headache. He was previously treated with potassium thiocyanate (three years). A, October 7, 1946; Blood pressure 212/110; weight, 62.8 Kg.; total PSP excretion in two hours, 32 per cent. Rice diet was started October 17, 1946, and strictly followed (4–9 mg. Cl. per 100 cc. of urine). No medication was given. B, May 2, 1947; Blood pressure 122/74; weight, 64.4 Kg. No appreciable drop in blood pressure after forty-one days of diet. The patient was working. A definite drop in blood pressure was noted after 105 days of diet. (Fig. 5.) The patient was asymptomatic and retinal hemorrhages had disappeared. There was a reduction in heart size with change in transverse diameter of 28 per cent and a reduction in size of great vessels with change of 22 per cent.

TABLE X

SULFATE EXCRETION IN URINE OF FOURTEEN PATIENTS (TEN MEN, FOUR WOMEN) WITH HYPERTENSIVE VASCULAR DISEASE—NO RENAL FAILURE

	Range		Average		
	Before Rice Diet	After 36 Days (Average) on Rice Diet	Before Rice Diet	After 36 Days (Average) on Rice Diet	Decrease (%)
	(Mg. S in 24 Hr.)		(Mg. S in 24 Hr.)		
Total sulfate	761–471	254–58	592	126	79
Inorganic sulfate	547–362	165–40	452	81	82
Ethereal sulfate	328– 52	115–15	140	45	56

TABLE XI

PHOSPHATE EXCRETION IN URINE OF SEVENTEEN PATIENTS (THIRTEEN MEN, FOUR WOMEN) WITH HYPERTENSIVE VASCULAR DISEASE—NO RENAL FAILURE

	Range		Average		
	Before Rice Diet	After 34 Days (Average) on Rice Diet	Before Rice Diet	After 34 Days (Average) on Rice Diet	Decrease (%)
	(Mg. P in 24 Hr.)		(Mg. P in 24 Hr.)		
Inorganic phosphate	1055–501	435–170	761	289	62

as salts of fixed base are converted there into ammonium salts and excreted as such in the urine; thus the fixed base in the body is conserved. Under pathologic conditions (e.g., at lowered oxygen concentrations) the rate of deamination of amino acids and of ammonia production in the kidney is decreased.[6,8] The acid must be excreted in the urine as salts of fixed base, the fixed base in blood and tissues decreases and uremic acidosis follows.[9,10] In considering the significance of the figures in Tables X and XI one might speculate about the possibility of forestalling an accumulation of acids in blood and tissue fluids by restricting

TABLE XII
AMMONIA EXCRETION IN URINE OF TEN PATIENTS WITH HYPERTENSIVE VASCULAR DISEASE

mg. NH_3 per twenty-four hr.		Change (Average)
Before Rice Diet	After 28 Days (Average) on Rice Diet	
479	139	−70%

sulfur and phosphorus in the diet, i.e., by reducing the quantity of acid formed. Or, in cases in which the kidney although functioning under pathologic conditions has retained its ability to form ammonia, one might speculate about the possibility of reducing the rate of oxygen consumption by reducing the rate of ammonia production. The amount of oxygen thus saved might lead to an increase in the oxygen concentration at the surface of kidney cells where the supply of oxygen is diminished. As Table XII shows the ammonia excretion in the urine is decreased by the rice diet.

Table XIII compares the quantities of solids excreted in the urine on the rice diet and on a normal diet.

Discussion of the "Active Principle" of the Rice Diet. Since the first reports on the rice diet (1944), the importance of the rigid restriction of protein, fat, sodium and chloride has been stressed. Up to that time the therapeutic effect of this diet on blood pressure, heart size, electrocardiogram, eyegrounds, non-protein nitrogen, edema, etc., had been determined in 150 patients with acute and chronic nephritis and hypertensive vascular disease.[1–4,(5)]

Grollman and Harrison (1945) believe that the effect of the rice diet is due to its low sodium content. They repeated some experiments with the rice diet on rats in which renal hypertension had been induced by the thread compression method. They confirmed our finding that the diet leads to marked blood pressure reduction. Since the hypotensive effect was not obtained when the strict rice diet was changed by the addition of NaCl (not of KCl), this

TABLE XIII
URINARY EXCRETION (GM. IN 24 HR.) ON "NORMAL" DIET AND ON RICE DIET

	Normal Diet	Rice Diet (2 Months or More)
Total nitrogen	15.0	2.3
Urea nitrogen	12.0	1.1
Uric acid nitrogen	0.3	0.08
Total creat. nitrogen	0.6	0.4
Ammonia nitrogen	0.6	0.1
Sodium	4.0	0.01
Potassium	2.0	3.0
Chloride	7.0	0.1
Inorganic phosphate	1.0	0.3
Total sulfate	0.80	0.13
Inorganic sulfate	0.72	0.08
Ethereal sulfate	0.08	0.05

hypotensive effect was ascribed by the authors to the sodium restriction.[21]

Selye and Stone (1946) kept the sodium chloride content of the diet high and varied the protein content. They produced nephrosclerosis with heart enlargement in rats by unilateral nephrectomy, lyophilized anterior pituitary gland and the substitution of a 1 per cent NaCl solution for drinking water. Each group of rats was fed exclusively on one of the following foods: skeletal muscle, cardiac muscle, "purina fox chow," peas, lentils, corn, lima beans or rice. They found that the degree of nephrosclerosis and the final organ weights were lowest in the rats fed with rice.[22]

Dock (1946) compares the relative infrequency of arteriosclerosis of the coronary arteries in the Chinese and Italian population with the high incidence of this disease in the American army and stresses the importance of cholesterol. "Diets high in cholesterol, such as the American servicemen had while in this country, may hasten the process and lead to death decades earlier than if the individual had been on a diet poor in cholesterol." "As hypertension and cholesterol metabolism become better understood and controllable there is every reason to believe that there will be a decline from the present appalling death rate from coronary disease to the insignificant level

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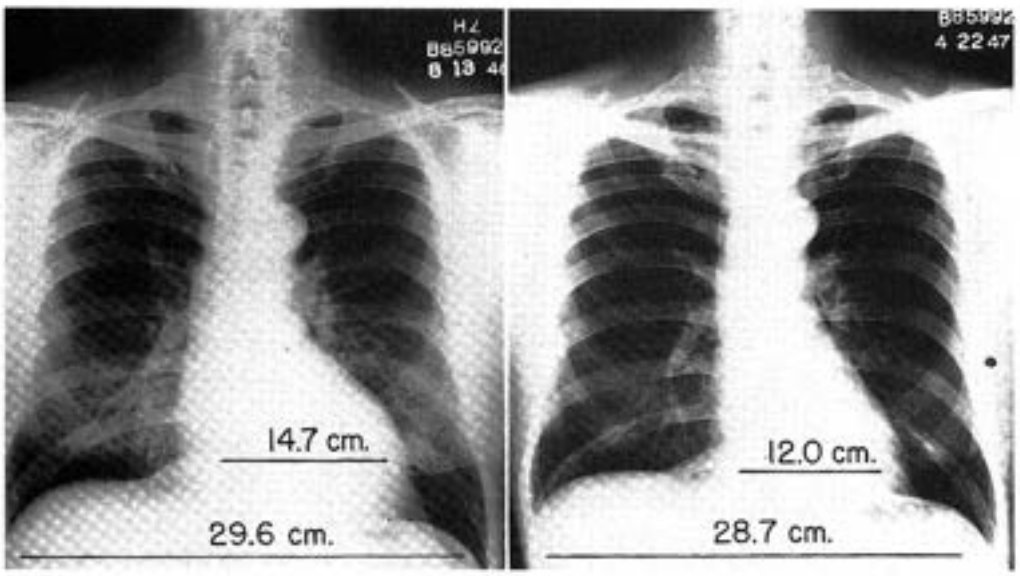

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FIG. 9. I. S., a male, forty-one years of age, had hypertensive vascular disease of three years' duration, retinal hemorrhages and exudates. Previous treatment consisted of rest and phenobarbital. Total PSP excretion in two hours, 60 per cent. A, August 13, 1946; Blood pressure 220/150; cholesterol 290 mg. per 100 cc. serum; EKG T_1 diphasic to inverted; weight, 72.5 Kg. Rice diet was started August 17, 1946 and strictly followed for two months (2–7 mg. Cl per 100 cc. of urine); then moderately well followed (35–36 mg. Cl per 100 cc. of urine). No medication was given; the patient was working. B, April 22, 1947; Blood pressure 128/88; cholesterol 155 mg. per 100 cc. of serum; EKG T_1 upright. Retinal hemorrhages and exudates had disappeared; weight 56 Kg._____There was decrease in blood pressure and reduction in heart size with change in transverse diameter of 22 per cent.

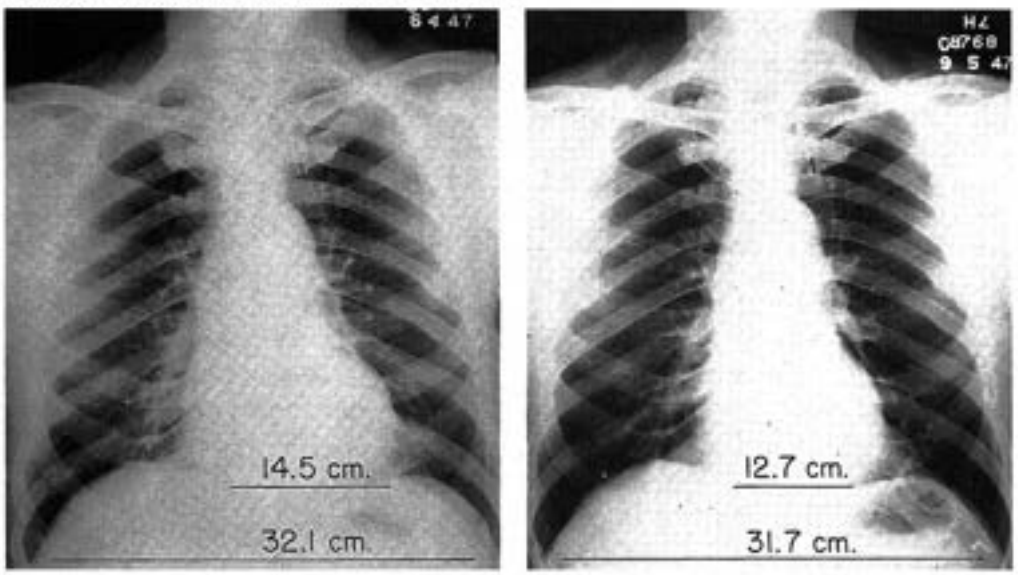

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FIG. 10. H. H., a male, sixty-three years of age, had hypertensive vascular disease of at least two and one-half years' duration and a stroke 1946. Previous treatment consisted of aminophyllin, rest, sedatives, weight reduction. Total PSP excretion in two hours 56 per cent. A, June 4, 1947; Blood pressure 217/124; weight, 76.3 Kg. Rice diet was started June 7, 1947, and strictly followed for three months (9-23 mg. Cl per 100 cc. of urine.) No medication was given. B, September 5, 1947; Blood pressure 170/98; weight, 70.7 Kg. _____There was a decrease in blood pressure and a reduction in heart size with change in transverse diameter of 14 per cent.

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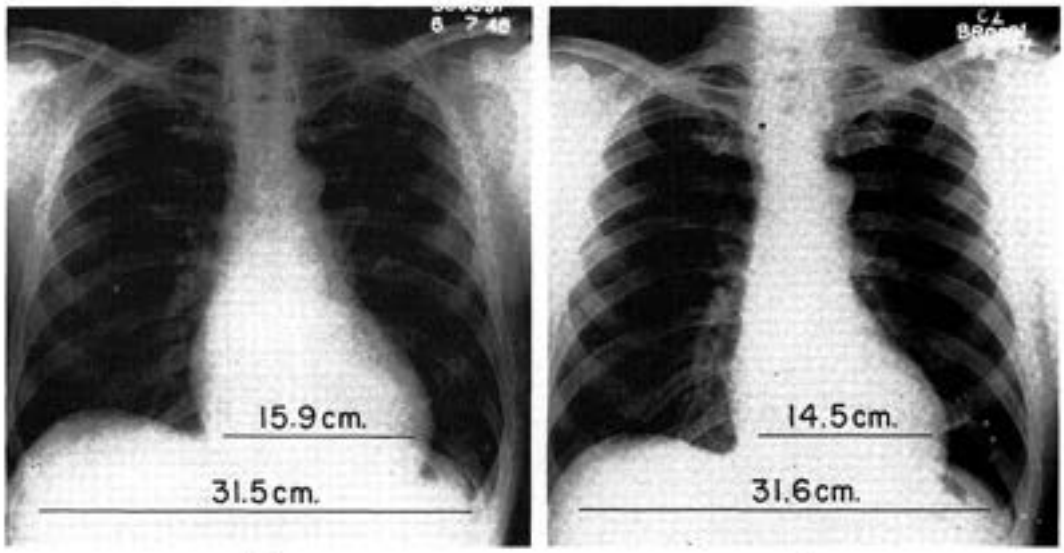
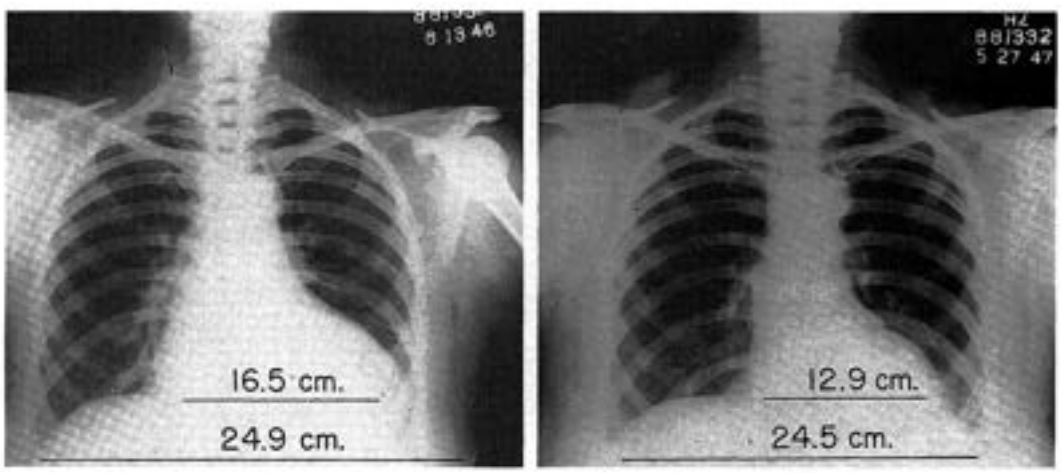


A B

FIG. 11. R. H., a male, fifty-two years of age, had hypertensive vascular disease of three years' duration and pulmonary edema. Was treated with digitalis, mercuhydrin, aminophyllin and morphine. Total PSP excretion in two hours 39 per cent. A, June 7, 1946; Blood pressure 222/130; weight, 78.7 Kg. Rice diet was started June 12, 1946, and strictly followed for four months (11–22 mg. Cl per 100 cc. of urine); then moderately well followed (43–48 mg. Cl per 100 cc. of urine). All medication except digitalis was discontinued at beginning of rice diet. Digitalis was discontinued 7–24–46. B, June 2, 1947; Blood pressure 178/106; weight 71.2 Kg.; the patient was asymptomatic and resumed his practice as surgeon._____There was a decrease in blood pressure and reduction in heart size with change in transverse diameter of 10 per cent.



A B

FIG. 12. A and B. G. H., a female, forty-five years of age, had hypertensive vascular disease of at least three years' duration, retinal hemorrhages and exudates. Total PSP excretion in two hours, 52 per cent. A, June 13, 1946; Blood pressure 258/138; EKG T_1 inverted; weight, 64.8 Kg. Rice diet was started June 20, 1946, and strictly followed for four months (4–13 mg. Cl per 100 cc. of urine); then moderately well followed (26–31 mg. Cl per 100 cc. of urine); no medication was given. The patient was active. B, May 27, 1947; Blood pressure 184/98; EKG T_1 upright; weight 59.6 Kg. No retinal hemorrhages or exudates were present._____There was a decrease in blood pressure and reduction in heart size with change in transverse diameter of 28 per cent.

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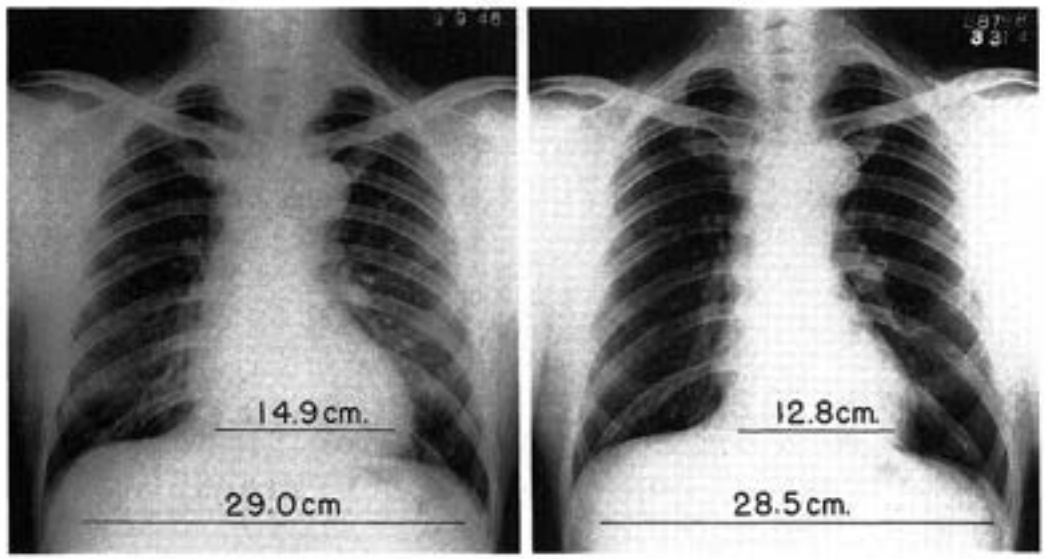
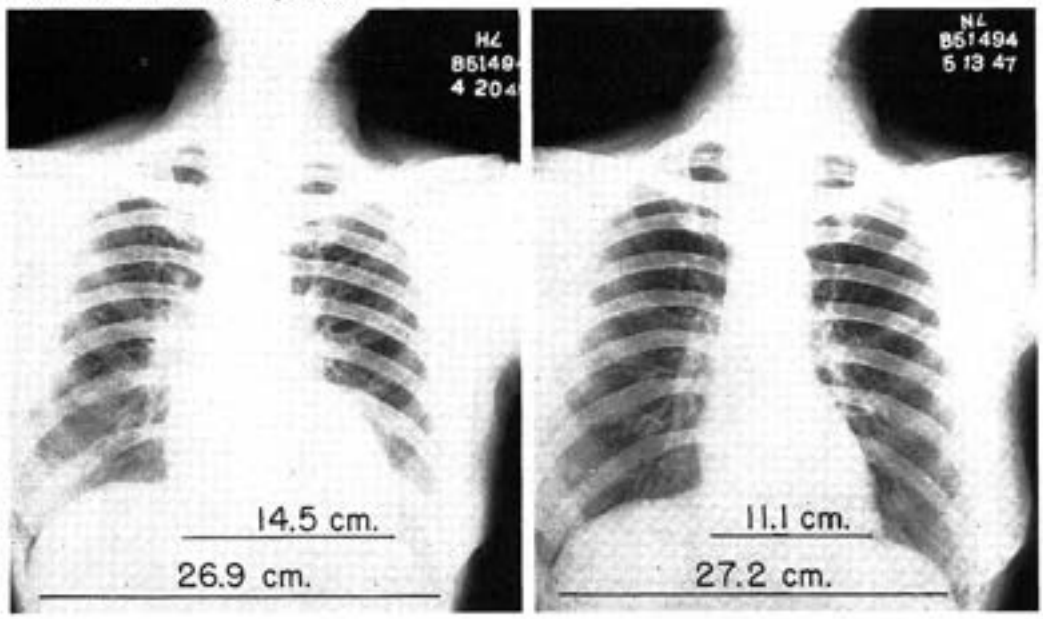


A B

FIG. 13. A and B. O. P., a male, forty-one years of age, had hypertensive vascular disease of five years' duration with severe headache. A, September 9, 1946; Blood pressure 186/122; EKG T_1 inverted; total PSP excretion in two hours 79 per cent; weight 68.7 Kg. Rice diet was started September 9, 1946; no medication was given. He was asymptomatic and able to do his work. B, March 31, 1947; Blood pressure 150/100; EKG T_1 upright; weight, 66.4 Kg.——There was a decrease in blood pressure and reduction in heart size with change in transverse diameter of 16 per cent.



A B

FIG. 14. A and B, R. Z., a female, fifty-three years of age, had hypertensive vascular disease (of at least five years' duration) and diabetes mellitus. Previous treatment: reduction diet (25 pound weight loss). A, April 20, 1945; Blood pressure 202/140; weight 53 Kg.; BMR +45 per cent; total PSP excretion in two hours 62 per cent, sugar, 231 mg. per 100 cc. blood (no insulin). Rice diet was started April 22, 1945; it was well followed through May, 1945, and from January, 1946 to February, 1947 (7–15 mg. Cl per 100 cc. of urine). No digitalis was given. From August, 1945 to December, 1946, 10–30 units of insulin were given daily. B, May 13, 1947: sugar, 113 mg. per 100 cc. blood (no insulin). Blood pressure 224/112; weight, 50 Kg.; BMR −10 per cent.——There was reduction in heart size with change in transverse diameter of 31 per cent in spite of persistence of high blood pressure.

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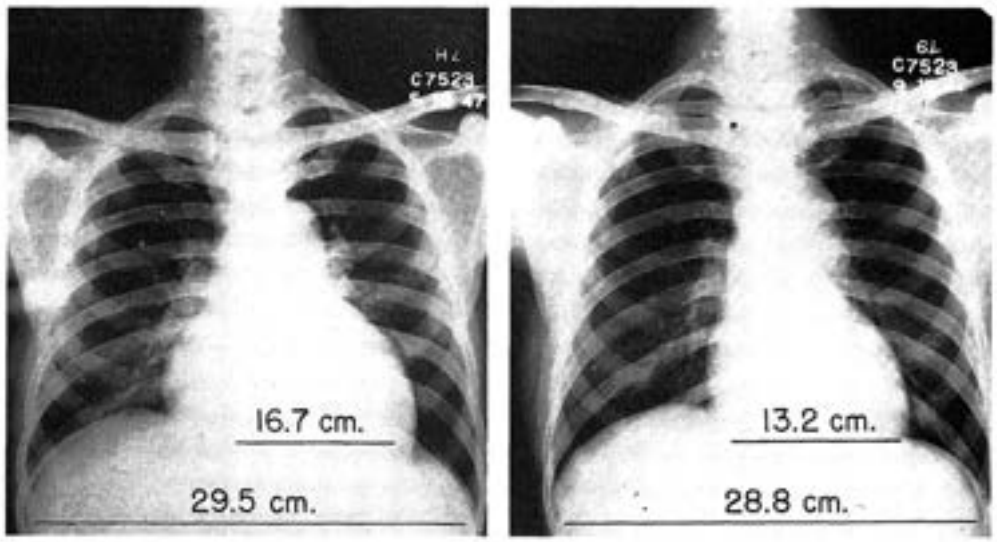

A B

FIG. 15. A and B, J. P., a male, forty-two years of age, had hypertensive vascular disease of ten years' duration and cardiac failure of six months' duration. Previous treatment: sympathectomy in 1940 and from 1940 to 1946 potassium thiocyanate and phenobarbital. In 1946 pituitary irradiation was given; since 1946, digitalis, mercurials and sedatives (0.6 Gm. sodium amytal daily). A, May 17 to 27, 1947; Total PSP excretion in two hours, 32 per cent; venous pressure 195 mm. of saline. Blood pressure 220/152; weight 60.3 Kg. Rice diet was started on May 17th and strictly followed for four months. All medication was discontinued on May 17th except digitalis which was discontinued June 9, 1947. B, September 15, 1947; Blood pressure 214/148; weight 57.1 Kg.——There was a reduction in heart size with change in transverse diameter of 27 per cent, in spite of persistence of high blood pressure.

FIG. 16. M. C., a male, forty-five. Planogram of myocardial aneurysm. (See Figure 17.)

now prevailing in other populations such as the Chinese."[23,24]

G. Dick and Schwartz (1947) measured the arterial pressure in dogs in which hypertension had been produced by a nephrosclerosis which followed the intravenous administration of streptococci. At the time when the rice diet was started the hypertension had been maintained for two to four years. Dick and Schwartz found an average decrease of the mean arterial pressure from 181.6 to 138 mm. Hg after eight weeks on the diet. They conclude: "It appears that the Kempner regime is capable of causing significant lowering of the arterial blood pressure of dogs made hypertensive through the induction of nephrosclerosis. The role of weight loss, salt restriction, and nitrogen balance in this result requires further study."[25]

INDICATIONS AND CONTRAINDICATIONS

The apparent simplicity of the rice diet has not infrequently proved a handicap.

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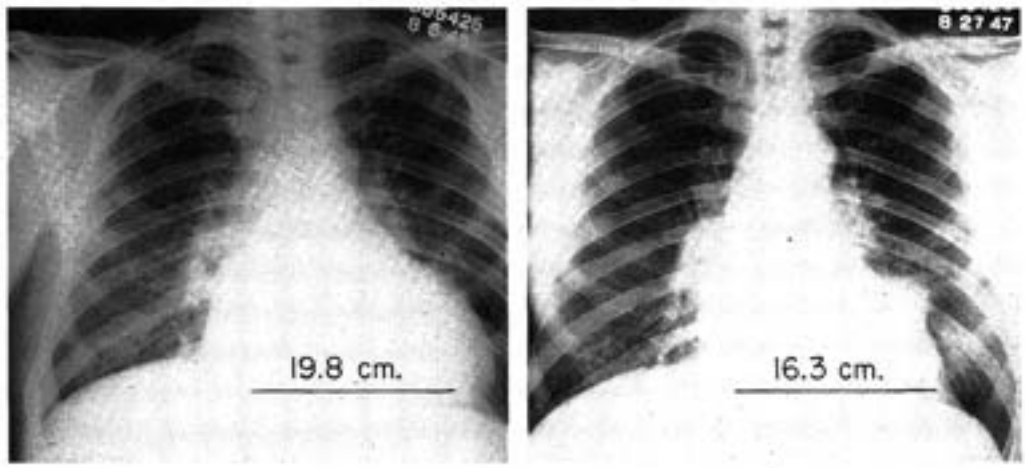

A B

FIG. 17. A and B, M. C., a male, forty-five years of age, had a history of hypertension in 1944, myocardial infarction in 1945, followed by myocardial aneurysm.[24] There was progressive cardiac failure with massive peripheral edema, ascites, liver enlargement, hypoproteinemia (Fig. 2), hypocalcemia, albuminuria, decubitus ulcer and dyspnea. Previous treatment: (four months' hospitalization) low-protein, salt-poor diet, oxygen, digitalis, salyrgan, aminophyllin, ammonium chloride, theominal, coramine, sedatives; i.v. glucose; paracentesis. Rice diet was started August 7, 1946, and strictly followed; paracentesis August 13th; oxygen inhalation. No medication was given except digitalis which was discontinued October 10, 1946. Blood pressure (A) August 6, 1946 was 138/94; (B) August 27, 1947, 118/94. Advanced myocardial failure unchecked by previous intensive treatment was compensated by rice diet. The patient became asymptomatic. There was a reduction in heart size with change in transverse diameter of 21 per cent.

We have seen patients who had been treated with the diet just because the manometer had shown blood pressure figures above normal and in whom tumors, infections, etc. had been overlooked.

The rice diet is indicated in all serious instances of acute and chronic nephritis;[1-5,11] in heart failure which does not respond to the customary treatment with salt restriction and drugs;[1-5,11,26] in arteriosclerotic and hypertensive vascular disease with cardiac, cerebral, retinal or renal involvement.[1-5,11,26]

The rice diet should be tried in uncomplicated hypertensive vascular disease when a more liberal regimen (fat-poor, salt-poor diets, weight adjustment, restriction of activities, regulation of bowel habits, sedation, etc.) has failed.

The rice diet should be used as a therapeutic test before sympathectomy is considered. If the dietary treatment proves ineffective, it can be discontinued.

In cases complicated by peptic ulcer the rice diet has to be modified. The rice is well tolerated, but raw fruit should be avoided and only cooked, strained fruit should be used. Water or dialyzed milk may be substituted for the fruit juices.

The rice diet is not contraindicated in cases complicated by diabetes mellitus. It may in fact have a special value because of the dangerous rôle played by hypercholesterolemia in this disease.[27] It was expected that in order to maintain the previous blood sugar levels larger amounts of insulin would have to be given. We found instead that in many cases the blood sugar decreased on the rice diet and the insulin dose had to be reduced.

The rice diet is contraindicated unless frequent checks of the patient's blood and urine chemistry are possible. This is of especial importance in patients with renal sodium chloride leakage as the following history may illustrate:

A patient with hypertensive heart disease (Figs. 18 and 19) had been on the diet for seven months. He had followed it very strictly. After three weeks on the diet the serum chloride was 95 and the serum

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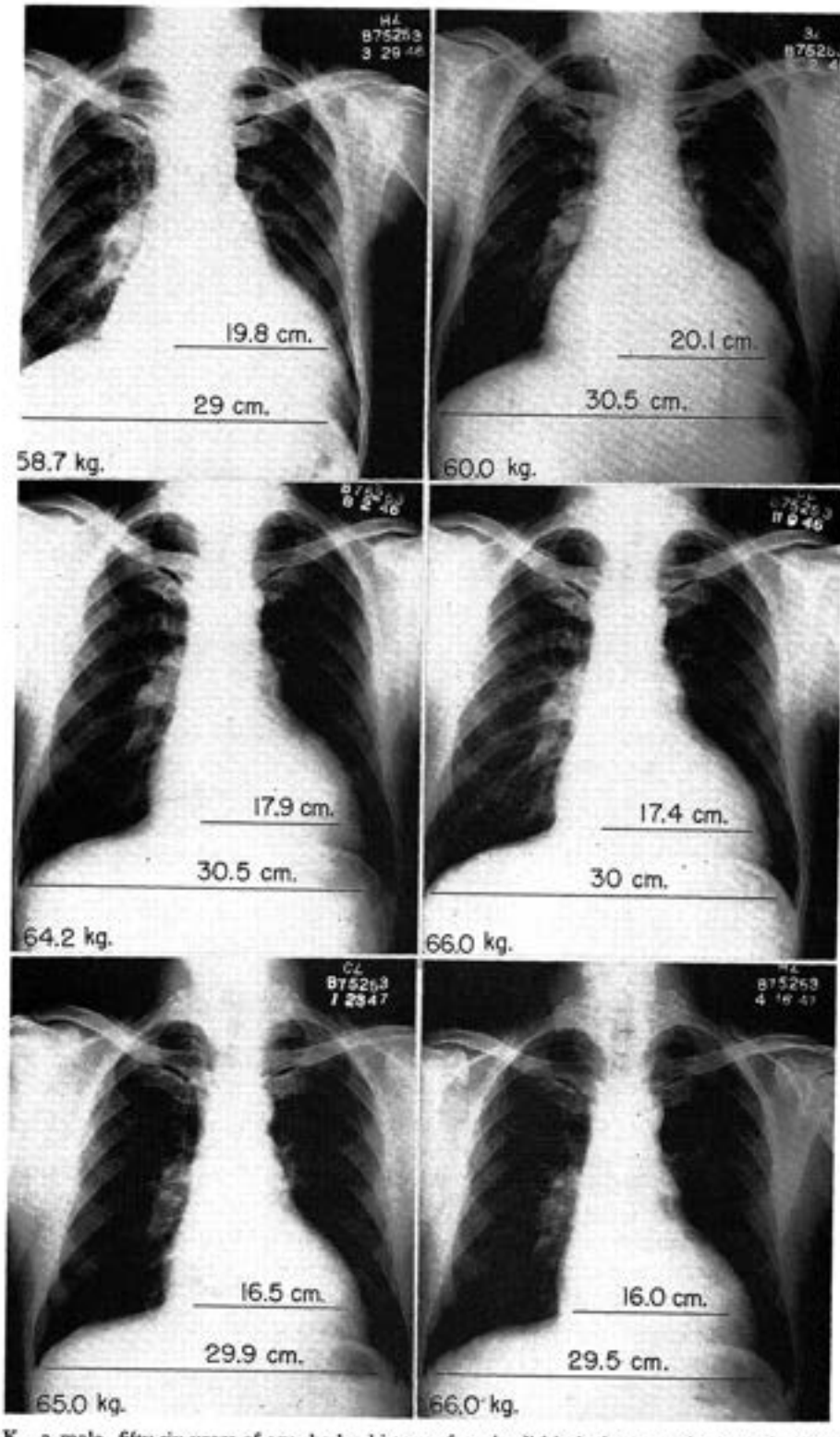

FIG. 18. P. K., a male, fifty-six years of age, had a history of nephrolithiasis, hypertensive vascular disease of more than ten years' duration, nephrectomy (left) in 1940, heart disease of three years' duration; left bundle branch block; dyspnea, edema. Previous treatment: salt-poor diet, digitalis, squill, salyrgan, mercupurin, ammonium chloride, sedatives. March 29, 1946; total PSP excretion in two hours, 24 per cent; NPN 45 mg. per 100 cc. of blood; blood pressure 145/90. Rice diet was started April 3, 1946, and strictly followed (1–10 mg. Cl per 100 cc. of urine). All medication discontinued except digitalis. Digitalis was discontinued April 20, 1946. There was a weight gain of 7.3 Kg. and a gradual reduction in heart size. (See also Fig. 19.)

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sodium 135 mEq. per liter; after four months, 87 and 138 mEq. respectively. From the fifth month on he had felt well and had been completely asymptomatic. One evening, after some hours work at carpentry, he suddenly became unconscious and remained so for many hours. His hands and feet were extremely cold and, on regaining consciousness, he felt very weak and "faint." The attending internist who was familiar with the treatment made a diagnosis of stroke. However, on the addition of a few vegetables to his diet, all the symptoms disappeared and three days later when the patient was brought to our hospital, examination of the serum revealed a chloride concentration of 69 and a sodium concentration of 125 mEq. per liter.

CLINICAL CHANGES PRODUCED BY THE RICE DIET

A great many patients on the rice diet have experienced relief from headache, giddiness, fatigue, dyspnea and substernal pain. Such subjective improvement has not been accepted as evidence of successful therapy. Only measured results such as decrease in blood pressure, reduction in heart size, loss of edema and reversion of electrocardiogram or eyeground changes have been used to determine the effect of the treatment.

The therapeutic results in eighty patients with acute or chronic primary kidney disease and in 130 patients with hypertensive vascular disease were reported in 1945.[8] By 1946 one hundred patients with primary kidney disease and 222 patients with hypertensive vascular disease had been treated with the rice diet.[11] This paper is limited to the changes obtained in patients with hypertensive vascular disease.

The effect of the diet has been determined in 500 patients most of whom were seriously ill and had failed to respond to other forms of treatment. The diet has been ineffective in 178 of these 500 patients if we include twenty-six patients who were in a critical condition when started on the diet and who died after an average period of thirty-nine days. In 322 of the 500 patients the diet has proved beneficial, i.e., it has produced one or more of the following effects: decrease in "mean" arterial blood pressure of at least 20 mm. Hg; reduction in heart size with change in the transverse diameter of 18 per cent or more; a change in T_1 from completely inverted to upright; disappearance of severe retinopathy.

Blood Pressure. Five hundred patients (207 women, 293 men) with hypertensive vascular disease whose "mean" arterial pressure (sum of systolic and diastolic pressures divided by 2) was 125 mm. Hg or more were treated with the rice diet. The age ranged from nineteen to seventy-three (average, fifty-one) years. Two hundred twenty-nine patients had signs of renal involvement; in 271 no conclusive evidence of renal involvement was found.

The systolic blood pressure levels before treatment ranged from 154 to 264 mm. Hg; the average was 199 mm. The diastolic blood pressure levels ranged from 72 to 172 mm. Hg; the average was 117 mm. Hg.

After they were regulated on the diet under our supervision, most of the patients followed the diet at home, returning at intervals of two to six months for reexamination.

The blood pressure was considered improved if the "mean" arterial pressure had decreased by at least 20 mm. Hg.

The results are summarized in Table XIV. The figures given are averages of the daily readings of three to twenty-four (average, eight) days before and after treatment.

Of the 229 patients in whom the diagnosis of hypertensive vascular disease with "secondary" renal involvement was made, twenty-five died six to ninety-six days (average, thirty-nine days) after the diet was started. Of the 271 patients without evidence of renal involvement, one patient died thirty-six days after the rice diet was started.

Table XV shows the difference in the percentage of improvement when these twenty-six patients who died are not included.

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TABLE XIV
EFFECT OF RICE DIET ON BLOOD PRESSURE OF 500 PATIENTS WITH HYPERTENSIVE VASCULAR DISEASE (PERIOD OF DIET 4–898 DAYS)
AVERAGES

No. of Patients	Blood Pressure: Before Rice Diet	Blood Pressure: After Rice Diet	Change in Systolic and Diastolic Pressure	Change in "Mean" Arterial Pressure	Days on Rice Diet
With Renal Involvement					
Hypertension Not Improved					
74	206/121	191/117	−15/−4	−9.5	71
25	226/147	Died	.....	.....	39
Hypertension Improved					
130	207/121	159/98	−48/−23	−35.5	81
Without Evidence of Renal Involvement					
Hypertension Not Improved					
89	186/109	167/102	−19/−7	−13	68
1	248/138	Died	.....	....	36
Hypertension Improved					
181	193/113	147/93	−46/−20	−33	85
Total					
Hypertension Not Improved					
163	195/114	178/109	−17/−5	−11	69
26	227/147	Died	.....	....	39
Hypertension Improved					
311	199/116	152/95	−47/−21	−34	83

TABLE XV
PERCENTAGE OF POSITIVE AND NEGATIVE BLOOD PRESSURE RESULTS (A) INCLUDING AND (B) NOT INCLUDING TWENTY-SIX PATIENTS WHO DIED

A	%	B	%
229 Patients with Renal Involvement		204 Patients with Renal Involvement	
Not improved	44	Not improved	37
Improved	56	Improved	63
271 Patients without Evidence of Renal Involvement		270 Patients without Evidence of Renal Involvement	
Not improved	33	Not improved	33
Improved	67	Improved	67
All 500 Patients		All 474 Patients	
Not improved	38	Not improved	35
Improved	62	Improved	65

TABLE XVI
INFLUENCE OF THE LENGTH OF TREATMENT WITH THE RICE DIET: BLOOD PRESSURE CHANGES IN PATIENTS WITH HYPERTENSIVE VASCULAR DISEASE

	Period of Treatment: 4–34 Days	Period of Treatment: 35–898 Days
	With Renal Involvement	With Renal Involvement
Number of patients	86	143
Not improved	49 = 57%*	50 = 35%†
Improved	37 = 43%	93 = 65%
	Without Evidence of Renal Involvement	Without Evidence of Renal Involvement
Number of patients	109	162
Not improved	47 = 43%	43 = 27%‡
Improved	62 = 57%	119 = 73%
	Total	Total
Number of patients	195	305
Not improved	96 = 49%	93 = 30%
Improved	99 = 51%	212 = 70%

* Including 13 patients who died.
† Including 12 patients who died.
‡ Including 1 patient who died.

TABLE XVII
CHANGES IN DIASTOLIC PRESSURE OF 406 PATIENTS WITH HYPERTENSIVE VASCULAR DISEASE INITIAL DIASTOLIC PRESSURE OF 100–159 MM. HG.

	No. of Patients	Percentage	Average Change
Decrease of 30 mm. Hg or more	52	13	−36
Decrease of 20–29 mm. Hg	101	25	−24
Decrease of 10–19 mm. Hg	158	39	−14
Decrease of 0–9 mm. Hg	77	19	− 5
Increase of 1–22 mm. Hg	18	4	+ 7
Total	406	100	−16.7

Figures 3 to 6 show typical blood pressure curves of patients on the rice diet.

The length of time required for the blood pressure to decrease varies from four days to ten months. The part played by the

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TABLE XVIII

EFFECT OF RICE DIET ON HEART SIZE: AVERAGE CHANGES IN TRANSVERSE DIAMETER OF HEART IN 286 PATIENTS WITH HYPERTENSIVE VASCULAR DISEASE

	No. of Patients	Percentage	Period of Rice Diet (Average) Days	Diameter of Chest (Averages)				Transverse Diameter of Heart (Averages)			
				Before Rice Diet Cm.	After Rice Diet Cm.	Change Cm.	Change % (Diameter of Chest of Smaller Heart = 100%)	Before Rice Diet Cm.	After Rice Diet Cm.	Change Cm.	Change % (Transverse Diameter of Smaller Heart = 100%)
Decrease of 20% or more	19	6.7	187	29.5	28.9	−0.6	−2.2	15.3	12.3	−3.0	−24.4
Decrease of 10.0–19.9%	106	37.1	114	29.2	29.1	−0.1	−0.3	14.5	12.7	−1.8	−14.2
Decrease of 0–9.9%	146	51.0	112	28.6	28.4	−0.2	−0.7	13.8	13.0	−0.8	−6.2
Increase of 0–8.0%	15	5.2	184	27.5	27.8	+0.3	+0.8	13.1	13.5	+0.4	+2.6
Total	286	100	122	28.8	28.6	−0.2	−0.7	14.2	12.9	−1.3	−10.1

TABLE XIX

CHANGES IN THE ANGLE OF THE ELECTRICAL AXIS IN 292 PATIENTS WITH HYPERTENSIVE VASCULAR DISEASE AFTER RICE DIET

No. of Patients	Percentage	Angle of Electrical Axis (Degrees)				Period on Rice Diet (Av.) Months
		Range of Change	Before Rice Diet	After Rice Diet	Change (Average)	
1	2	More than −25	−10	−55	−45	2
6		−15 to −25	+19	0	−19	4
173	60	±14	+13	+17	+ 4	6
70	38	+15 to +25	+13	+32	+19	7
42		More than +25	+ 6	+43	+37	8

TABLE XX

CHANGES OF T_1 IN 310 PATIENTS WITH HYPERTENSIVE VASCULAR DISEASE AFTER RICE DIET

No. of Patients	T_1 Before Rice Diet	T_1 After Rice Diet	Period on Rice Diet (Average) Months
	Change in Direction to Inverted		
2	diphasic	inverted	3
1	upright	diphasic	6
3	low upright	diphasic	4
1	upright	low upright	2
	No Change		
52	inverted	inverted	5
21	diphasic	diphasic	4
5	low upright	low upright	2
136	upright	upright	6
	Change in Direction to Upright		
19	low upright	upright	5
4	diphasic	low upright	7
19	diphasic	upright	8
17	inverted	diphasic	7
5	inverted	low upright	7
25	inverted	upright	10

length of time the diet was followed is evident from Figures 3 to 6 and Table XVI.

In 125 of the 500 patients (forty with and eighty-five without evidence of renal involvement) the blood pressure figures returned to normal or almost normal values (below 145/95 mm.). The blood pressure of these patients before the rice diet ranged from 222/148 to 158/98, average 181/107 mm.; the average pressure after four to 898 days, average ninety-four days, of rice diet was 132/85 mm. Seven patients are

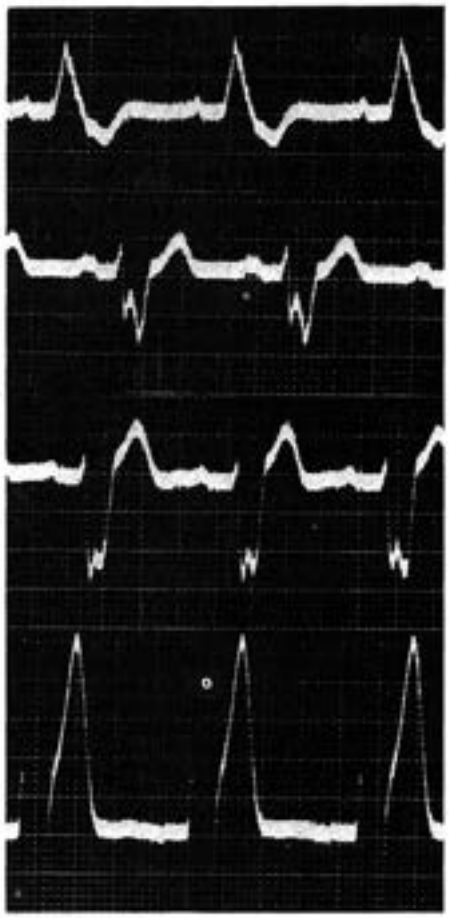

FIG. 19. P. K., a male, fifty-six, had left bundle branch block. The EKG did not change. (See also Fig. 18.)

included in this group whose "mean" arterial pressure dropped less than 20 mm. Hg and who therefore are counted as "not improved" in the previous paragraphs and tables.

The changes in diastolic pressure are analyzed separately in Table XVII.

Of 406 patients whose initial diastolic pressure was 100 mm. Hg or more 388, i.e., 96 per cent, had a decrease of 1 to 62 mm., average 18 mm., whereas only eighteen patients, i.e., 4 per cent, had an increase of 1 to 22, average 7 mm.

It has been assumed that the lowest blood pressure figure obtained after 0.6 Gm. sodium amytal indicates the maximum decrease which could be expected in the individual patient from any form of treatment. Figure 7 shows in three typical charts that the blood pressure values obtained without sodium amytal after rice diet may be far lower than the lowest values reached during the sodium amytal test before the diet.

Heart Size. The assumption that cardiac enlargement in hypertensive vascular disease is desirable in order to overcome the increased peripheral resistance has been a pious self-deception of the physician who had no means of influencing the disease and preventing the progressive cardiac breakdown.

Cardiac enlargement in hypertensive vascular disease has been found to disappear when the patient is given the rice diet. Chest films taken before and after rice diet show decreases in the heart sizes with changes in the transverse diameter up to 30 per cent. Decrease in heart size does not necessarily coincide with decrease in blood pressure. In a number of patients whose blood pressure remained at a constant high level or showed only an insignificant reduction, a considerable decrease in heart size was found. (Figs. 14 and 15.)

Six foot chest films of 286 patients taken before and after one month or more of dietary treatment (no digitalis or other drugs) are available for comparison. Table XVIII combines the averages of the measurements of the transverse diameter of the heart and of the chest diameter grouped according to the extent of change.

Before the rice diet the transverse diameters of the hearts of the 286 patients ranged from 10.2 to 19.4 cm.; the average was 14.2 cm. After the rice diet they ranged from 9.4 to 18.2 cm.; the average was 12.9 cm.

In 15 of the 286 patients (5 per cent) the heart became larger. In these patients the transverse diameter of the heart showed an average increase of 2.6 per cent. The chest diameter (average) increased by 0.8 per cent. The average period on the diet was

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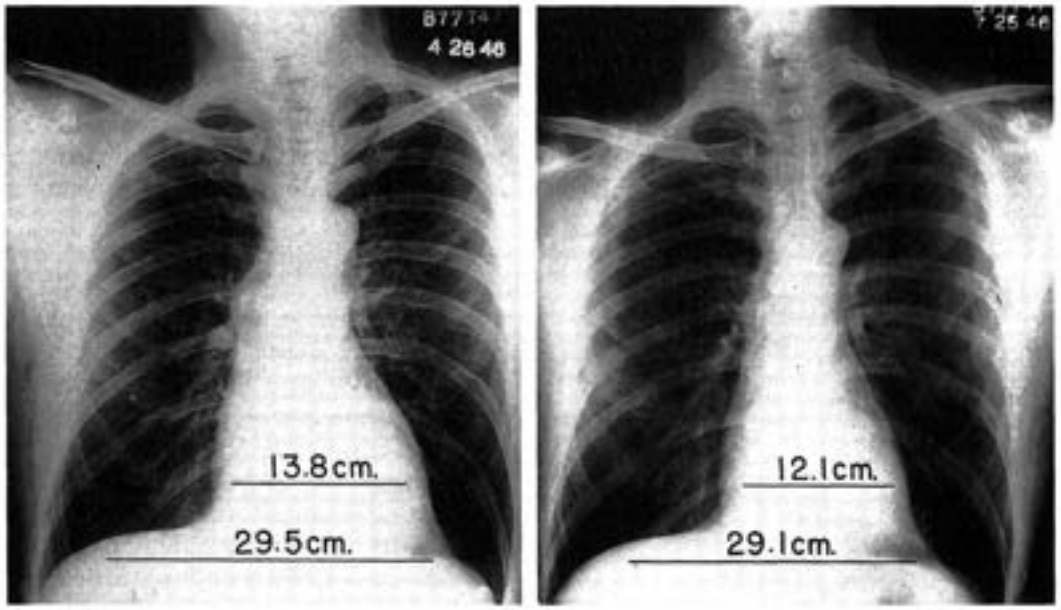

A B

FIG. 20. A and B, C. O. a male, forty-three years of age, had hypertensive vascular disease of ten years' duration, left bundle branch block and dyspnea. Total PSP excretion in two hours, 57 per cent. Rice diet was started May 4, 1946, and strictly followed (10–11 mg. Cl per 100 cc. of urine). No medication was given. The patient became asymptomatic. There was a decrease in blood pressure and reduction in heart size with change in transverse diameter of 14 per cent. (See also Fig. 21.)

184 days. The average heart size in this group before treatment was the smallest found.

In 271 of the 286 patients (95 per cent) the heart became smaller with an average change in the transverse diameter of 10.6 per cent. The chest diameter decreased by 0.6 per cent (average). The average period on the diet was 118 days.

Figures 8 to 15, 17, 18, 20 show typical changes in the heart picture produced by the rice diet.

Electrocardiograms. The blood supply to the heart muscle will be inadequate whenever the coronary blood flow is decreased without a simultaneous decrease in the myocardial energy requirements, or whenever the myocardial energy requirements are increased without a simultaneous increase in the blood supply through the coronaries. In either case the effects of the deficiency in oxygen and nutrient substances, with the resulting chemical changes and consequent clinical manifestations, are easily predictable.[7,28] The natural course of these events is recorded by the electrocardiographic findings which indicate advancing myocardial impairment: left axis deviation, T_1 inversion, arrhythmias, conduction defects or myocardial infarction.

An attitude of resignation has prevailed with regard to the abnormal electrocardiogram in hypertensive heart disease. "It is a pertinent feature of records denoting left ventricular strain that the changes are slow in their evolution and more or less permanent once they have appeared."[29] "When once established the T-wave and the RS-T defects described persist and remain unaltered until the death of the patient."[30]

Electrical axis and T_1 waves were studied in the electrocardiograms of 310 patients with hypertensive vascular disease before and after the rice diet. None of these patients received digitalis or any other drug. All electrocardiograms were made with the patient at rest in a recumbent position. The period between the two electrocardiograms compared was one month to thirty-three months, an average of six months. In 18

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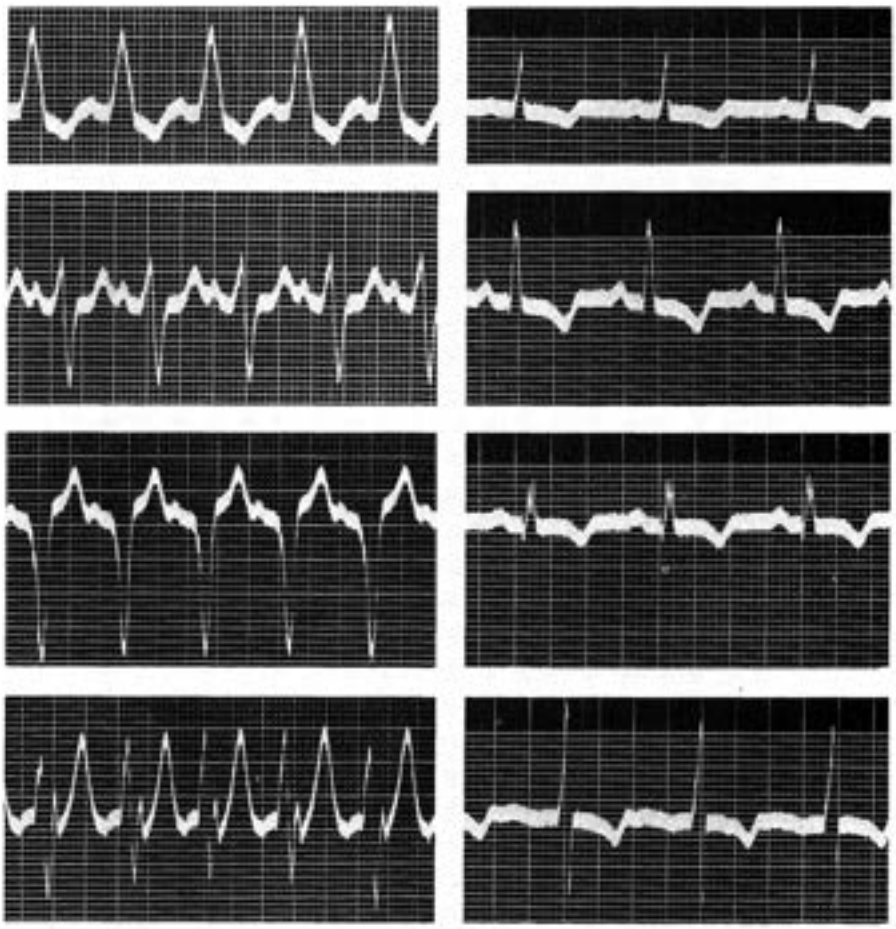

FIG. 21. C. O., a male, forty-three years of age, had hypertensive vascular disease of ten years' duration and dyspnea. April 29 to May 8, 1946: blood pressure, average, 179/126; total PSP excretion in two hours, 57 per cent. Rice diet was started May 4, 1946, and strictly followed (10–11 mg. Cl per 100 cc. of urine). No medication was given. July 24 to July 25, 1946: blood pressure, average, 157/110.——The patient became asymptomatic and there was disappearance of left bundle branch block. (See Fig. 20.)

of the 310 patients the electrical axis could not be evaluated. In the remaining 292 patients the angles of the electrical axis were:

	Before Diet	After Diet
More than +30 degrees	in 89 patients	in 131 patients
0 to +30 degrees	in 97 patients	in 91 patients
Less than 0 degrees	in 106 patients	in 70 patients

The changes in the angle of the electrical axis of these patients are summarized in Table XIX.

Of the 119 patients whose electrical axis changed more than ±14° during the treatment 7, i.e., 6 per cent, showed a decrease; 112, i.e., 94 per cent, showed an increase in the angle of the electrical axis.

The T waves in lead I were evaluated in 310 patients. Before the rice diet was started T_1 was normally upright or low upright in 165, diphasic or inverted in 145 patients. The changes during the treatment are shown in Table XX.

In seven patients there was a change of T_1 in the direction from upright to inverted. In 89 patients there was a change of T_1 in the direction from inverted to upright. In

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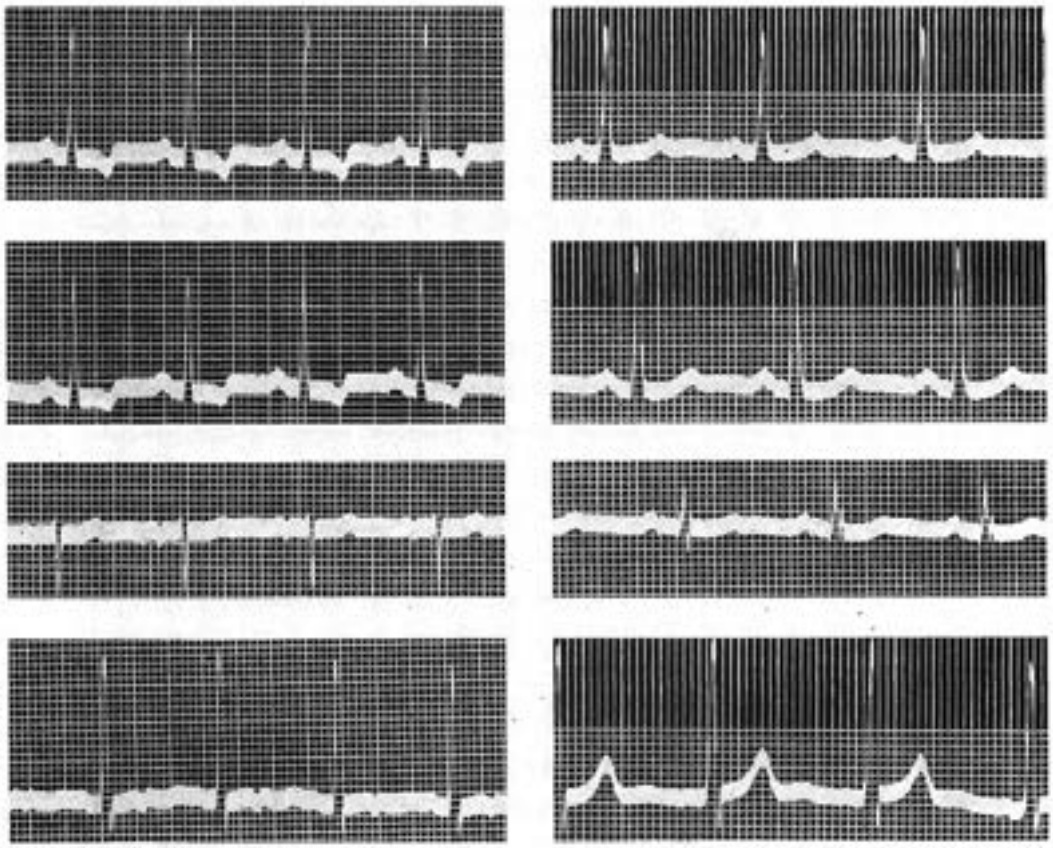

12-19-45 1-18-46

FIG. 22. R. L., a male, twenty-three years of age, had hypertensive vascular disease of three years' duration with advanced retinopathy; total PSP excretion in two hours: 2.5 per cent. No digitalis was given. Rice diet was started on December 18, 1945. Blood pressure, average, December, 18 to December 24, 1945: 222/148; January, 15 to January 21, 1946: 153/112. March, 11 to March 22, 1946: 134/94. Inverted T_1 became upright within one month. The lowest blood pressure was reached two months later. (Figs. 3 and 30.)

ninety-nine patients the T_1 waves were completely inverted before treatment. In thirty of these ninety-nine patients T_1 became upright with the diet. In no patient did the reverse occur.

Excluding the patients who at the start of the rice diet already had an inverted T_1 (and in whom there could be no further change for the worse according to the grouping of Table xx), the percentage of those changing for the worse during the rice diet was three. Excluding the patients who at the start of the diet already had an upright T_1 (and in whom there could be no further improvement according to the grouping of Table xx), the percentage of those changing for the better was fifty-two.

The shortest time in which an inverted T_1 became normally upright was one month. (Fig. 22.) The average was ten months. In the patient whose EKG is shown in Figure 23 it took three years.

Of the 292 patients in whom it was possible to evaluate the changes both in electrical axis and in T_1, eighty-seven patients (30 per cent) had an initial electrical axis above $+10°$ and an upright T_1. Of these eighty-seven patients 7 (8 per cent) showed a change for the worse in that the electrical axis decreased below $+10°$ and/or T_1 became diphasic; 80 (92 per cent) did not change with the rice diet.

Of the 292 patients 205 (70 per cent) had an initial electrical axis below $+10°$ and/or

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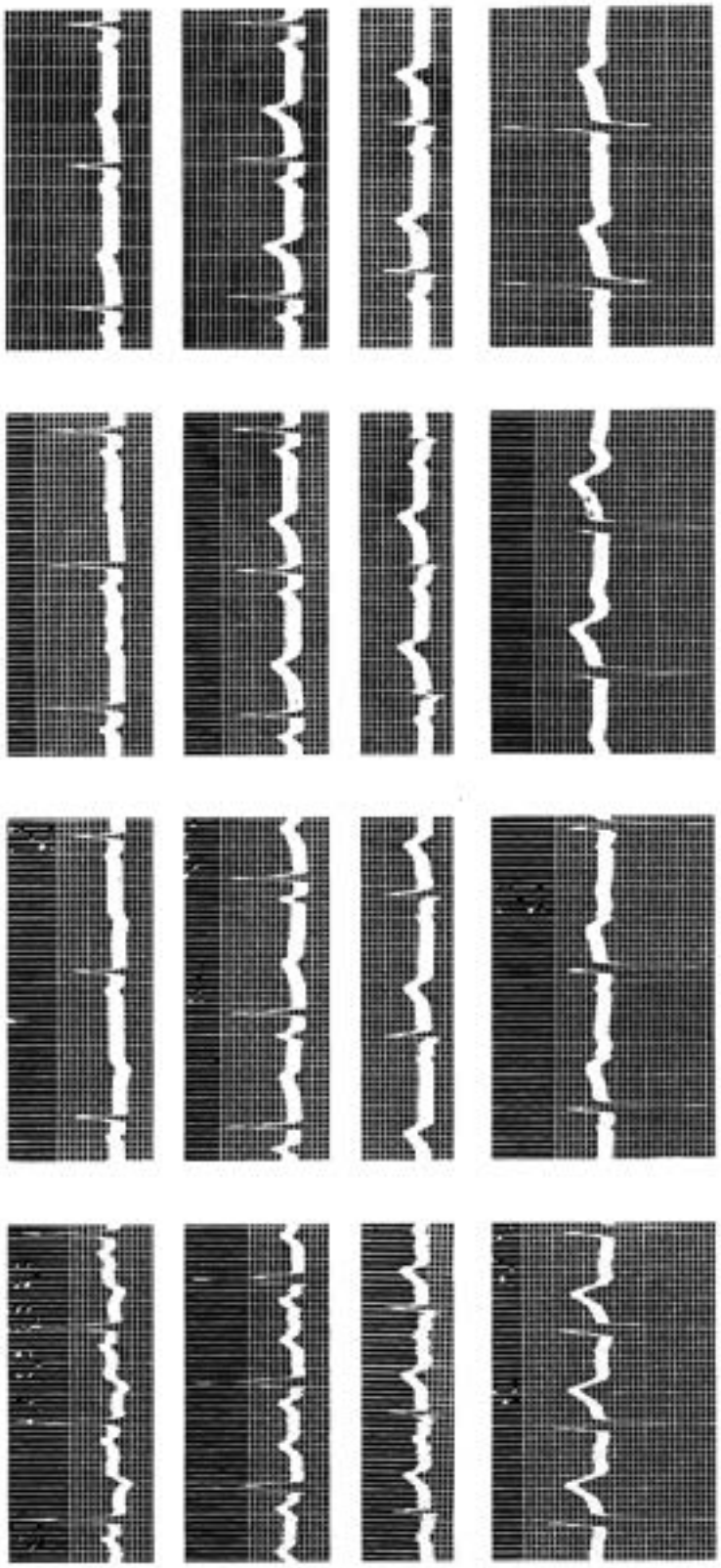

FIG. 23. A. E. H., female, thirty-six years of age, had hypertensive vascular disease of one year's duration. Chronic pyelonephritis was present. There were severe headaches and retinal hemorrhages and "silver wire arterioles." Previous treatment with salt-poor diet; no digitalis was given. Total PSP excretion in two hours: 9–25 per cent. Rice diet was started April 13, 1943: it was moderately well followed. No medication was given. Patient was asymptomatic and working. Blood pressure averages: April 5 to April 26, 1943: 223/149; March 8 to March 10, 1944: 116/92; Feb. 20 to March 3, 1945: 159/109; May 23 to May 29, 1946; 118/79. Inverted T; has become normally upright three years after decrease of blood pressure.

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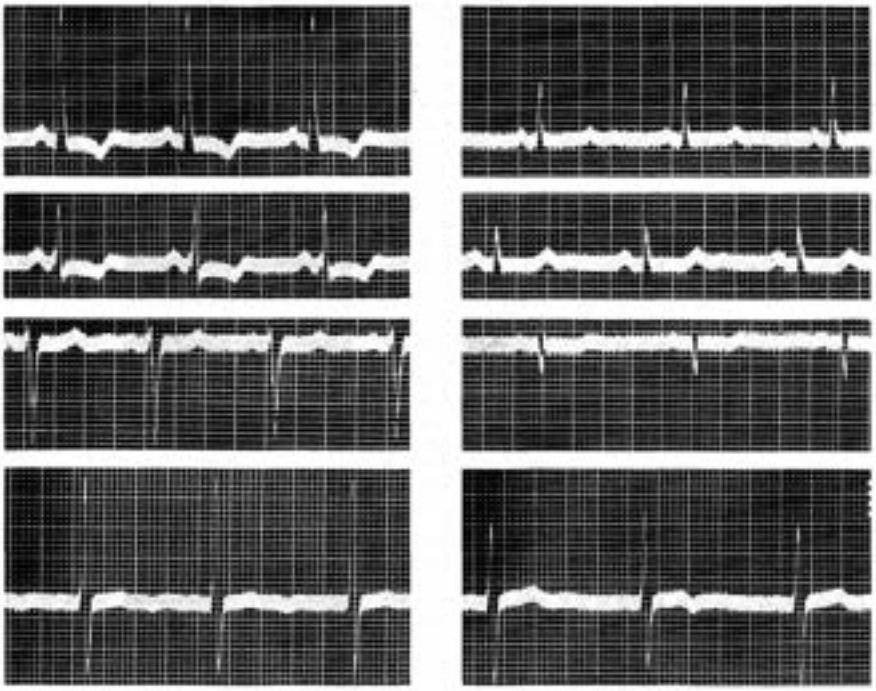

4-9-45 10-8-45

FIG. 24. C. G., a male, forty-nine years of age, had hypertensive vascular disease of two years' duration with severe headache. Two strokes occurred in 1944. He was treated with sedatives; was given no digitalis; April 6 to April 22, 1945: blood pressure average, was 196/105; total PSP excretion in two hours: 48 per cent. Rice diet was started April 24, 1945: it was followed strictly (5–20 mg. Cl per 100 cc. of urine). October 8 to October 11, 1945: blood pressure average was 136/80._____There was a decrease in the blood pressure and an increase in the angle of electrical axis. Inverted T_1 became upright.

a diphasic or inverted T_1. Of these 205 patients 119 (58 per cent) remained unchanged; eighty-six patients (42 per cent) showed an increase in the electrical axis to more than +10° and/or a change of T_1 from diphasic or inverted to upright.

Retinopathy. Advanced retinopathy with papilledema, hemorrhages or exudates is a danger signal in hypertensive vascular disease. "Hemorrhages associated with white spots in the retina (hypertensive neuroretinopathy) are ominous signs. Death commonly follows within a year."[31]

Vascular retinopathy has been found to disappear with the rice diet. The retinal improvement does not necessarily coincide with decrease in blood pressure. Very severe retinopathy has disappeared in patients when the blood pressure remained at a constant high level or showed only an insignificant reduction. (Figs. 27 to 29.)

Papilledema, hemorrhages or exudates, frequently in combination, were present in 140 of the 500 patients. In eighty-eight of these, eyeground photographs taken both before and after the rice diet (one to thirty months) are available for comparison. Papilledema was found in twenty-three of the eighty-eight patients. In seventeen it disappeared completely, in five partially and in one remained unchanged. Hemorrhages were found in fifty-five of the eighty-eight patients. In thirty-nine they disappeared completely, in fifteen partially and in one remained unchanged. Exudates were found in seventy of the eighty-eight patients. In forty-two they disappeared completely, in twenty-three partially and in five remained unchanged. In one of the patients in whom the exudates cleared up partially small hemorrhages occurred after a period of twelve

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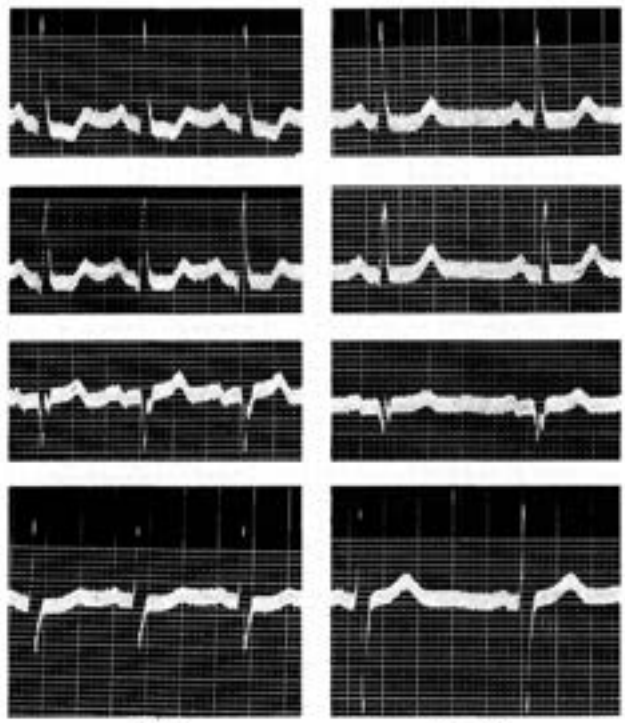

8-8-46 12-2-46

FIG. 25, F. G., a female, fifty-two years of age, had hypertensive vascular disease of twelve years' duration which began in toxemia of pregnancy. There were severe headaches. She had a stroke in May, 1946. She had previous treatment in a hospital with bedrest and a reduction diet. She had been given sedatives for the past three years. No digitalis was given. August 8, 1946: blood pressure was 238/128; total PSP excretion in two hours: 57 per cent. Rice diet was started August 10, 1946; it was strictly followed for six weeks (5 mg. Cl per 100 cc. of urine). September 20, 1946 to September 26, 1946: blood pressure, average, was 150/100. October and November, 1946, diet was poorly followed (194 mg. Cl per 100 cc. of urine). December 2–3, 1946: blood pressure average was 179/103. _____There was a decrease in blood pressure. The diphasic T_1 has become upright.

months on the diet (which had not been strictly followed).

Those patients in whom the retinopathy remained unchanged had been on the diet from one to three and one-half months except for one patient with exudative stippling who was on the rice diet for nineteen months. The patients in whom the retinopathy cleared up only partially had been on the rice diet from one to seventeen months, an average of five months. The period of time in which the retinal changes disappeared completely ranged from two to thirty months, an average of fourteen months.

Figures 26 to 30 show typical eyeground photographs before and after the diet.

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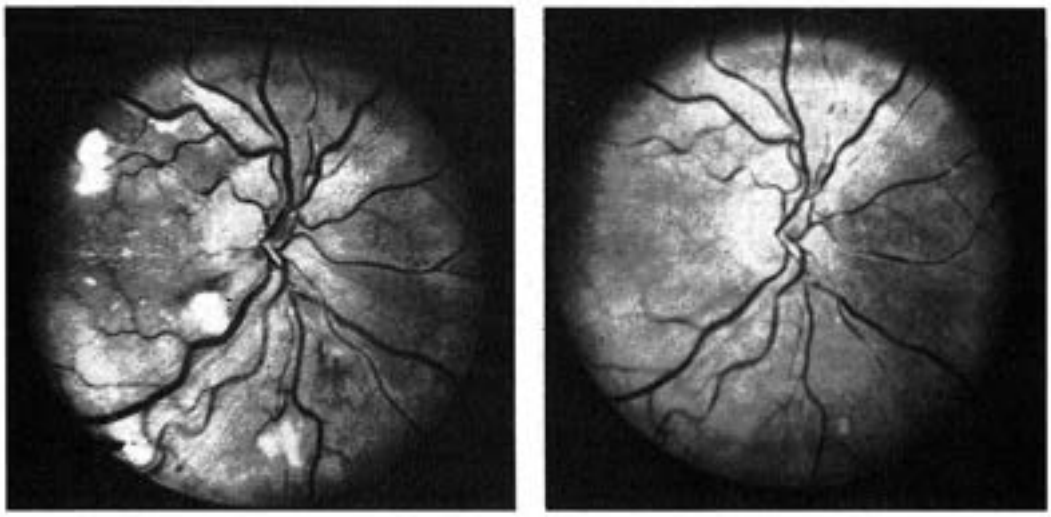
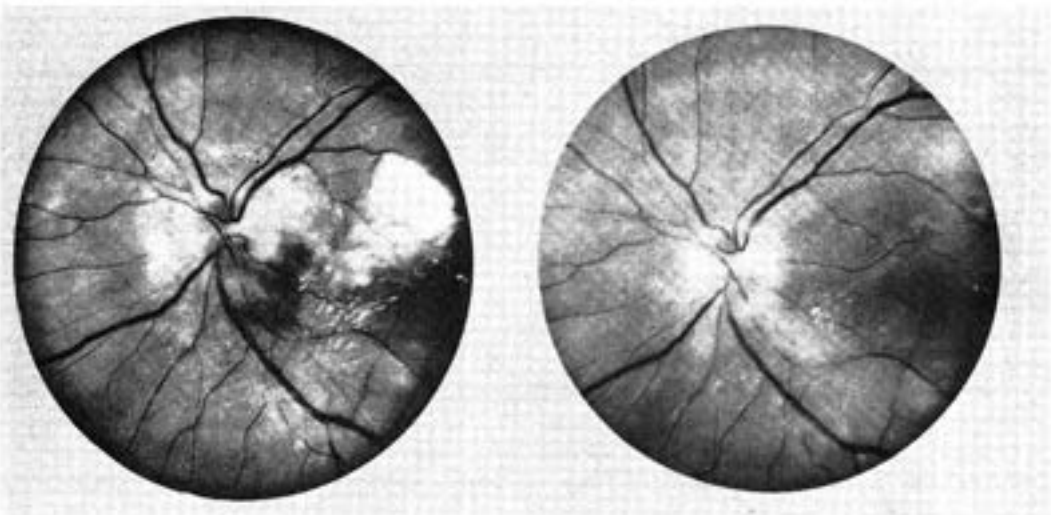


4-19-46 Right 3-26-47

FIG. 26. D. L., a male, fifty-four years of age, had hypertensive vascular disease of at least six months' duration. His previous treatment consisted of low-fat, low-protein diet and sedatives. April 19, 1946 to May 6, 1946: blood pressure average was 221/144; EKG T_1 inverted; total PSP excretion in two hours: 35 per cent. Rice diet was started April 26, 1946; it was strictly followed (5–13 mg. Cl per 100 cc. of urine). March 25 to March 26, 1947: Blood pressure, average, was 177/112; EKG T_1 was upright. September 22 to September 24, 1947: blood pressure, average, was 149/106; EKG T_1 upright._____There was a disappearance of papilledema and exudates before lowest blood pressure level was reached.



2-21-47 Left 9-23-47

FIG. 27. W. A., a male, thirty-two years of age, had hypertensive vascular disease of eighteen years' duration. Sympathectomy was performed in the Mayo Clinic in 1945. Since July, 1946, there had been progressive impairment of vision in the left eye. February 19 to February 21, 1947: blood pressure average was 255/158; total PSP excretion in two hours: 40 per cent. Rice diet was started February 21, 1947; it was moderately well followed (12–51 mg. Cl per 100 cc. of urine). September 22 to September 26, 1947 blood pressure, average 230/138._____There was a disappearance of papilledema, almost complete disappearance of hemorrhages and exudates in spite of persistence of high blood pressure.

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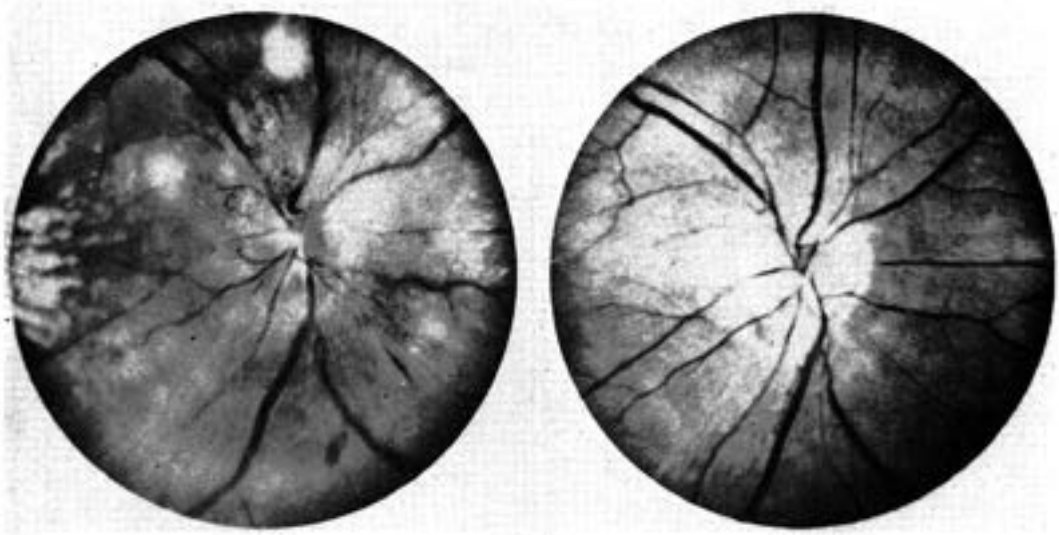
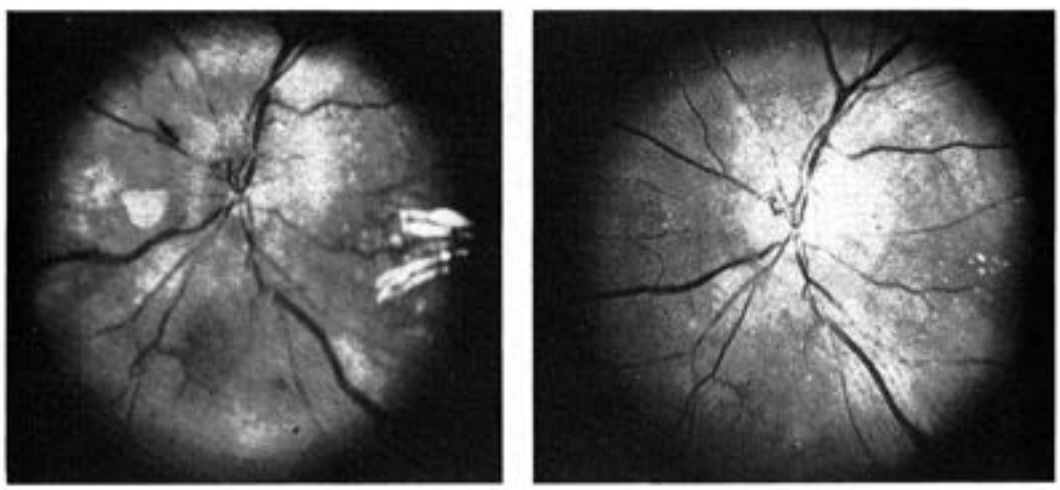


8-4-44 Right 8-11-45



8-4-44 Left 8-11-45

FIG. 28. L. W., a female, forty-five years of age, had hypertensive vascular disease of at least four months' duration. July 16 to August 5, 1944: blood pressure, average, 225/153; total PSP excretion in two hours, 59 per cent. Rice diet was started July 23, 1944 and strictly followed (4–24 mg. Cl per 100 cc. of urine). August 8 to August 13, 1945: blood pressure, average, 215/138_____There was a disappearance of papilledema, hemorrhages and exudates in spite of persistence of high blood pressure.

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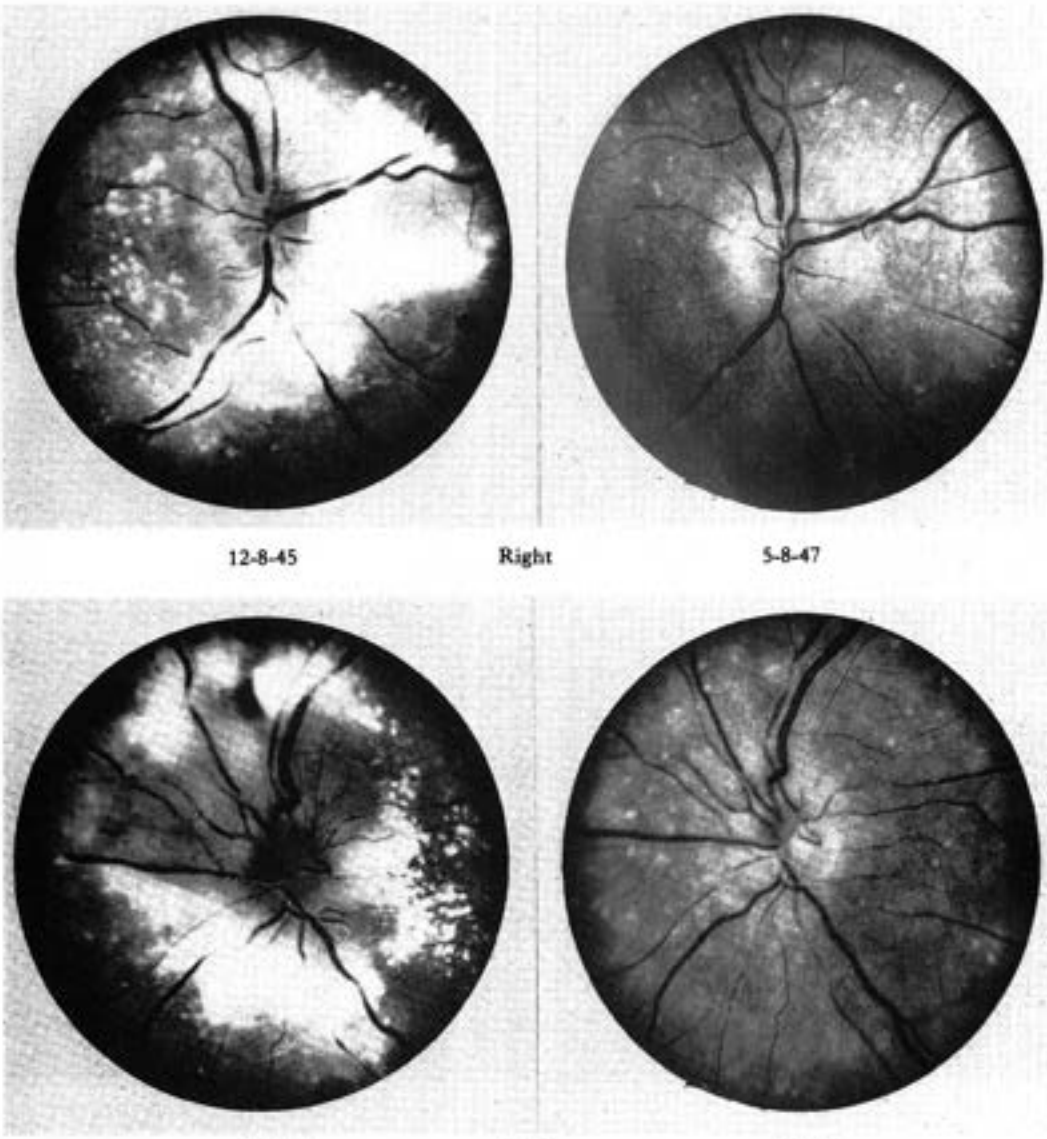

12-8-45 Right 5-8-47

12-8-45 Left 5-8-47

FIG. 29. A. McA., a male, thirty-eight years of age, had hypertensive vascular disease of at least one years' duration. He was previously treated with sedatives and low-salt diet. December 8 to 20, 1945: blood pressure, average, 216/132; EKG T_1 inverted; total PSP excretion in two hours, 58 per cent. Rice diet was started, December 13, 1945 but was not strictly followed (28–55 mg. Cl per 100 cc. of urine). May 5 to 8, 1947: blood pressure, average, 208/123; EKG T_1 upright.——Papilledema, hemorrhages, exudates disappeared in spite of persistence of high blood pressure.

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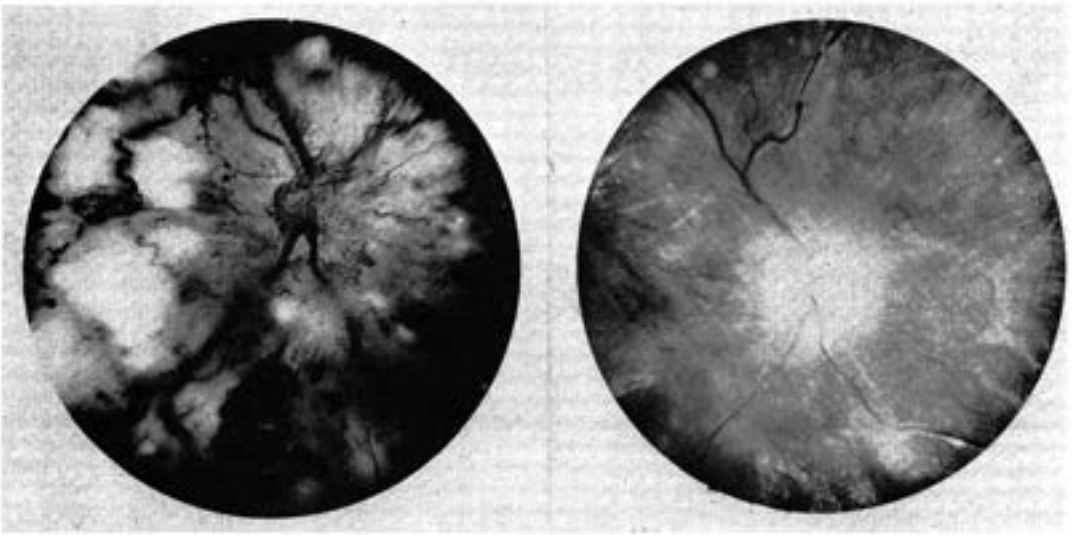
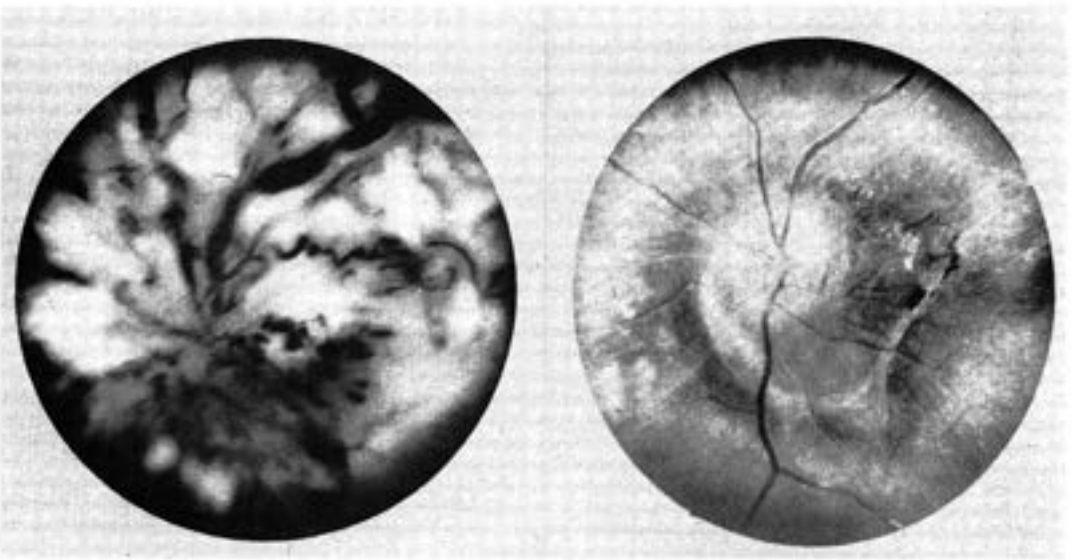


1-8-46 Right 8-17-46



12-18-45 Left 10-3-46

FIG. 30. R. L., a male, twenty-three years of age, had hypertensive vascular disease of three years' duration. Previous treatment consisted of a "modified rice diet." December 18 to December 24, 1945: blood pressure, average, 222/148; EKG T_1 inverted; total PSP excretion in two hours, 2.5 per cent; NPN 79 mg. per 100 cc. blood; cholesterol 340 mg. per 100 cc. serum. Rice diet was started December 18, 1945 and strictly followed for three months (8–21 mg. Cl per 100 cc. of urine). March 11 to 22, 1946: blood pressure, average 134/94; EKG T_1 upright. After March, diet was poorly followed (192–255 mg. Cl per 100 cc. of urine). August 15 to 21, 1946 and October 2 to 5, 1946: blood pressure, average, 194/133; EKG T_1 upright; NPN 60 mg. per 100 cc. blood; cholesterol 173 mg. per 100 cc. serum._____There was a disappearance of papilledema, hemorrhages, exudates and no recurrence of retinopathy although diet was broken and hypertension recurred.

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Pseudotumor Cerebri Treated by Rice/Reduction Diet

Pseudotumor Cerebri Treated

Barbara Newborg, MD, Durham, NC

Pseudotumor cerebri has been described in association with a variety of conditions. One of the more common associations has been with obesity. Despite the usual benignity of this condition, many patients with this disorder have been subjected to various surgical procedures. Surgery was not without complications. This report of nine patients treated with a rice/reduction diet demonstrates that the condition can be reversed by salt restriction and weight reduction with diet alone. Complete reversal of the papilledema and improvement in accompanying metabolic and vascular abnormalities is shown.

Pseudotumor cerebri (benign intracranial hypertension) is a syndrome of increased intracranial pressure in the absence of a space-occupying lesion or focal neurologic signs. Although the condition was first described in 1897 by Heinrich Quincke,

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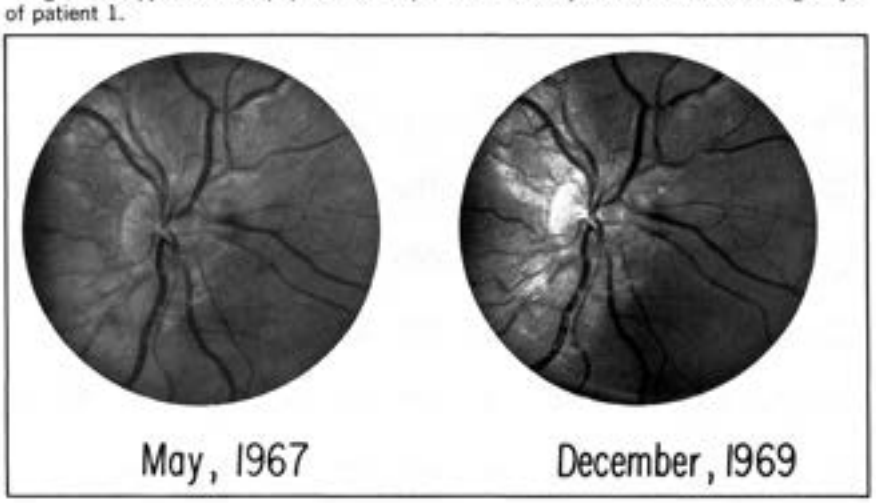
Patient, Age (yrs), Sex	Height, cm	Phenosulfonphthalein % Total Excretion in 2 hr	Weeks of Treatment
1, 21, F	167.6 (5 ft 6 in)	68	135 (interrupted)
2, 47, F	167.6 (5 ft 6 in)	75	10
3, 18, F	167.0 (5 ft 5¾ in)	45	20
4, 17, M	174.0 (5 ft 8½ in)	57	60 (interrupted)
5, 24, F	167.0 (5 ft 5¾ in)	47	26
6, 28, M	172.7 (5 ft 8 in)	62	48 (interrupted)
7, 22, F	156.2 (5 ft 1½ in)	83	22
8, 30, F	167.0 (5 ft 5¾ in)	80	13
9, 44, F	163.8 (5 ft 4½ in)	48	49
Mean	167.0 (5 ft 5¾ in)	63	

* Expressed as sodium chloride per 100 ml of urine.

Fig 1.—Disappearance of papilledema in patient treated by rice/reduction diet. Right eye of patient 1.

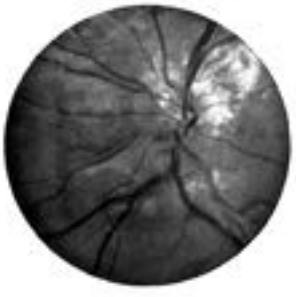


by Rice/Reduction Diet

Changes of Patients on Rice/Reduction Diet

Chloride Excretion in Urine*		Weight, kg (lb)		Blood Pressure, mm Hg		Heart Rate		Heart/Chest Ratio (%)		Longitudinal Diameter of Right Lung, cm		Blood Glucose, mg/100 ml				Serum Cholesterol, mg/100 ml		Serum Triglycerides, mg/100 ml		Serum Uric Acid, mg/100 ml	
												Fasting		2 hours after 100 gm glucose							
Highest Before	Lowest After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
1,000+	1	107 (235)	77 (170)	160/80	120/80	94	83	45	45	20.8	21.5	90	85	114	...	139	149	...	...	5.0	4.1
790	2	75 (165)	64 (142)	124/80	94/62	80		40	40	21.1	22.3	98	86	168	130	222	198	...	...	5.8	4.5
420	1	95 (210)	66 (145)	110/60	94/64	100	70	38	35	18.3	20.7	95	97	107	...	142	...	...	...	5.2	5.0
560	18	158 (347)	137 (302)	145/90	145/70	107	90	36	38	20.2	20.1	90	101	105	...	187	161	182	201	11.6	11.7
566	4	104 (228.5)	65 (143)	115/73	101/68	74	80	44	37	16.0	20.0	95	95	96	...	225	142	136	84	5.3	5.7
400	5	147 (323)	91 (201)	155/101	119/61	112	48	43	43	15.9	18.6	95	105	95	...	277	229	439	172	5.7	8.6
900	60	94 (206)	72 (160)	140/70	118/75	83	55	46	45	16.8	18.4	100	85	104	88	159	199	90	132	5.1	3.6
580	19	128 (281)	100 (221)	130/60	115/80	79	68	50	45	18.3	19.3	105	110	128	84	148	160	83	72	8.1	7.5
520	10	158 (348)	106 (235)	152/97	120/85	86	57	53	47	19.3	19.2	99	100	118	...	170	226	105	85	10.0	7.4
637	13	119 (261)	(85) (187)	137/79	114/72	91	69	44	42	18.5	20.1	96	96	115	101	185	183	172	124	6.9	6.5

Fig 2.—Left eye of patient 1.



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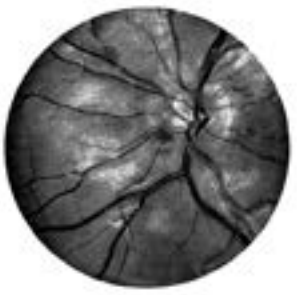

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Fig 3.—Disappearance of papilledema in patient treated by rice/reduction diet. Left eye of patient 2.

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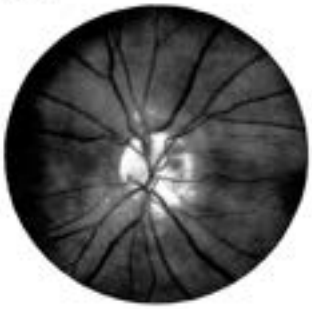

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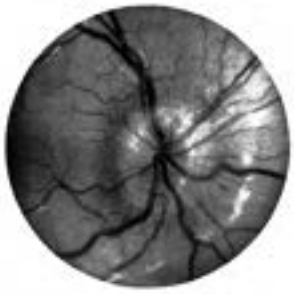

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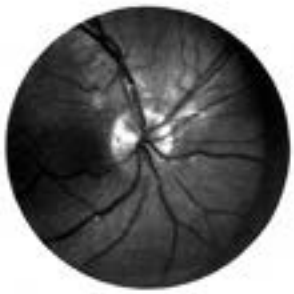
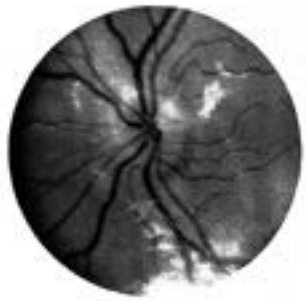


February, 1969

Fig 4.—Disappearance of papilledema and hemorrhage in patient with obesity treated by rice/reduction diet. Right eye of patient 3.



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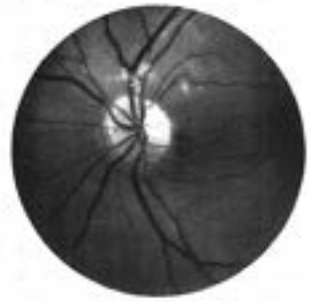
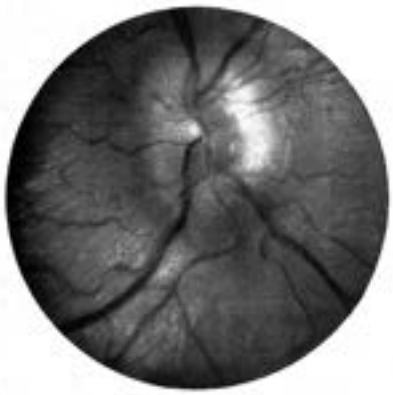


February, 1969

Fig 5.—Left eye of patient 3.



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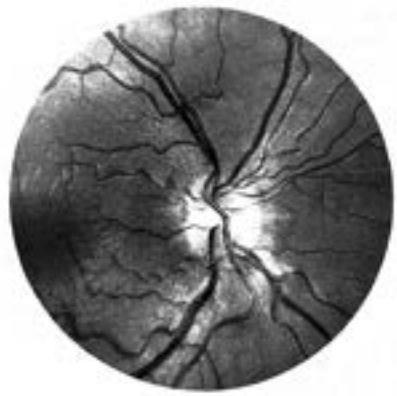
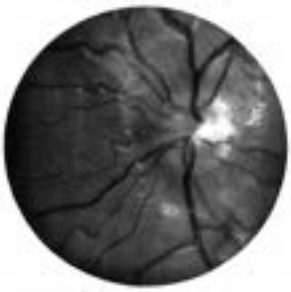


July, 1971

Fig 6.—Disappearance of papilledema in patient treated by rice/reduction diet. Right eye of patient 4.



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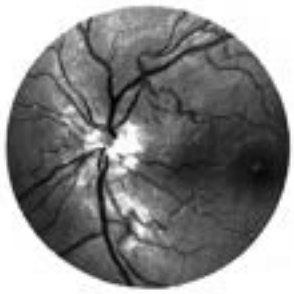
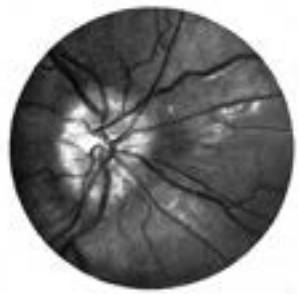


July, 1971

Fig 7.—Left eye of patient 4.



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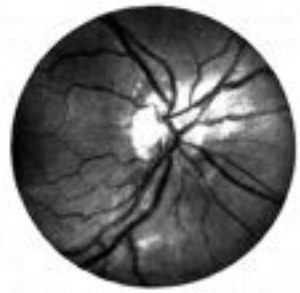
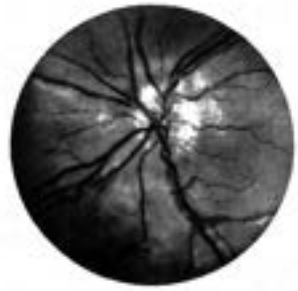


December, 1970

Fig 8.—Disappearance of papilledema in patient treated by rice/reduction diet. Right eye of patient 5.

Fig 9.—Left eye of patient 5.

June, 1970



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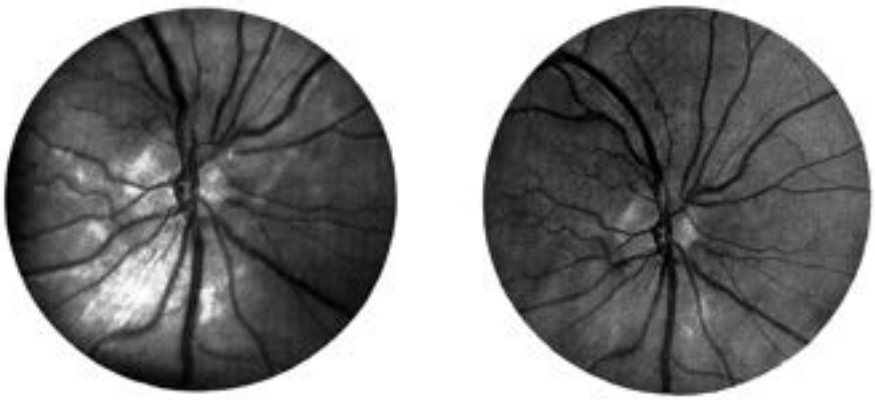
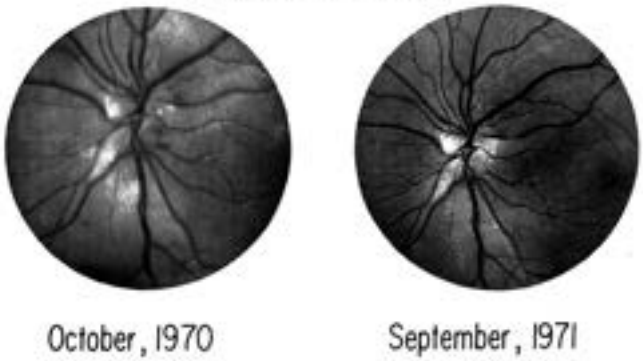


Fig 10.—Disappearance of papilledema in patient treated by rice/reduction diet. Right eye of patient 6.

Fig 11.—Left eye of patient 6.



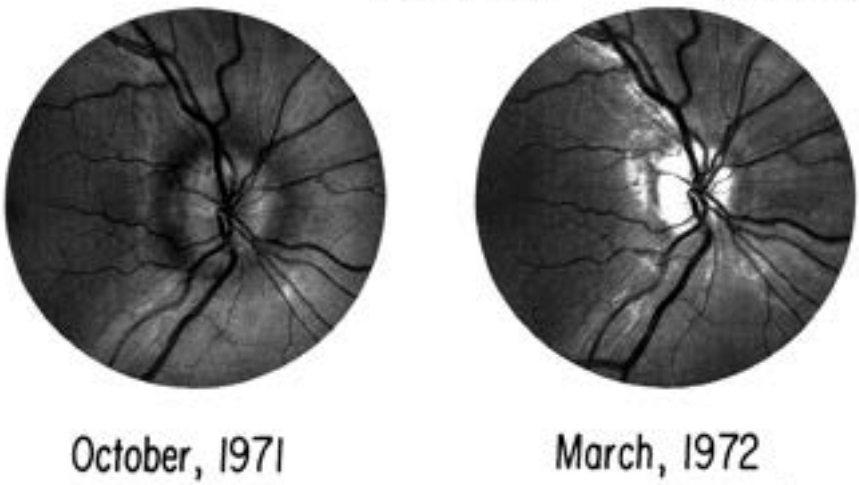
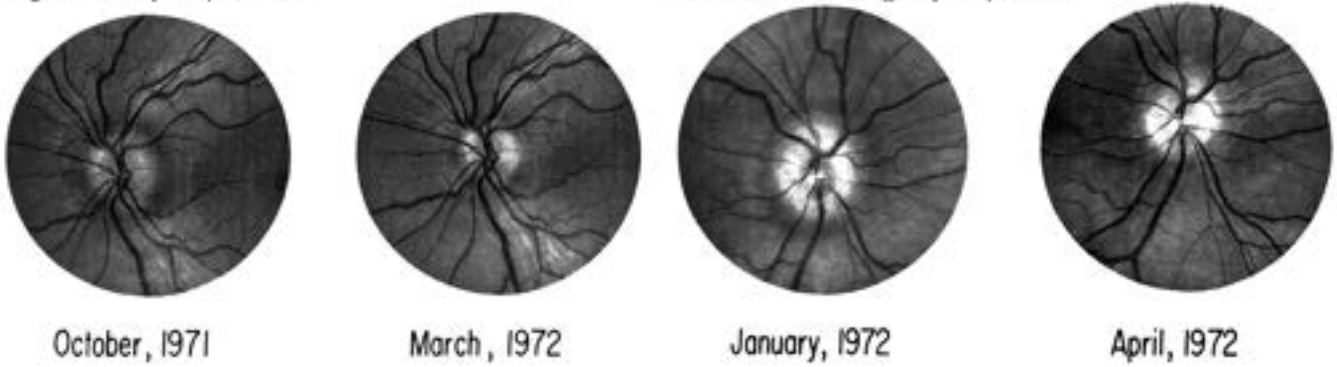
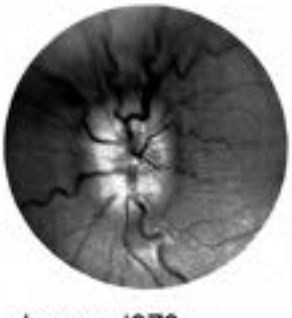


Fig 12.—Disappearance of papilledema in patient treated by rice/reduction diet. Right eye of patient 7.

Fig 13.—Left eye of patient 7.

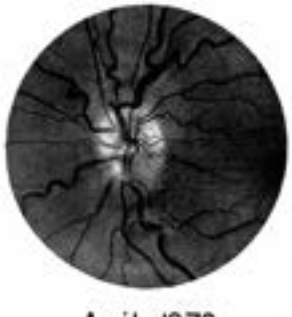
Fig 14.—Disappearance of papilledema in patient treated by rice/reduction diet. Right eye of patient 8.





January, 1972

Fig 15.—Left eye of patient 8.



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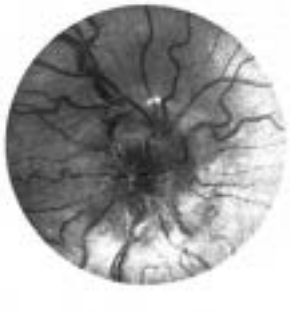

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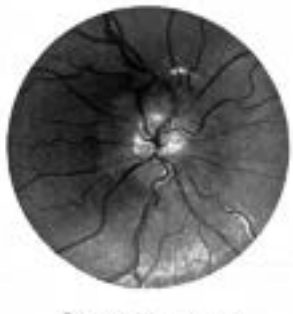
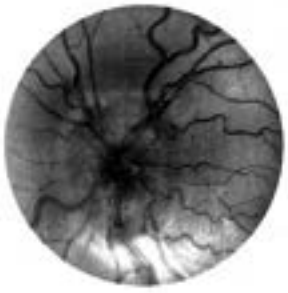


December, 1972

Fig 16.—Disappearance of papilledema in patient treated by rice/reduction diet. Right eye of patient 9.

Fig 17.—Left eye of patient 9.



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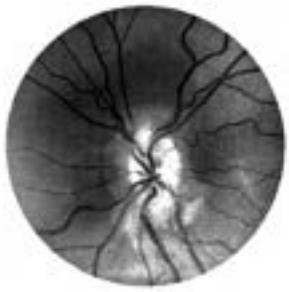

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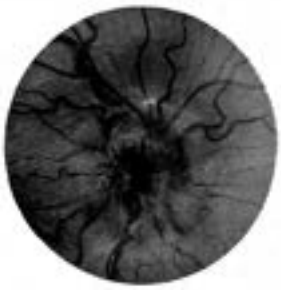

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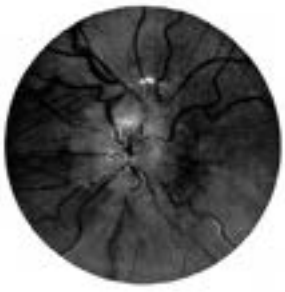
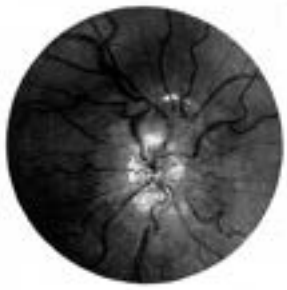


March, 1972



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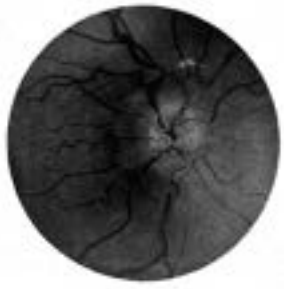
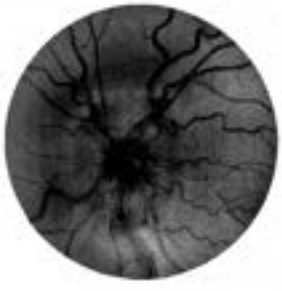


August, 1972

Fig 18.—Gradual disappearance of papilledema in patient treated by rice/reduction diet. Right eye of patient 9.

Fig 19.—Left eye of patient 9.



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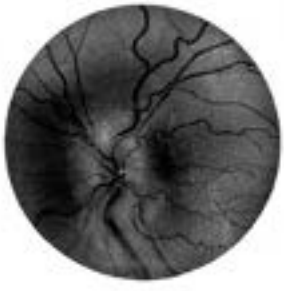

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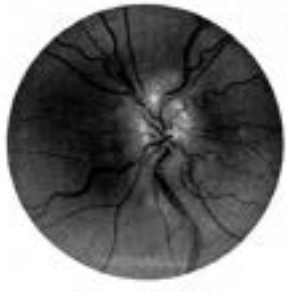

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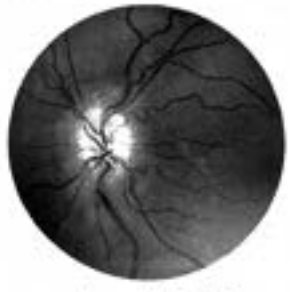

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the pathophysiology is still not understood completely.

Most patients with the condition are women, many of whom have been obese. Although Greer[1] has advocated weight reduction for the long-term management of such patients, 15 of his 20 patients had surgical procedures (either subtemporal decompression [12] or open craniotomy [3]). In addition, serial lumbar punctures were used by Greer and have been advocated by others. Diuretics and steroids have also been recommended despite the association of the syndrome with steroid administration in some patients. A series of nine patients, all quite obese, who had resolution of papilledema and clinical symptoms by treatment with diet alone is reported here.

Patients and Methods

Seven female and two male patients, aged 17 to 47 years (mean age, 28), with pseudotumor cerebri were studied. All were obese. All had papilledema. None had evidence of focal neurologic signs. None had clinical evidence of adrenal, ovarian, pituitary, or thyroid disease.

All patients were treated with a low-calorie adaptation of the rice diet originated by Kempner.[2,3] The diet consisted of 400 to 1,000 calories daily, provided by fruits, rice, vegetables, and in some cases 1 to 2 oz of meat, all of which were prepared without salt. Fluids were limited to 750 to 1,250 ml/day and sodium to less than 100 mg/day.

Figures 1 to 19 show eyeground photographs of these nine patients before and after treatment. Only two patients had symptoms. One had dizziness and menstrual irregularities, while the other patient, a physician, had shortness of breath, somnolence and visual disturbances that were so severe that she had to give up her medical practice and was even unable to drive a car. (After treatment she has been in perfect health, has resumed her practice, and drives her car.) None of the other seven patients had symptoms, nor did they know of any eye trouble. One patient also had a linear hemorrhage (Fig 4); this also disappeared with the dietary treatment. In addition to these nine patients, there were a number of patients with pseudotumor for whom no follow-up photographs are available and a much greater number in whom the discs were hazy or not quite sharply outlined or in whom marked venous engorgement was present initially and disappeared after treatment.

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1. Greer M: Benign intracranial hypertension. *Neurology* 15:382-388, 1965.
2. Kempner W: Treatment of kidney disease and hypertensive vascular disease with rice diet, I. *NC Med J* 5:125-133, 1944.
3. Kempner W, Newborg B: Analysis of 177 cases of hypertensive vascular disease with papilledema. *Am J Med* 19:33-47, 1955.

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Treatment of Massive Obesity with
Rice/Reduction Diet Program

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Walter Kempner, MD; Barbara C. Newborg, MD; Ruth L. Peschel, MD; Jay S. Skyler, MD

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Treatment of Massive Obesity With Rice/Reduction Diet Program

An Analysis of 106 Patients With at Least a 45-kg Weight Loss

Walter Kempner, MD; Barbara C. Newborg, MD; Ruth L. Peschel, MD; Jay S. Skyler, MD

• One hundred six massively obese patients, who each lost at least 45 kg, were treated as outpatients with the rice/reduction diet, exercise, and motivational enhancement under daily supervision. Average weight loss was 63.9 kg. Forty-three patients achieved normal weight. Men lost weight at a greater rate than women. Concomitant with weight reduction, there were significant decrements in blood pressure; fasting and two-hour postprandial blood glucose, serum triglyceride, and serum uric acid levels, and heart-chest ratio as evidenced on chest x-ray film. Electrocardiographic and retinal venous changes improved. Serum cholesterol level did not change significantly. This study demonstrates that massively obese persons can achieve marked weight reduction, even normalization of weight, without hospitalization, surgery, or pharmacologic intervention. Accompanying cardiovascular risk factors show great decrements concomitant with weight loss.

(*Arch Intern Med* 135:1575-1584, 1975)

Obesity is one of the leading public health problems in the United States. This is attested to by (1) the high prevalence of obesity; (2) an associated increased mortality; and (3) the high incidence of associated clinical abnormalities (elevated blood pressure, carbohydrate intolerance, lipid abnormalities, hyperuricemia and gout, cardiovascular disease, gallbladder disease, and others).[1-10] The importance of obesity is increased by the great difficulty physicians have had in treating affected patients. Since morbidity and mortality appear to increase with the degree of obesity, and since treatment also becomes more difficult, massive obesity is an even more complex problem for the physician and the patient. The usual approaches of diet and pharmacologic manipulation (eg, appetite suppression) have met with little success in the treatment of massive obesity. Therefore, many groups have resorted to seemingly extreme measures in treating this problem. These approaches have included intestinal bypass surgery, surgical extirpation of the panniculus, and prolonged fasts.[11,12]

In the 1940s, Kempner developed the rice diet for the treatment of renal insufficiency and severe hypertensive cardiovascular disease.[13-15] Later, he adapted this diet for the treatment of diabetes mellitus, especially with vascular complications.[16] In more recent years, Kempner adapted his rice diet for the treatment of obesity, as a lower calorie, "rice/reduction" diet. This report describes his application of the rice/reduction diet program to the treatment of patients with massive obesity. It demonstrates that massive obesity can be corrected, and without the necessity of surgical intervention, prolonged fasting, hospitalization, or pharmacological manipulation. It further shows that some of the associated abnormalities—elevation of blood pressure, carbohydrate intolerance, hypertriglyceridemia, hyperuricemia, increased heart size, electrocardiographic changes, and retinal vascular changes—show improvement concomitant with the weight loss achieved with the rice/reduction diet program.

METHODS

Treatment Program

Diet.—The initial diet prescribed for most patients ("unmodified rice/reduction diet") is a low-calorie (400 to 800 kilocalories [kcal]/day, average, estimated) adaptation of the rice diet originally described by Kempner for treatment of hypertensive cardiovascular and renal disease, and subsequently used successfully for the treatment of diabetes mellitus.[13-16]

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From the Department of Medicine, Duke University Medical Center, Durham, NC.

Part of this work was read before the First International Congress on Obesity, London, Oct 10, 1974.

Reprint requests to Department of Medicine, Duke University Medical Center, Durham, NC 27710 (Dr Kempner).

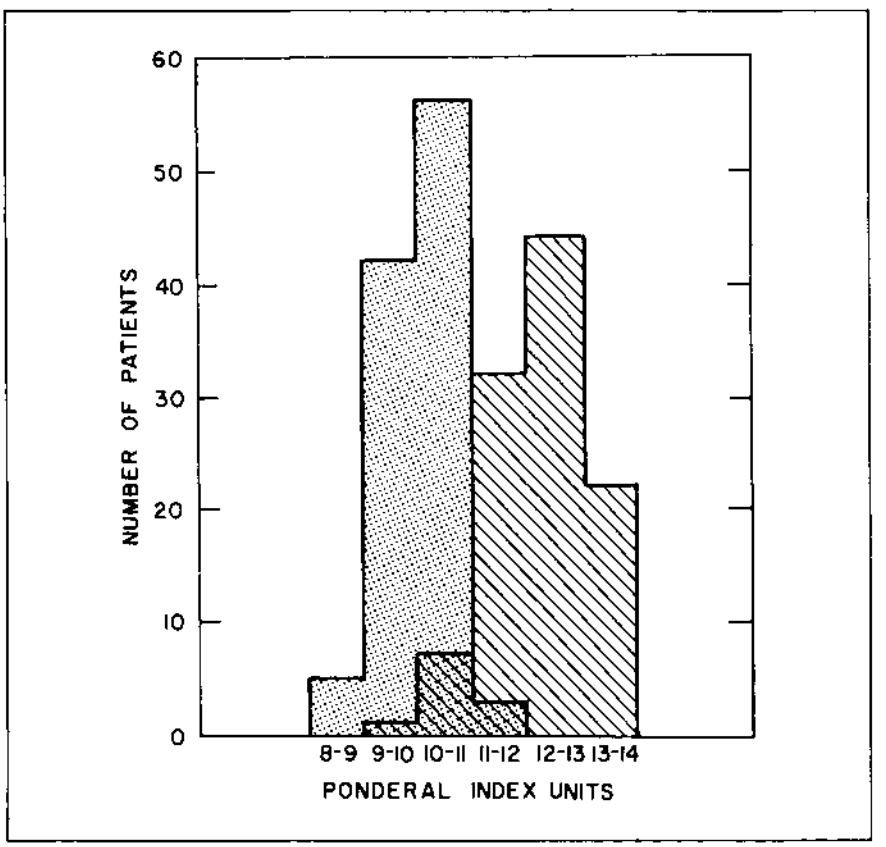
Table 1.—Weights and Indexes of Weight Before and After Weight Loss

Clinical Data	Before Loss, Mean ± SD (Range)	After Loss, Mean ± SD (Range)
Weight, kg	143.9 ± 29.3 (91.4-231.6)	80.0 ± 21.7 (44.4-145.5)
Relative weight	2.28 ± 0.39 (1.64-3.85)	1.26 ± 0.29 (0.87-2.60)
Ponderal index	10.03 ± 0.57 (8.43-11.17)	12.26 ± 0.83 (9.38-13.77)
Body mass index	6.87 ± 1.17 (5.10-11.30)	3.81 ± 0.87 (2.50-7.60)
Weight-height ratio	4.66 ± 0.82 (3.24-7.58)	2.58 ± 0.62 (1.58-4.76)

Table 2.—Weights and Relative Weights by Sex

Weight Data	Men, Mean ± SD	Women, Mean ± SD
Initial weight, kg	160.8 ± 26.2	130.5 ± 24.3
Final weight, kg	91.2 ± 19.2	71.1 ± 19.5
Change in weight, kg	−69.6 ± 20.8	−59.3 ± 11.8
Initial relative weight	2.22 ± 0.36	2.32 ± 0.41
Final relative weight	1.25 ± 0.23	1.26 ± 0.33

Fig 1.—Distribution of ponderal index before (dotted area) and after (hatched area) weight loss. Ponderal index was calculated as height (inches) divided by cube root of weight (pounds). Ranges of ponderal index units are used in this histogram.



In the unmodified initial diet, 90% to 95% of the caloric intake is carbohydrate, taken as rice and fruit. As in the original rice diet, salt intake is exceedingly low (less than 60 mg of sodium per day), and fluid intake is thus markedly reduced to prevent water intoxication. Thus, the initial diet is low-calorie, low-salt, low-protein, low-fat, and essentially free of cholesterol.

Later, usually at least one month after the initial phase of treatment, some additions, such as vegetables, are made to the diet, and still later, others, such as lean poultry or meats, are added. Always, the prescribed diet is low in calories (less than 1,000 kcal/day) and very low in sodium (less than 100 mg/day). The diet is supplemented daily with multivitamins to prevent any possible nutritional deficiencies.

Exercise.—A daily minimum exercise program is prescribed for the patients, and they are encouraged to exercise to the point of maximum tolerance in terms of subjective comfort. Exercise prescription is individualized and varies with the age and sex of the patient, the history of any known disabilities, and the results of resting or ten-flight exercise electrocardiograms, or both.

Environment.—While on the treatment program, patients obtain accommodations in a motel, rooming house, or apartment in the Durham area. Except for initial, final, and special evaluations at Duke University Private Diagnostic Clinic, patients report daily to a satellite facility (known as a "rice house") seven mornings a week. Here, they undergo daily checks of weight and blood pressure and have daily discussions with physicians or "patient counselors," or both. The satellite facility serves meals in accordance with the patients' diet prescriptions. Although patients are encouraged to eat most of their meals at the satellite facility, many choose not to. Most restaurants in the Durham area have some form of special menu. Although these menus do not necessarily adhere exactly to the prescribed regimen, at least they include items that have limited salt, fat, and caloric values.

Motivational Enhancement.—Adherence to the regimen is monitored not only by daily weight checks, but also by measurement of 24-hour urinary chloride or sodium excretion, or both, twice weekly. Since it is possible to predict the urinary chloride or sodium excretion, or both, of patients following the rice diet exactly, nonadherence to the diet can be detected by the finding of high values or by the failure of the patient to provide a specimen. Not only can physicians and counselors encourage the patient to adhere better, but also peer group pressure, since the results are

Fig 2 (left).—Left, Patient 3 (54-year-old man) who at start of regimen weighed 141.4 kg. Blood pressure was 198/123 mm Hg while he was receiving 50 mg hydrochlorothiazide and 250 mg methyldopa twice a day. Blood glucose determinations were 125 mg/100 ml (fasting) and 265 mg/100 ml (two-hour postprandial), with glycosuria (4+) at two hours. Values were as follows: serum uric acid, 8.4 mg/100 ml; serum cholesterol, 282 mg/100 ml; serum triglycerides, 156 mg/100 ml. Electrocardiogram showed first-degree heart block. Right, After 144 days on regimen, patient weighed 81.4 kg. Blood pressure was 130/86 mm Hg without medication; fasting and two-hour postprandial blood glucose values were 95 mg/100 ml and 130 mg/100 ml, respectively, without glycosuria. Values were as follows: serum uric acid, 6.8 mg/100 ml; serum cholesterol, 277 mg/100 ml; serum triglycerides, 100 mg/100 ml; ECG was within normal limits. (Also see Fig 8.)

posted with high values circled in red, can aid the patient to maintain the diet. Peer group pressure is apparent as patients compare accumulated weight loss.

Additional motivational enhancement is applied by continual emphasis on the health hazards of obesity. Each patient is given a defined goal (an "ideal" weight), and although all weight losses are recognized as indicating some improvement, patients are not considered "successful" until they achieve a "normal" weight.

Patients

The 106 patients analyzed in this study were selected from the total population of obese patients undergoing treatment on Dr. Kempner's service. Criterion of selection was loss of at least 45 kg (100 lb); the 100 patients who most recently qualified at the time this report was initiated were studied. Six additional patients attained this weight loss while the first 100 charts were being reviewed and were also included in the analysis. The 45-kg minimal loss criterion was chosen to assure both that the patients were massively obese ini-

Fig 3 (left).—Left, Patient 26 (25-year-old man) who at start of regimen weighed 212.3 kg. Blood pressure was 140/96 mm Hg; two-hour postprandial blood glucose level, 114 mg/100 ml; serum cholesterol, 240 mg/100 ml; serum triglycerides, 187 mg/100 ml. Right, After 379 days on regimen, patient weighed 85.9 kg. Values were as follows: blood pressure, 120/80 mm Hg; two-hour blood glucose, 60 mg/100 ml; serum cholesterol, 195 mg/100 ml; serum triglycerides, 85 mg/100 ml.

tially and that they had lost a marked amount of weight.

There were 47 men and 59 women in this series, with ages at entry into the program ranging from 16.6 to 65.1 years (mean age, 34.2 ± 12.0 [SD] years).

"Relative weight" was calculated by dividing the patient's weight by the "ideal" weight, which was derived from the mean value of the desirable weight range for individual height and sex for a medium body frame (the latter information was taken from Metropolitan Life Insurance Company Tables [1959]).[17] Ponderal index was calculated as height (inches) divided by the cube root of weight (pounds).[18] Body mass index was calculated as 100 times weight (pounds) divided by the square of the height (inches).[19] Ratios of weight (pounds) to height (inches) were also calculated.[18] Pounds and inches were used in these calculations to facilitate comparison with published data.[18-19]

Analytical Methods

All blood samples were obtained with the patient in the fasting state, with the exception of those obtained for the two-hour postprandial blood glucose test (they were obtained after 100 gm of glucose was administered orally). Samples were analyzed by standard clinical procedures for blood glucose,[21] serum triglycerides,[22,23] serum cholesterol,[24] serum uric acid,[25] and lipid phosphorus.[26,27]

Heart-chest ratios were derived from measurements of the maximum widths of heart and chest on standard roentgenograms of the chest.

Retinal changes were assessed by both funduscopy and fundus photography.

Statistical Methods

The two-tailed paired Student *t* test for comparison of changes in individuals and the two-tailed unpaired test for comparison between groups were employed. Correlation coefficients were calculated by the product-moment correlation method. All analyses were performed in the facilities of the Computer Center Branch, Division of Computer Research and Technology, National Institutes of Health, Bethesda, Md.

RESULTS

Weight Loss

The mean weight lost per patient was 63.9 ± 17.2 (SD) kg, with a maximum loss of 137.0 kg. Initial and final means and ranges of weight and weight indexes are shown in Tables 1 and 2. All patients initially had a relative weight of at least 1.64, with

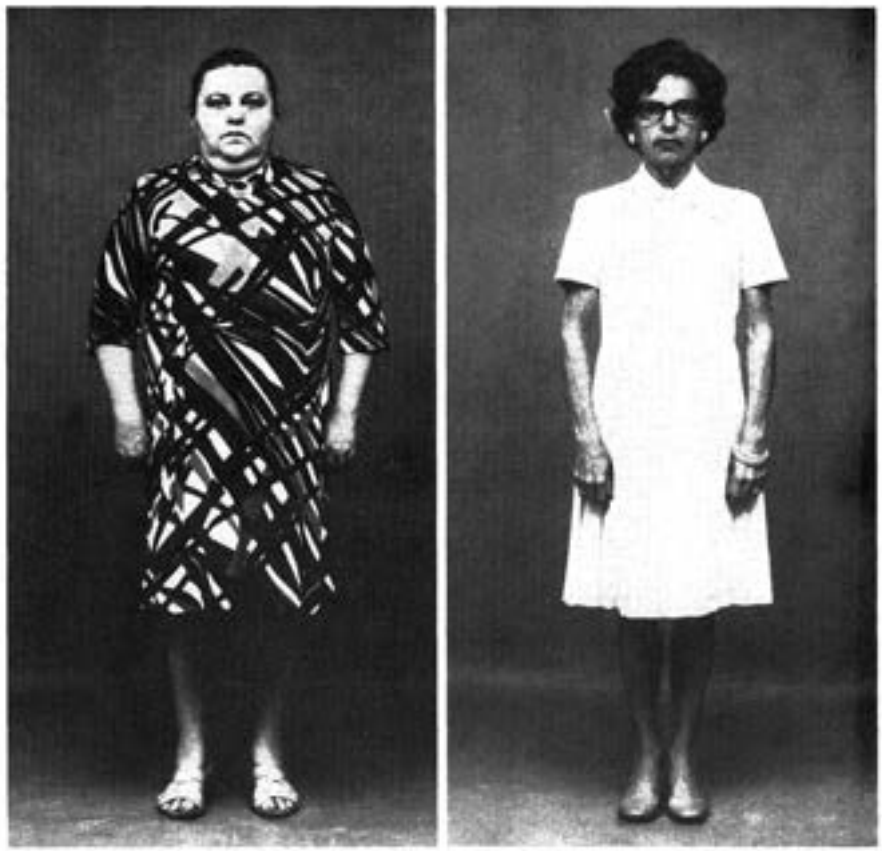


Fig 4.—Left, Patient 64 (48-year-old woman) who at start of regimen weighed 96.6 kg. Blood pressure was 140/90 mm Hg while patient was receiving antihypertensive medication; fasting and before lunch and supper blood glucose levels were 315 mg/100 ml, 350 mg/100 ml, and 408 mg/100 ml, respectively, while patient was receiving 90 units isophane insulin suspension (NPH Insulin) daily. Values were as follows: serum cholesterol, 223 mg/100 ml; serum triglycerides, 516 mg/100 ml; heart-chest ratio, 0.503, as shown on x-ray film. Right, After 234 days on regimen, patient weighed 44.5 kg. Administration of antihypertensive medication and insulin had been discontinued. Fasting and preprandial blood glucose levels had fallen to 100 mg/100 ml, 75 mg/100 ml, and 80 mg/100 ml. Blood pressure was 102/62 mm Hg. Serum cholesterol and triglyceride levels ultimately fell to 217 mg/100 ml and 79 mg/100 ml, respectively. Heart-chest ratio improved to 0.410.

79 patients having an initial relative weight of at least 2.00 and three patients having one greater than 3.00. After weight loss, only two patients continued to have a relative weight greater than 2.00. There is little overlap between initial and final values of weight indexes, as is demonstrated for ponderal index in Fig 1. Nevertheless, if one defines obesity as a relative weight in excess of 1.15 (Metropolitan Life standards),[17] then the mean final relative weight of the entire group of patients, 1.26 ± 0.28 (SD), exceeds this criterion. Therefore, for analysis, patients were subdivided into those who achieved a final "relative weight" less than 1.15 (group 1) and those who did not fulfill this requirement (group 2). There were 43 patients (16 men, 27 women) in group 1 and 63 patients (31 men, 32 women) in group 2. The mean final relative weight for group 1 was 1.02 ± 0.08 (range, 0.86 to 1.14), and that for group 2 was 1.42 ± 0.26 (range, 1.15 to 2.59). Since there was no significant difference in magnitude of weight loss of the two groups, the differences apparently reflect the significantly greater ($P < .001$) initial weight of group 2 patients (155.2 ± 26.8 kg) vs group 1 patients (127.4 ± 24.8 kg).

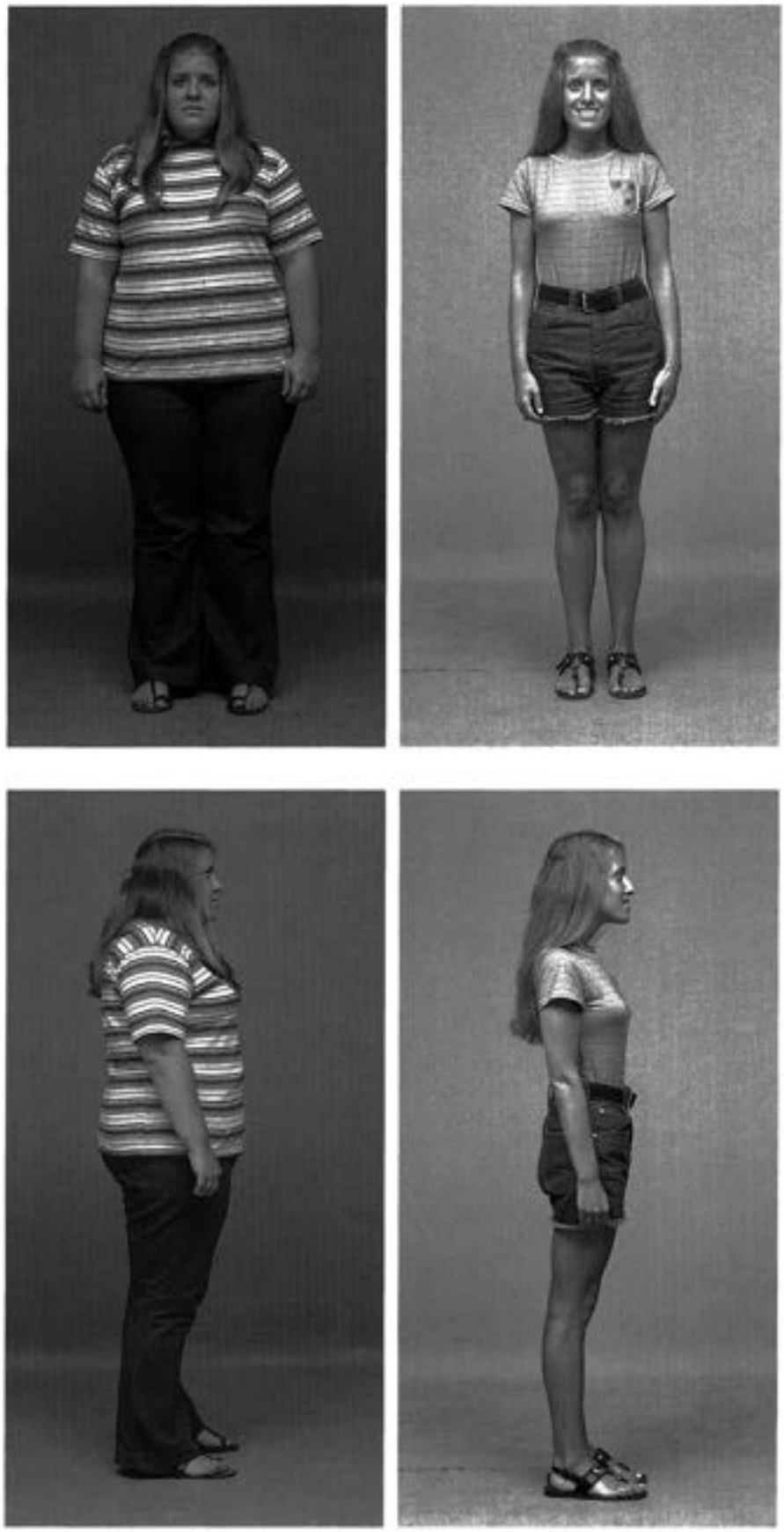


Fig 5 (right).—Left (top and bottom), Patient 2 (19-year-old woman) who at start of regimen weighed 100.2 kg. Serum uric acid level was 8.3 mg/100 ml. Right (top and bottom), After 352 days on regimen, patient weighed 44.4 kg, and serum uric acid level had fallen to 4.9 mg/100 ml. (Also see Fig 7.)

Illustrations of four of the patients in this series, before and after weight loss, are shown in Fig 2 to 5.

Rate of Weight Loss

The mean rate of weight loss was 0.24 ± 0.09 (SD) kg/day, with men having a significantly greater ($P < .001$) rate of weight loss (0.28 ± 0.08 kg/day) than women (0.20 ± 0.08 kg/day). This greater rate of weight loss for men was seen in all age groups (Fig 6), while within each sex, there was no difference in rate of loss between one age group and another. The difference in rate of weight loss does not reflect a difference in relative weight of men and women, since there was no significant difference in either initial or final relative weight between sexes. However, both the initial and final absolute weights of men were higher, as was the magnitude of their weight loss (Table 2), despite the fact that women remained in the program significantly longer ($P < .005$) than did men (334.9 ± 127.6 days vs 261.6 ± 91.9 days). Twenty-six patients were in the program longer than one year.

There was no significant difference in mean rate of weight loss between group 1 and group 2 patients. However, the sex difference in rate of weight loss can be accounted for entirely by the greater ($P < .001$) rate of loss of group 2 men (0.29 ± 0.08 kg/day) vs group 2 women (0.20 ± 0.05 kg/day). This was true despite the fact that group 2 women had a somewhat higher ($P < .02$) initial relative weight than did group 1 men (2.55 ± 0.41 vs 2.31 ± 0.32).

Examples of individual rates of weight loss for two patients are shown in Fig 7.

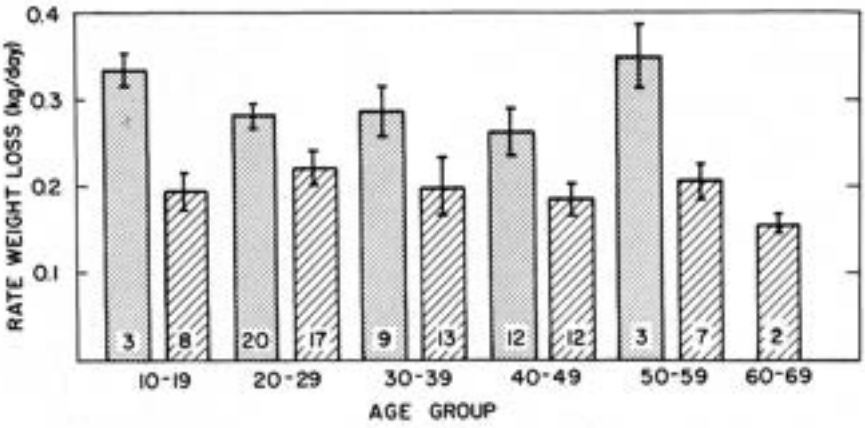


Fig 6.—Rate of weight loss by age group and sex (men, dotted bars; women, hatched bars). Standard error of the mean is also shown. Number in each bar corresponds to number of patients in that age and sex group. For all age groups, rate of weight loss for men is significantly greater than that for women.

Associated Clinical and Chemical Criteria

Table 3 lists the mean initial and final values and mean changes in blood pressure, the blood glucose level, serum triglycerides, serum cholesterol, serum uric acid, and heart size (as indicated by the heart-chest ratio on a roentgenogram of the chest that were noted concomitant with weight loss. Also listed is the incidence of abnormalities in these variables before and after weight loss. As can be seen, there were highly significant ($P < .001$) decrements in both systolic and diastolic blood pressure, both fasting and two-hour postprandial blood glucose levels, and in heart size. There were also significant decreases in serum triglyceride ($P < .05$) and serum uric acid ($P < .02$) values. The serum cholesterol level remained unchanged.

Further analysis of cholesterol changes revealed that in those patients with normal initial cholesterol concentration (81 patients), there was a mean increase in cholesterol of 10.5 mg/100 ml, whereas patients with high initial cholesterol concentration (21 patients) showed a mean decrease in cholesterol of 28.6 mg/100 ml. Patients with an initial serum cholesterol value of less than 220 mg/100 ml (our "desired" level) showed a mean increase of 15.1 mg/100 ml (53 patients), whereas those with an initial value greater than 220 mg/100 ml showed a mean decrease of 11.2 mg/100 ml (49 patients). There was a wide scatter among cholesterol values, with some patients showing marked decrements and others sharp increases. A total of 58 patients showed decreases in serum cholesterol, while in 44 patients cholesterol concentration increased.

Comparing group 1 and group 2 patients, there was no significant difference in magnitude of change of any of these variables (blood pressure, blood glucose, serum triglycerides, serum cholesterol, serum uric acid, and heart-chest ratio). Group 2 patients, however, did have somewhat higher absolute values of initial ($P < .001$) and final systolic blood pressure ($P < .001$), final diastolic blood pressure ($P < .05$), final serum uric acid ($P < .005$), and final heart-chest ratios ($P < .005$). Complete data for all factors in both groups are shown in Table 4.

An example of improvement in heart size and heart-chest ratio is shown in Fig 8.

In addition to the abnormal variables just noted, 45 patients (42%) had some electrocardiographic change on initial examination (usually left axis deviation or voltage criteria of left ventricular hypertrophy).[28] After weight loss, only six patients (6%) continued to have abnormalities. Before weight loss, 14 patients (13%) had papilledema (pseudotumor cerebri) or marked retinal venous fullness. In all of these patients, the retinal changes resolved with the rice/reduction diet, as described by Newborg.[29] Patients 6 and 9 of Newborg's report are included in this series.

Correlation coefficients were calculated between values for blood glucose and blood lipids. These were especially striking for the initial values. Lipid phosphorus, which was measured only initially, showed a highly significant ($P < .001$) correlation with cholesterol ($r = .834$). Other values are shown in Table 5.

COMMENT

The treatment of massive obesity is a perplexing problem for both patient and physician.[30,31] The more conservative methods of caloric restriction and starvation (usually in-hospital treatment) have not met with great success.[32,33] Furthermore, appetite suppressants have not been found to be very useful, probably because of the refractoriness that develops to their pharmacologic effects.[34,35] This has led to a proliferation of more drastic invasive approaches, including jejunocolic and jejunoileal shunting,[36,37] gastroplasty,[38] panniculectomy,[39] stereotaxic hypothalamic stimulation of feeding centers,[40] and wiring of the jaws. All of these surgical procedures have definite associated morbidity and mortality. Furthermore, the results of these procedures at the present cannot be said to be striking.

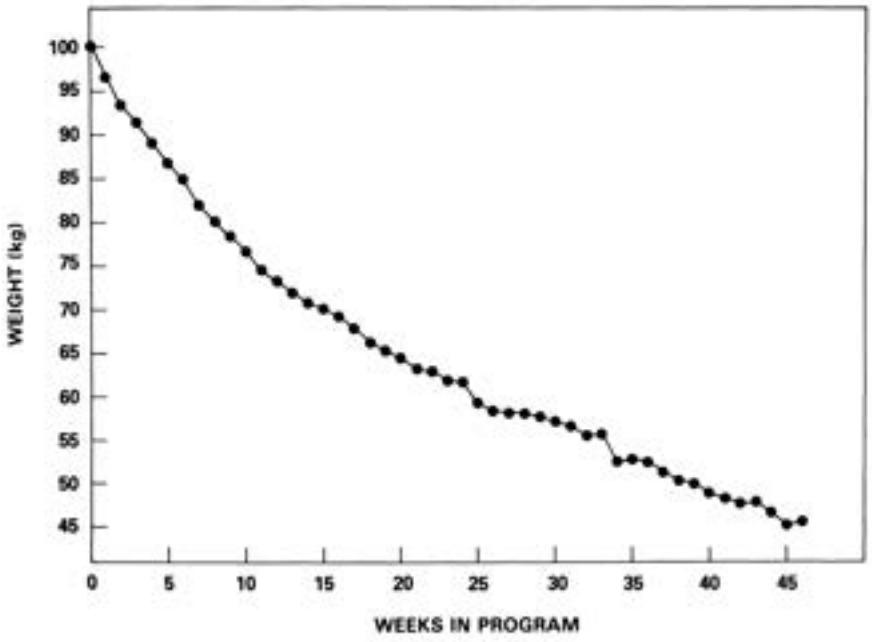
In recent years, there have been a growing number of reports on the use of behavioral modification for the treatment of obesity.[41-43] Although such therapy appears quite useful for the mildly or moderately obese, no reports to date describe extensive experience for the treatment of massive obesity.

This report demonstrates that massive obesity can be corrected without resorting to invasive techniques and without either hospitalization or pharmacological intervention. The approach represents an extension of Kempner's earlier dietary programs for renal insufficiency, hypertensive

cardiovascular disease, and diabetes mellitus.[13-16] It involves a combination of dietary manipulation, exercise, environmental alteration, and motivational enhancement. Each factor appears to be important. The reduction of calories is obviously the cornerstone of any weight reduction program. The rather severe caloric restriction allows for reasonably rapid weight reduction, which is important if the patient is to remain motivated until normal weight is achieved. The sodium restriction appears to be important for four reasons: (1) it aids in correction of associated abnormalities, eg, elevated blood pressure; (2) it prevents accumulation of fluid that may replace adipose tissue and, because of the higher density of water than fat, may mask true reduction in adiposity (a phenomenon manifested by loss of girth without loss of weight)[43]; (3) it provides a means of monitoring patient adherence to the regimen through the measurement of urinary chloride or sodium excretion, or both; and (4) it may reduce the stimulatory effect of salt on food intake.[44] The use of carbohydrate as the caloric source takes advantage of its protein-sparing effects and its inhibition of excessive sodium excretion.[45] Exercise may only slightly increase caloric utilization; however, it is important in improving both muscle tone and cardiovascular-pulmonary capacity and in preventing boredom.

The Durham environment is singularly conducive to weight reduction not only because most of the patients are removed from their home stresses, but also because there are so many massively obese patients there that the local population does not pay special attention to them. The camaraderie of other patients in the same situation leads to increased willingness to participate. The gathering of others with the same problem allows social interaction, which may have been lacking in the home environment.

Maintenance of the patient's motivation to continue on a monotonous dietary program until normal weight is achieved is a difficult but important problem. We recognize that our patients are a self-selected, highly motivated group to begin with. Otherwise, they would not leave their homes for months at a time (and at some expense) to participate in such a program. Despite this and the various motivational enhancement techniques outlined previously (see "Methods"), many patients tire of the regimen and have difficulty maintaining interest. We do not consider them successful unless normal weight is achieved. Thus, it is possible to lose even several hundred pounds and still



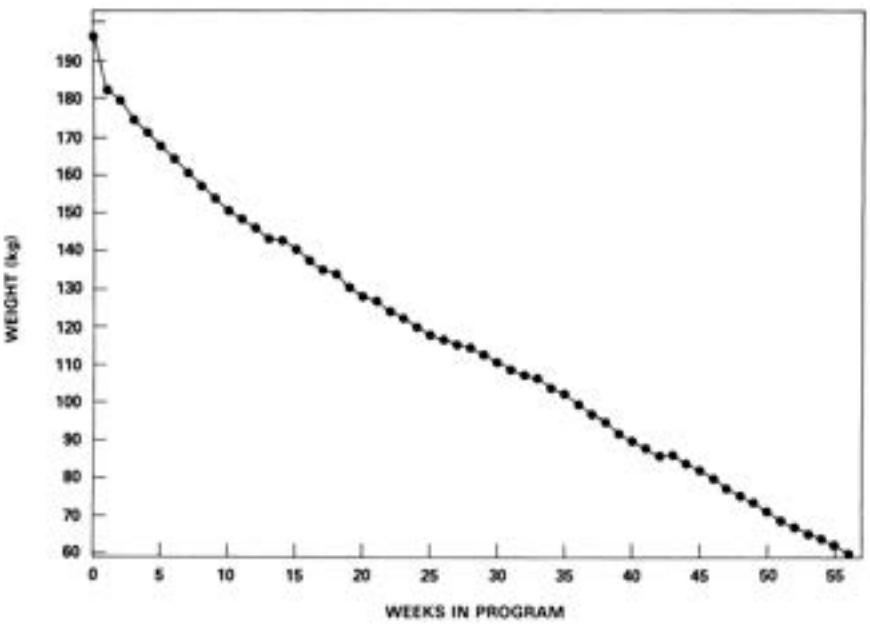


Fig 7.—Top, Weekly weights of patient 2 (see Fig 5) while she was losing 55.8 kg on regimen. Bottom, Weekly weights of patient 8 (31-year-old man) who lost 137.0 kg in 56 weeks on regimen.

be considered "unsuccessful."

In addition to the benefit of motivational enhancement, frequent monitoring of the patients is an important consideration in protecting against potential side-effects of rapid weight loss. The daily discussion serves to detect potentially dangerous symptoms, including those of postural hypotension. Daily measurement of blood pressure is also important in this regard. The inclusion of frequent monitoring is an important element of any overall weight reduction program. We do not recommend application of drastic dietary therapy and weight loss for any patient without appropriate medical supervision.

Weight Loss

The measurement of success of any regimen for treatment of obesity depends on the criteria selected for making such an assessment. This has been the subject of much discussion in the literature and remains unresolved.[17-20,46,47] Although our selection of patients for this study assured us of a population that was clearly massively obese and that had lost a relatively large amount of weight, we are uncertain about the best way of reporting our data. We have concentrated on the most widely used yardstick, relative weight in comparison with the normal values obtained from the Metropolitan Life Insurance Company Tables.[17] We recognize, however, the great limitations of this criterion.[46,47] Nevertheless, it does enable us to demonstrate the failure of the majority of our patients (group 2) to achieve a normal weight, despite relatively great weight loss.

Seltzer related ponderal index to mortality, with the use of the build and blood pressure study.[20] Thus, we have included ponderal index in our analysis and demonstrate that the patients who have lost weight have distinctly different indexes from those at entry.

The greater rate of weight loss in men than in women, despite equal magnitude of loss, confirms the clinical observation that women have a more difficult time with weight reduction programs than do men. Whether this reflects some physiological differ-

Table 3.—Clinical Findings Associated With Weight Loss

Clinical Values*	Before Weight Loss, Mean ± SD	After Weight Loss, Mean ± SD	Change, Mean ± SD
Blood pressure, mm Hg			
Systolic	150.0 ± 24.2 58% abnormal (No. = 106)	114.2 ± 17.0 2% abnormal (No. = 106)	−35.9 ± 25.2 P < .001 (No. = 106)
Diastolic	91.5 ± 14.2 39% abnormal (No. = 106)	72.7 ± 12.2 3% abnormal (No. = 106)	18.9 ± 16.1 P < .001 (No. = 106)
Blood glucose, mg/100 ml			
Fasting	118.7 ± 50.2 35% abnormal (No. = 106)	96.4 ± 14.3 14% abnormal (No. = 97)	−23.5 ± 50.7 P < .001 (No. = 97)
2-hr postprandial	140.7 ± 72.0 63% abnormal (No. = 106)	90.9 ± 24.5 14% abnormal (No. = 57)	−74.9 ± 79.8 P < .001 (No. = 57)
Serum triglycerides, mg/100 ml	147.6 ± 87.4 37% abnormal (No. = 71)	126.4 ± 67.6 30% abnormal (No. = 67)	−29.3 ± 101.2 P < .05 (No. = 63)
Serum cholesterol, mg/100 ml	227.7 ± 51.0 21% abnormal (No. = 106)	231.4 ± 65.3 21% abnormal (No. = 102)	+ 2.4 ± 66.6 NS† (No. = 102)
Serum uric acid, mg/100 ml	7.5 ± 1.9 68% abnormal (No. = 106)	7.0 ± 2.0 54% abnormal (No. = 101)	−0.5 ± 2.2 P < .02 (No. = 101)
Heart-chest ratio × 100	44.9 ± 4.4 17% abnormal (No. = 106)	39.8 ± 4.1 2% abnormal (No. = 98)	−4.9 ± 4.2 P < .001 (No. = 98)

* Normal values used in calculating percentage abnormalities follow: blood pressure—systolic, <140 mm Hg and diastolic, <90 mm Hg; blood glucose—fasting, <110 mg/100 ml and two-hour postprandial, <110 mg/100 ml; serum triglycerides—<140 mg/100 ml if less than 30 years old and <150 mg/100 ml if 30 or more years old; serum cholesterol—<230 mg/100 ml if less than 20 years old, <240 mg/100 ml if 20 through 29 years old, <270 mg/100 ml if 30 through 39 years old, <290 mg/100 ml if 40 or more years old; serum uric acid, <7.3 mg/100 ml for men and <5.9 mg/100 ml for women; heart-chest ratio (× 100), <50.0.

† NS, not significant.

Table 4.—Values for Group 1 and 2 Patients

Clinical Data	Group 1, Mean ± SD	Group 2, Mean ± SD
Weight, kg		
Before loss	127.4 ± 24.8	155.2 ± 26.8
After loss	63.9 ± 12.6	91.1 ± 19.6
Change	−63.5 ± 17.7	−64.1 ± 16.9
Relative weight		
Before loss	2.05 ± 0.27	2.43 ± 0.38
After loss	1.02 ± 0.09	1.42 ± 0.27
Ponderal index		
Before loss	10.35 ± 0.47	9.81 ± 0.54
After loss	13.02 ± 0.36	11.74 ± 0.64
Blood pressure, mm Hg		
Systolic		
Before loss	139.8 ± 16.8	157.0 ± 26.1
After loss	107.1 ± 15.5	119.0 ± 16.3
Change	−32.7 ± 20.2	−38.0 ± 28.1
Diastolic		
Before loss	86.7 ± 12.5	93.5 ± 15.1
After loss	69.7 ± 11.1	74.7 ± 12.7
Change	−18.9 ± 13.3	−18.8 ± 17.9
Blood glucose, mg/100 ml		
Fasting		
Before loss	121.1 ± 63.8	117.1 ± 38.7
After loss	93.5 ± 14.5	98.6 ± 23.6
Change	−28.7 ± 65.2	−19.7 ± 36.9
2-hr postprandial		
Before loss	140.4 ± 76.5	140.9 ± 69.4
After loss	86.7 ± 25.5	94.0 ± 23.6
Change	−82.7 ± 94.0	−69.3 ± 68.6
Serum triglycerides, mg/100 ml		
Before loss	162.6 ± 116.1	139.4 ± 67.1
After loss	119.0 ± 45.9	131.1 ± 78.5
Change	−59.1 ± 112.5	−12.1 ± 91.2
Serum cholesterol, mg/100 ml		
Before loss	236.8 ± 63.4	221.5 ± 39.8
After loss	228.1 ± 66.6	233.8 ± 64.9
Change	−8.7 ± 75.1	+10.5 ± 59.0
Serum uric acid, mg/100 ml		
Before loss	7.1 ± 2.0	7.7 ± 1.7
After loss	6.2 ± 1.6	7.5 ± 2.1
Change	−0.9 ± 1.8	−0.3 ± 2.4
Heart-chest ratio		
Before loss	44.5 ± 4.3	45.2 ± 4.5
After loss	38.4 ± 4.0	40.9 ± 3.9
Change	−5.8 ± 4.2	−4.3 ± 4.1

Table 5.—Correlation Coefficients Between Glucose and Lipid Levels

	Fasting Blood Glucose	2-hr Postprandial Blood Glucose	Serum Cholesterol	Serum Triglycerides	Lipid Phosphorus*
Correlations of Initial Values					
Fasting blood glucose		.759	.464	.431	.579
2-hr postprandial blood glucose			.383	.396	.515
Serum cholesterol				.280	.834
Serum triglycerides					.370
Correlations of Final Values					
Fasting blood glucose		.315	227	.252	
2-hr postprandial blood glucose			.217	.308	
Serum cholesterol				.275	
Correlations of Changes					
Fasting blood glucose		.790	.271	.255	
2-hr postprandial blood glucose			.271	.322	
Serum cholesterol				.230	

* Lipid phosphorus was measured only initially.

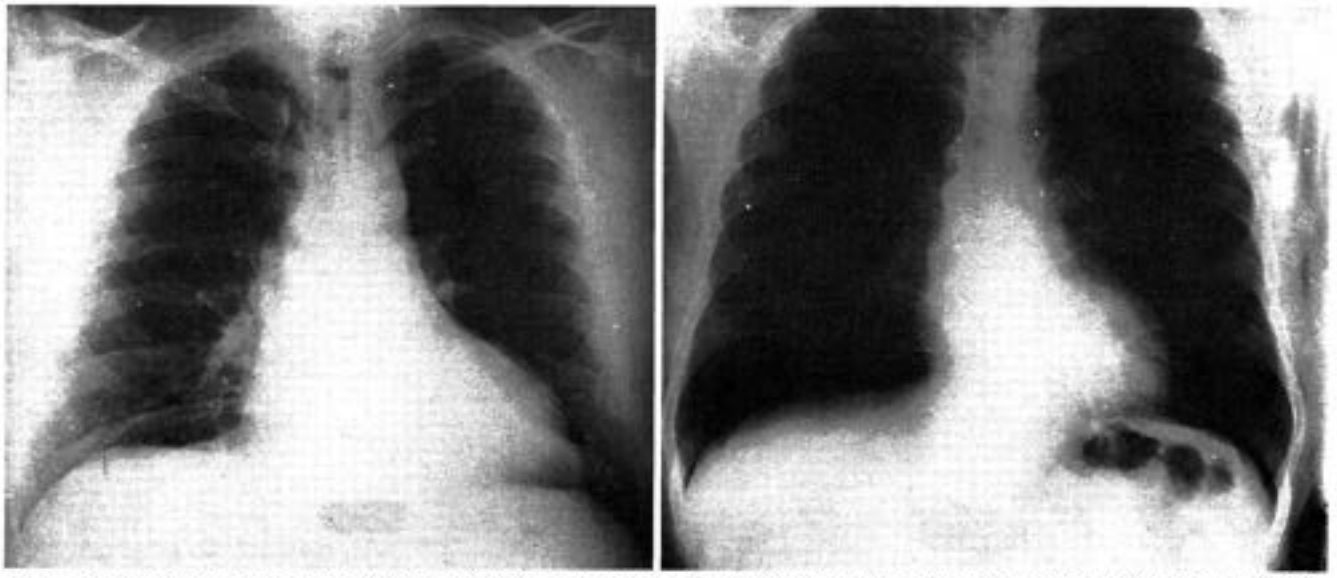


Fig 8.—Chest x-ray films of patient 3 (see Fig 2) showing improvement in heart-chest ratio from 0.524 to 0.431. Left, Initially on Nov 7, 1972, transverse diameter of heart was 19.9 cm and internal chest diameter, 38.0 cm. Right, After loss of 60.0 kg, on March 26, 1973, transverse diameter was 15.5 cm and internal chest diameter, 36.4 cm.

ence between men and women or simply better adherence to the regimen by men is not known.

Associated Clinical Determinants

The decrements in blood pressure, blood glucose value, serum triglycerides, serum uric acid level, and heart size and the improvement in retinal findings and electrocardiograms, concomitant with weight loss, tend to support the notion that some of the abnormalities in these criteria may be directly related to obesity.[1-10] A causal relationship, however, cannot be implied from these findings, especially in view of the known efficacy of the rice diet in the treatment of hypertension and diabetes mellitus.[13-16] Nevertheless, the significant decrements in these factors show that they are not irreversible and support the view that weight reduction can be important in decreasing morbidity. If some of these measurements do represent risk factors for cardiac or other disease, their improvement may also mean that there is decreased risk of cardiac disease and death as well.

The absence of significant change in the serum cholesterol level is probably related, in part, to the relatively normal initial cholesterol values seen. The slight increases in those patients with low initial cholesterol values and the decreases in those with high initial values may reflect regression toward the mean.[48] The rises in cholesterol values are not surprising during periods of weight reduction, and there may not yet have been equilibration at the time final values were measured.

Likewise, the relatively small changes in serum triglycerides and serum uric acid may reflect mobilization of fat during weight loss, with keto acids (derived from mobilized free fatty acids) competing with uric acid for renal tubular secretion.[49]

The finding that group 1 and group 2 patients had equal magnitudes of change in the various clinical and chemical variables studied shows that the changes are related to degree of change in weight. The higher final values of some variables in group 2

patients indicate that correction to normal weight is also important in normalizing concomitant abnormalities of obesity. This is consistent with the actuarial data that, with increasing degree of obesity, there is increased morbidity and mortality.[3] It would also support those who argue in favor of promoting as much weight loss as possible, even though that does not completely resolve the problem.

The correlation between levels of blood glucose and blood lipids is consistent with the hypothesis that these are under common control, perhaps both under control of insulin.[10]

Conclusion

The criterion of ultimate success of any weight reduction program is dependent on long-term maintenance of weight loss. Such data are not yet available for the patients analyzed in this report. Nevertheless, one important fact to be gained from this study is that, despite the misconception to the contrary, massive obesity is not an uncorrectable malady. Weight loss can be achieved, massive obesity can be corrected, and it can be done without drastic intervention. Treatment is worthwhile, since weight reduction is associated with improvement in many of the associated clinical abnormalities that are present in obese patients—elevation of blood pressure, carbohydrate intolerance, elevated serum triglyceride levels, hyperuricemia, cardiomegaly, electrocardiographic changes, and retinal vascular changes.

Mercedes Gaffron, MD, PhD, and Clotilde Schlayer, PhD, participated in the care of these patients. Edith Anne Scoggins aided in the chart review. George Shakarji and Ray Danner, of the Math-Stat Section, Division of Computer Research and Technology, National Institutes of Health, aided in the statistical analysis.

This work was supported by the Walter Kempner Foundation. Dr Skyler was a Public Health Service trainee in endocrinology and metabolism (grant 5-T1-AM-5074) at the time this study was done.

For each of the patients in this series, data for weight; relative weight; ponderal index; blood pressure; blood glucose, serum cholesterol, serum triglyceride and serum uric acid values; and heart-chest ratio appear in a table titled Appendix 1. See NAPS document 02711 for 22 pages of this supplementary material. Order from ASIS/NAPS, c/o Microfiche Publications, 440 Park Ave S, New York, NY 10016. Remit with order $3 for microfiche or $5.50 for a photocopy. Make checks payable to Microfiche Publications. Outside the United States and Canada, postage is $1 for a fiche and $2 for a photocopy.

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Effect of Weight Loss on Arterial Oxygen Pressure (pO_2)

EFFECT OF WEIGHT LOSS ON ARTERIAL OXYGEN PRESSURE (pO_2)

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PHYSIOLOGY

Energy Metabolism and Metabolic Diseases

EFFECT OF WEIGHT LOSS ON ARTERIAL OXYGEN PRESSURE (pO_2).

Barbara Newborg*(SPON: Walter Kempner).
Duke University Medical Center, Durham, N.C. 27710

In 250 obese out-patients, without breathing difficulties or heart failure, in whom the initial pO_2 was found to be below 85 mm.Hg., the pO_2 was determined again after weight loss on a rice/reduction diet. In 105 of these patients, the pO_2 before and after weight loss varied more than $\pm$ 7 mm.Hg. (lesser variations considered to be within the limits of technical error). In 18 of the 105 patients, there was a decrease in the arterial pO_2: -8 to -18, avg. -10.4 mm.Hg.; in 87 of the 105 patients, there was an increase: +8 to +35, avg. +14.6 mm.Hg. The avg. change in the 105 patients was an increase of 10.3 mm.Hg. (A paired t test on the 105 differences shows the overall increase to be highly significant.) The avg. weight loss in the two groups was 45 pounds in 90 days and 51 pounds in 102 days. The avg. arterial carbon dioxide pressure was unchanged: 37-38 and 37-37 mm.Hg., respectively. How much of the increase in the arterial pO_2 was caused by a decrease in the amount of fatty tissue and its blood supply or by an increase in the lung volume or by other factors will not be discussed in this report. But since the rate of cellular respiration varies with variation of pO_2 (Kempner, Cold Spring Harbor Symposia on Quantitative Biology, 1939), it is surmised that a great deal of the beneficial results of weight reduction (improvement in function of the brain, retina, heart, kidney, testis, etc.) might be due to an increase in the rate of respiration of cells oxidizing in a milieu of higher oxygen pressure.

Obesity Destabilizes the System

Obesity Destabilizes the System

Barbara Newborg, M.D.

The lungs normally contain a large volume of air. When we hold our breath the air in the lungs allows the continued oxygenation of blood and allows the CO_2 to occupy the space from which the oxygen is being removed. This reserve volume of air stabilizes the system much as a flywheel can stabilize an energy producing system. In very obese persons, this flywheel-like stabilizing function is lost. Moreover, the obese body extracts more oxygen and adds more CO_2 per unit of time. The loss of air volume in the lungs reduces the effectiveness of the flywheel-like stabilizing effect and the increased body mass depletes the available oxygen supply more quickly. Short periods of apnea produce large changes in blood gases. Sophisticated lung function studies are not needed to establish the large loss in lung capacity. A glance at the x-rays shown in figure 1 is sufficient.

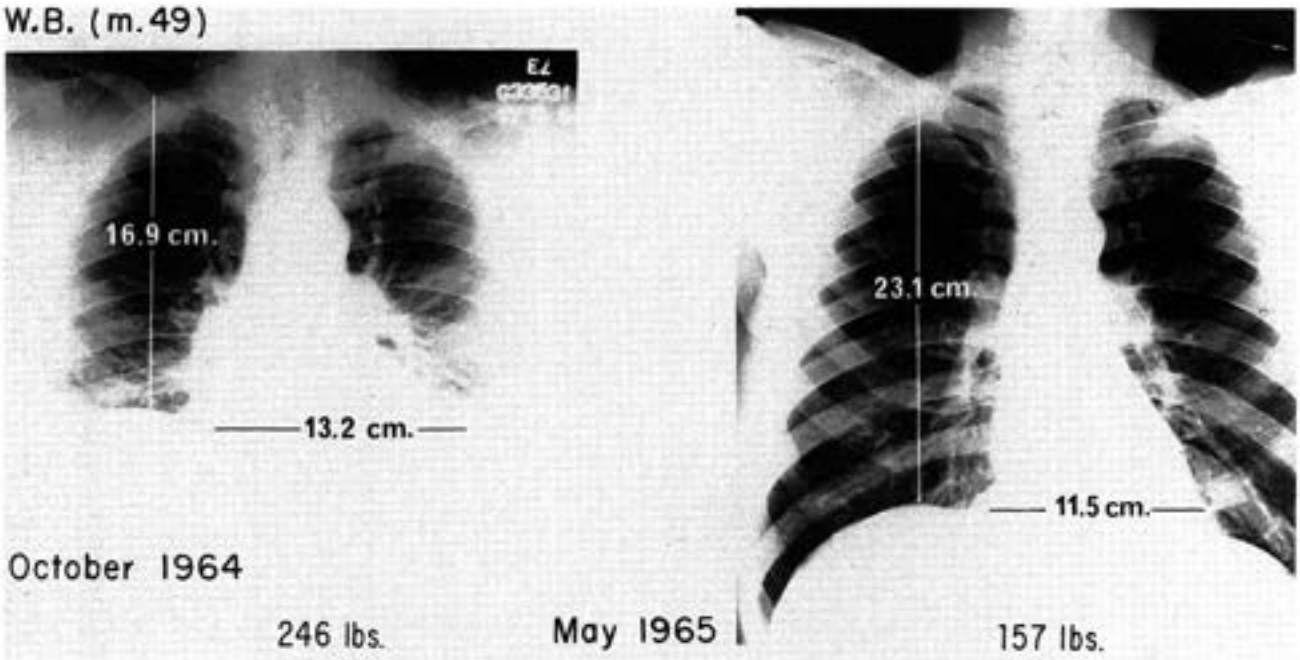

Figure 1. Increase in lung capacity and decrease in heart size in a patient treated by rice/reduction diet.

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Kempner Revisited

North Carolina
MEDICAL JOURNAL
for doctors and their patients

The Official Journal of the NORTH CAROLINA MEDICAL SOCIETY April 1983, Volume 44, No. 4

Kempner Revisited

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

The original descriptions of the effects of the rice diet were published in the *North Carolina Medical Journal*.[1-3] Editors of other, more widely read national journals did not appreciate that the Kempner articles would come to be recognized as classics and that here in North Carolina Dr. Kempner was making medical history. The editor of the *North Carolina Medical Journal* was wiser and published his work.

On my arrival at Duke in 1947, Walter Kempner and the rice diet were in the news. The students and house staff at Duke helped care for Kempner's patients as well as those of the rest of the staff. Each morning I had to answer the question of why Kempner's patients with destructive hypertension did better than mine or those of other members of the staff. With the help of the Durham chapter of the North Carolina Heart Association and my colleague Bernard Holland (presently Professor of Psychiatry at Emory), I started my own rice house. As Kempner had done originally, we served patients who did not have the means to pay a private doctor. We discovered several things. Twenty-four hour care of very sick hypertensive heart and kidney patients is time-consuming and difficult. The disease responded in the manner described by Kempner. The long-term care of patients who stayed for six weeks or longer in our "rice establishment" was simplified. All dieters are liars, and chemical analysis of the urine to determine oral intake is essential.

After two years we disbanded our "rice house" and from that time I have sent patients who would profit by the dietary regimes of Kempner to him.

In a letter written in 1958, I summarized Kempner's contributions as follows:

> Dr. Walter Kempner showed that our ideas regarding protein requirements were erroneous and that, in the presence of a high caloric intake, nitrogen balance can be reached on as little as 25 grams of protein per day; that man can remain in sodium and chloride balance on as little as 5 mEq per day; that the cholesterol levels in the blood can be lowered by rigid dietary restrictions.
>
> He showed that rigid dietary restriction has a favorable effect in congestive heart failure, kidney disease and

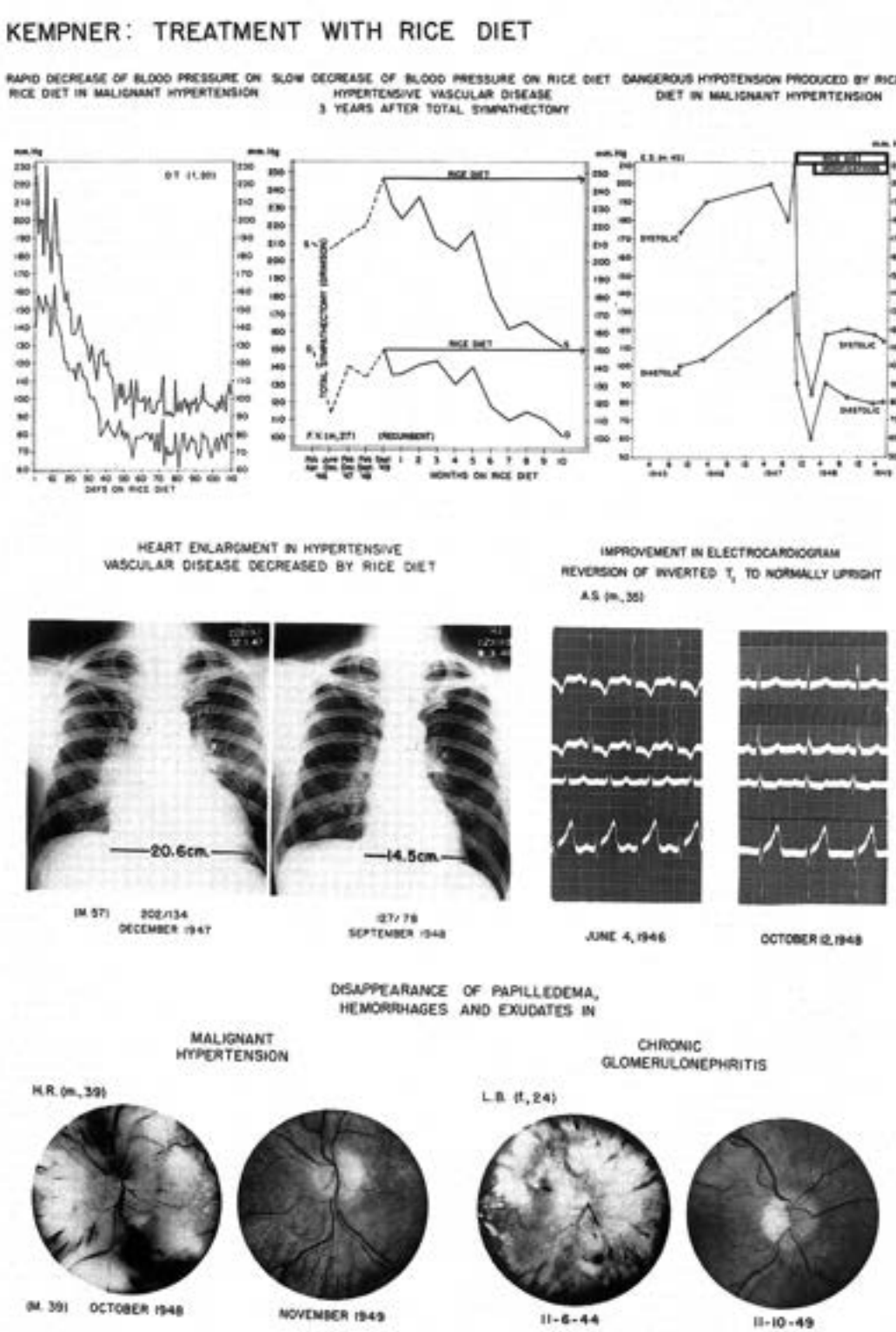

Figure 1. *Changes in several systems in several patients during treatment on Kempner's rice diet.*

hypertension, and that it affects not only subcutaneous edema but reduces cerebral edema seen in malignant hypertension, with disappearance of papilledema and retinal edema.

He demonstrated that in many patients the rice diet could reverse the course of hypertensive vascular disease in both benign and malignant states.

In his studies on the course of treated and non-treated malignant hypertension, he demonstrated that renal damage was not necessarily irreversible but that an appreciable return of kidney function was possible in many patients, provided the time of treatment is measured in years rather than weeks or months.

He has shown that, in malignant hypertension, multiple factors are at work in producing the brain, heart, retinal and renal lesions; that the blood pressure is only one factor, but that even without any change in blood pressure, favorable changes may occur with rigid dietary

treatment in the brain, heart, retina, and kidney.

In patients with nephrosis with heavy albuminuria, he has demonstrated that recovery may occur on the rice diet. The protein decreases in the urine, and the albumin content of the plasma returns to normal in the presence of a protein intake not exceeding 25 grams. Before Dr. Kempner's work, we believed that a patient with little protein in the blood who was losing a large amount of protein in the urine would have died on such a protein intake.

He has shown that diabetics with complicating vascular disease improve not only in regard to the vascular disease, including severe diabetic retinopathy, but that they tolerate the high-carbohydrate diet well; and that the diabetes mellitus itself is often favorably affected, as evidenced by decreasing insulin requirements and decreasing blood sugar levels.

The above record is one for which we at Duke have respect and admiration. It has required an immense amount of work and large sums of money.

Kempner has dedicated his life to the study of vascular disease and his strikes have all been made in areas where the experts said there was no gold. Who in his right mind would have ever thought that rice and fruit could modify vascular disease appreciably? Who would have fed a protein-deficient patient, losing large quantities of protein in his urine, a protein-poor diet? Who would have dared to give a more than 90% carbohydrate diet to a diabetic? Every expert knew that cholesterol levels were not influenced by diet. Nevertheless, all these leads have paid off richly.

Figure 1 shows examples of the responses Kempner described in the *North Carolina Medical Journal*.

With the permission of Drs. Kempner and Newborg, I am re-publishing an updated 42-year-old blood pressure chart of Katherine Ormston, the first executive secretary of the North Carolina Heart Association (figure 2). Miss Ormston was referred to Kempner by a well-known New York cardiologist (Dr. Irving Wright) after bilateral sympathectomy (by Dr. Reginald Smithwick in Boston) failed to control her hypertension. In 1953, while she was still following the Rice Diet, I had a talk with her concerning the patient's viewpoint of this treatment. She assured me that while a salt-free diet was inconvenient, especially in conjunction with an active job requiring considerable travel, it was certainly possible. She pointed out, too, that since she had been Dr. Kempner's patient she had taken no medication except regular multivitamins, and occasional aspirin and antibiotics for severe winter colds.

She continued:

> More important to me personally is the fact that since September 1, 1948, I have been steadily engaged in earning my own living, with only the usual vacations and holidays; and the only time I have lost through illness during that time was because of the above-mentioned colds. In August 1950, I became executive secretary of the North Carolina Heart Association which was in the beginning stage of establishment in this state. This work has required steadily increasing activity and responsibility, long hours of work and considerable travel. I've driven my car about 34,000 miles during these years,

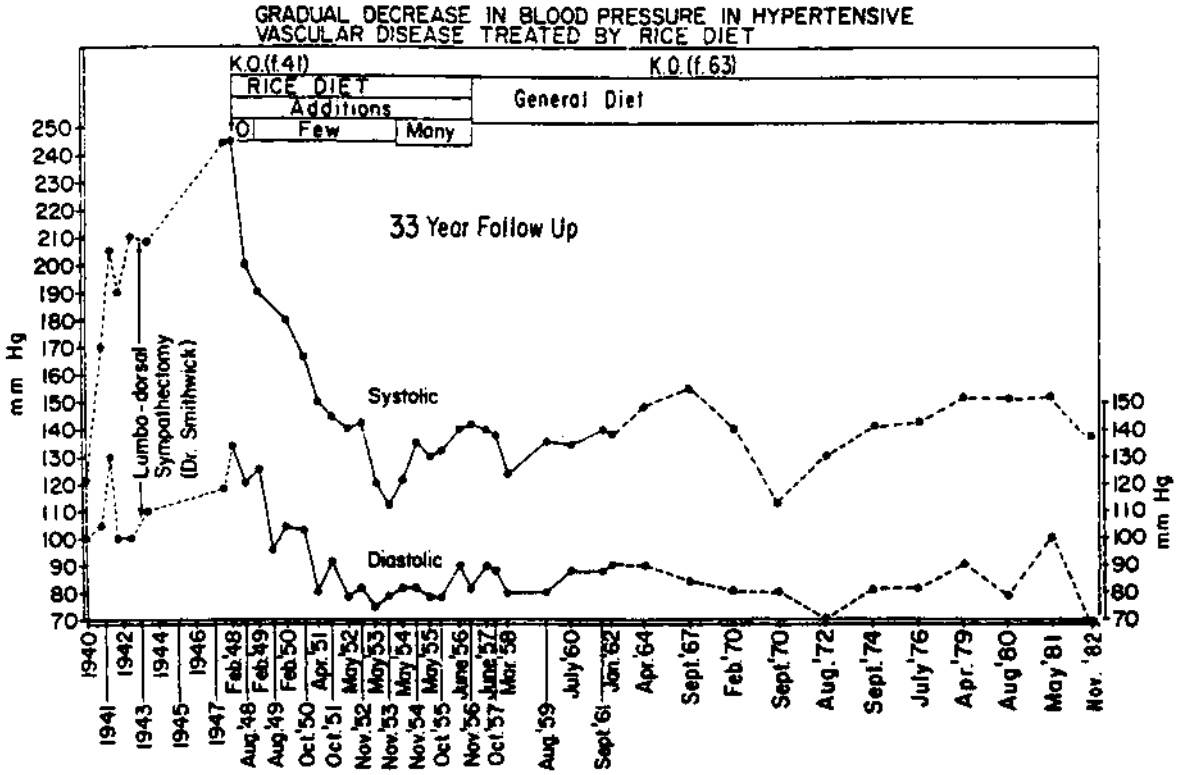

Figure 2. *Forty-two year followup of Katherine Ormston.*

much of it for organizational and fund-raising work. Looking back, it seems to me that my blood pressure decreased as my work and responsibility increased.

Another point which seems to interest doctors is loss of weight. My height is 5′ 4½″ and my build is rather slight. For a good many years my normal weight was around 110 pounds. When I started the modified rice diet in New York, I weighed about 118 pounds. Four months later, when I first came to Durham, I weighed 105 pounds. At the end of 100 days on the "basic" rice-fruit-sugar diet, I weighed 115 pounds. Since then my weight has fluctuated between 98 and 110 pounds, apparently depending upon such factors as the amount of energy I was expending or how hot the summer was.

Best of all, to me, has been the consistent feeling of well-being. I have, throughout the past 5 years, slept well each night (with no medication whatever) and wakened with sufficient energy to carry me through a busy day without difficulty. I am, in fact, living a normal, busy, happy life; I just can't eat everything I'd like to have. Perhaps in the future even that will be remedied.

A few days ago, 30 years after the conversation described above, I chatted with Miss Ormston again. Now 76 years old, she has been working continuously since that time, and only recently reduced her work week to three days instead of five. In 1954, Dr. Kempner allowed her to discontinue the Rice Diet, gradually at first. For many years she has eaten as she chooses, but voluntarily limits her intake of salt, fat and red meat, and prefers food that is prepared simply. Her highest weight in 30 years was 126 pounds for a short period; it now fluctuates a little above or below 115 pounds. She has made nine trips to Europe, and recovered without complication from two major operations. The reduction in work week has not decreased her activity; for the past three years her housekeeping duties have been doubled by care of an invalid sister who came to live with her.

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Otto Warburg 1883-1970: Thoughts Upon Looking at the 1983 Commemorative Issue of the Postal Service of West Germany in Honor of His Hundredth Birthday

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Otto Warburg 1883-1970

Thoughts upon looking at the 1983 commemorative issue of the Postal Service of West Germany in honor of his hundredth birthday, by Walter Kempner, M.D., page 25

HANDS ACROSS THE SEA

The Durham Connection to Germany

Walter Kempner M.D.

Thoughts Upon Looking at the 1983 Commemorative Issue of the Postal Service of West Germany in Honor of The Hundredth Birthday of Otto Warburg, the Father of Cellular Physiology

"HERE in the Medical School of Heidelberg everybody wants to be a Professor and wants to teach and wants to talk. There was never anybody here who wanted to work. When something finally has to be done, they shout: 'Mr. Ziegler, Mr. Ziegler!' Doctor, I get sick to my stomach when I hear my name."

Mr. Ziegler was the janitor who cleaned my glassware when I was an intern in Heidelberg where I did blood sugar determinations on dogs I had made diabetic by the injection of phlorizine. Mr. Ziegler had a fine upright character and I learned a lot from his pearls of wisdom, even when he was not completely sober and wore his hat on the back of his head while washing the pipettes and flasks.

I said, "Really, really, Mr. Ziegler, in all the time you were here wasn't there ever anyone who did some work?" After a lot of deliberation he said, "Yes, several years ago there was one, but he left pretty soon and never became a Professor; and one never heard anything about him anymore."

Sitting in the library a few days later, I looked to see if he had ever published a scientific paper and came across something about sea urchin eggs, nucleated red blood cells, and metabolic reactions of cancer cells. All of a sudden I found myself writing a letter to this unknown man whose address was in Dahlem, a suburb of Berlin, asking him whether I could work in his laboratory. He answered me politely that unfortunately he had only a very small laboratory where there was no space, but he would be glad to talk with me if I should come sometime to Berlin.

My ward consultant said that this was the most complete nonsense he had ever heard especially in my case since the big boss, Dr. von Krehl who had written the famous first book about pathological physiology (which incidentally was translated into English with an introduction by Osler), wanted to put me on the Staff as soon as I finished my internship. But I protested and said that I first wanted to learn something. My superior said, "It is much more important for your career to have been on the boss's Staff a few years than to learn everything." Anyway, I took the train to Berlin and Warburg talked with me in his small office. He was 43 years old, I was 24. He asked me, "Do you know any mathematics?" I said no. "Any physics?" I said no. "Any chemistry?" I said no. He said, "What actually do you know?" I said, "I graduated from the Medical School in Heidelberg and completed my internship there, and I published a paper about diabetes and did more than 650 blood sugar determinations on a dozen dogs and a few rabbits. (The methods were not so simple then and I had to do all the determinations myself without the help of technicians.) So I really don't know anything." Warburg said, "At least you are honest. But you will see for yourself what I already wrote you that this is a very small laboratory and there is no space for anybody else. However, you can stay here for a couple of weeks and learn our methods."

There were three young men without any previous training working there and three who had doctoral degrees. One was Dr. Wind who died of tuberculosis shortly afterwards; the second was Dr. Hans Gaffron, later well known for his work on photosynthesis, who was for many years Professor of Biochemistry at the University of Chicago; the third was Dr. Hans Adolf Krebs who became famous for his citric acid cycle and got the Nobel Prize a few years later. (Two other Nobel laureates had also started in Warburg's laboratory: Otto Meyerhof and Hugo Theorell).

After the two weeks were over, Warburg asked me, "Did you learn our methods?" I said no. He asked "Why not?" I said I would need much more time to learn them. He asked, "How much time would you need?" I said, "Maybe one or two years." "All right," he said, "then stay here." And I stayed there 1927 and 1928 in his small laboratory in the upper floor of the Kaiser Wilhelm Institute of Biology in Berlin-Dahlem and again in 1933 after an interval of five years in which I had been an Assistant Physician in the Medical School of Berlin.

In 1931 Warburg had got the Nobel Prize for his work on the respiration ferment and had been given a beautiful new institute of his own — the Kaiser Wilhelm Institute for Cellular Physiology in Dahlem.

Up until then he had published two books: *Metabolism of Tumors* (1926) and *Catalytic Effects of Living Substance* (1928). These books do not contain any opinions or discussions but are merely collections of the original papers he had written about the methods and results of his new experiments. One of his favorite remarks when he read the "literature" was, "There are two kinds of chemistry — experimental chemistry and paper chemistry."

The titles of his later books (1948-1962) (also collections of original papers) are: *Heavy Metals as Active Groups of Enzymes, Hydrogen-Transferring Enzymes,* and *Further Developments in Methods of Cellular Physiology.*

In 1933, after Hitler came to power in Germany, a gentleman from the Rockefeller Foundation visited Warburg in his laboratory in order to persuade him to come to the United States. Warburg looked around and said, "Here

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I know where each piece of apparatus is; here I can put my hand on everything I need," whereupon the visitor replied, "We will photograph the whole laboratory just as it stands down to the last detail. We will present you with an exact duplicate of your Institute." But Warburg couldn't make up his mind and remained in Germany throughout the rather unpleasant years before and during World War II.

Great scientists can be very average and boring people. Warburg was interesting. In 1927, my first year with him, I discussed in the evening with Dr. Krebs the results of an experiment I had just made that day. "There must be a mistake," Krebs said. I questioned why and he answered, "This is against all the laws of cellular physiology." The next morning when Warburg had come in, he asked me for the results of my experiment. I showed it to him and he said in English, "That's very exciting." I argued with my newly acquired wisdom, "But it can't be true; this is against all the laws of cellular physiology." Warburg pondered a moment and then said, "Of course you have to repeat it six or seven times, but if it always comes out the same the laws of cellular physiology have to be changed."

In 1968, the year he became 85 years old, he sent me a letter for my 65th birthday and wrote, "In many respects I found that age is better than youth. The fight for existence is over and, if one possesses luck and reason, one can still live for many years. A bank account is desirable, a house of one's own is desirable, the possibility to do scientific work is desirable. I assume that you have all of this in ample measure. And so I dare to congratulate you."

"Luck and reason." But I think I would never have been lucky in any endeavor in medicine without those years 1927, 1928, and 1933 with Otto Warburg.

Reprinted from pages 25 and 26 of the January 1984, North Carolina Medical Journal

The Role of Oxygen Pressure in the Fight Against the Chief Killers in the First and in the Last Half of the 20th Century

The Role of Oxygen Pressure in the Fight Against the Chief Killers in the First and in the Last Half of the 20th Century

By
Barbara Newborg, M.D.

Reprinted from pages 47 and 48 of the January 1985
North Carolina Medical Journal

LEARNING WITHOUT WORDS

The Role of Oxygen Pressure in the Fight Against the Chief Killers in the First and in the Last Half of the 20th Century

Barbara Newborg, M.D.

• *The fashionable therapies for tuberculosis patients used earlier in this century had a common physiological effect: they reduced oxygen pressure which in turn inhibited the oxidative processes of the tubercle bacillus.*

WHY were patients with tuberculosis, the chief killer until the 1940s, urged to have maximal weights?

The accepted dietotherapy for patients in the tuberculosis sanitariums consisted in giving large amounts of butter, cream, eggs, cheese and other high caloric items to promote all possible weight gain. The plausible explanation was that, due to the chronic fever, the patients burned up more calories and unless they were overfed they would die of "galloping consumption."

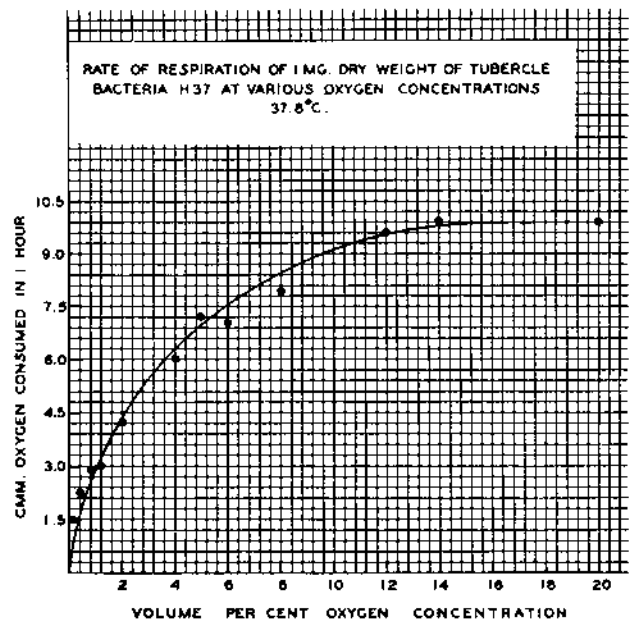
The second fashionable and obviously helpful treatment was sending the patients to high altitudes, the explanation being that the air was purer there and there was more ultraviolet light.

The third type of treatment that had proved successful was pneumothorax, or cutting the phrenic nerve to elevate the diaphragm, or rib resection. The explanation here was that thereby the affected lung tissue was given less work to do and more rest.

After the discovery of antibiotic therapy these forms of treatment were almost relegated to books about the history of medicine. However, from a scientific point of view it was interesting to establish the physiological rationale of these therapies.

In 1939, W. Kempner published a paper about "Oxygen Tension and the Tubercle Bacillus" in the *American Review of Tuberculosis*, in which he reported that contrary to Warburg's "all or nothing law" of cellular respiration, a considerable decrease of the oxidative processes of the tubercle bacillus was found under conditions of lowered oxygen pressure (figure 1).

Since these oxidations are virtually the only energy-supplying mechanism of the tubercle bacillus, its power to harm would be greatly inhibited by conditions like high altitude, pneumothorax, etc., which lower the oxygen pressure at the site of the infected tissue.



But what has this dietotherapy, the insistence on maximal weight, to do with high altitude and pneumothorax?

We have determined* the oxygen pressure in the arterial blood of 105 overweight patients before and after a period on a weight reduction diet. While some of the patients had no complaints except their overweight, quite a few showed symptoms of narcolepsy, lack of alertness, failing memory, impotence, inability to burn calories, etc., which improved with the weight reduction. The outcome of the determinations was an average increase of the oxygen pressure in the arterial blood from 71.1 to 81.4 mmHg after an average weight loss of 49 pounds in an average period of 100 days. (Incidentally, the chest films of obese patients

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* Barbara Newborg, Fed Proc (Physiology) 1977; 36.

often look like those of patients with bilateral artificial pneumothorax: see *North Carolina Medical Journal*, page 242, April 1983.)

This shows that the practical approach of the dietotherapy of maximal feeding in tuberculosis had the same physiological basis — the decrease of oxygen pressure — as that of high altitude and pneumothorax therapy, though a quantitative explanation was not available at the time it was advised. One is reminded of what E. A. Stead wrote in 1978 in a paper about "Holistic Health": "It is sounder to determine by proper observation whether the treatment is beneficial. If it is, rationale will be developed in time to make the venture fit into the mold of biologic science."

If the bacteriostatic therapy which we are lucky enough to have now at our disposal did not offer so much better means to kill the tubercle bacillus, the treatment by decreasing the oxygen pressure would probably still be the most efficient.

With regard to tuberculosis, oxygen pressure is no longer of paramount importance. It remains, however, one of the most decisive factors in another therapeutic approach, though exactly in the opposite direction: today we are faced with the task not of *decreasing* but of *increasing* the oxygen pressure in the body in our fight against the chief killer of *our* time, the so-called cardiovascular diseases in which a decrease of oxygen pressure in the cells, for instance by overweight, has occurred, not only in the case of intermittent claudication of the leg muscles but also in the intermittent or permanent claudication of the testes, the kidneys, the myocardium or the brain.

Disappearance of Psoriatic Lesions on the Rice Diet

SCIENTIFIC ARTICLE

Disappearance of Psoriatic Lesions on the Rice Diet

Barbara Newborg, M.D.

SOME time ago one of our Cardiology Professors stopped Dr. Kempner in the corridor and said, "I believe in the Rice Diet." Suspecting that his colleague wanted to tease him, Dr. Kempner replied: "You'd better tell me why." His colleague answered, "Every time my psoriasis flares up, I put myself on the Rice Diet until the psoriasis has disappeared. This occurs often within a short time."

The Rice Diet contains no more than 20 grams of protein — mostly derived from rice, 20-50 mg of sodium and very little fat with a relatively large percentage of linoleic acid. Figure 1 shows a comparison with a "so-called" normal diet.

Results of the treatment with the Rice Diet in kidney, hypertensive vascular and heart diseases and diabetes were first published by Dr. Kempner in the forties.

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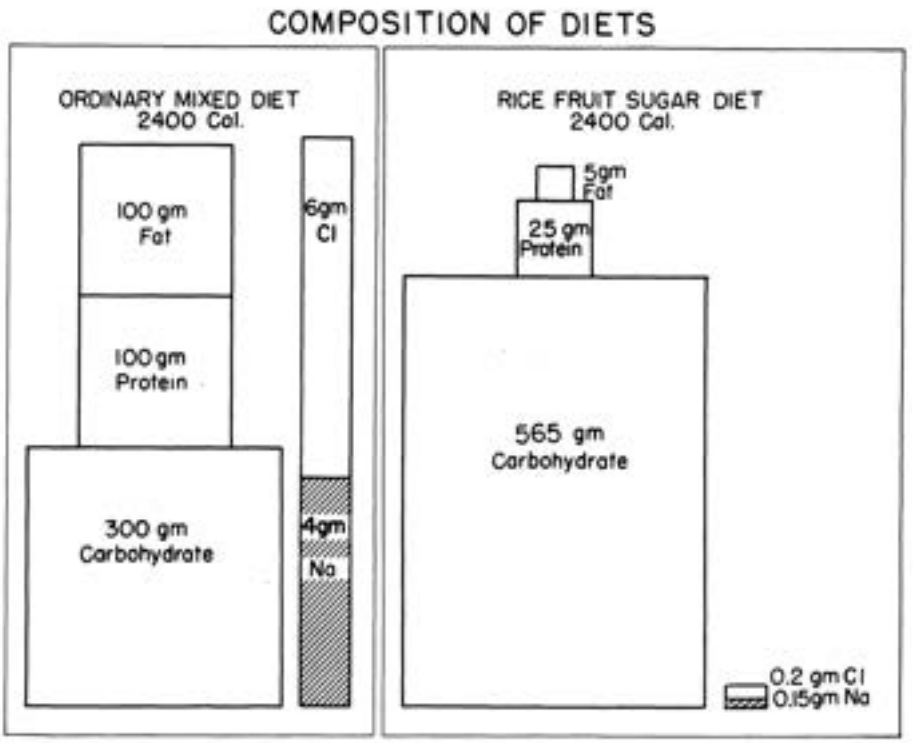
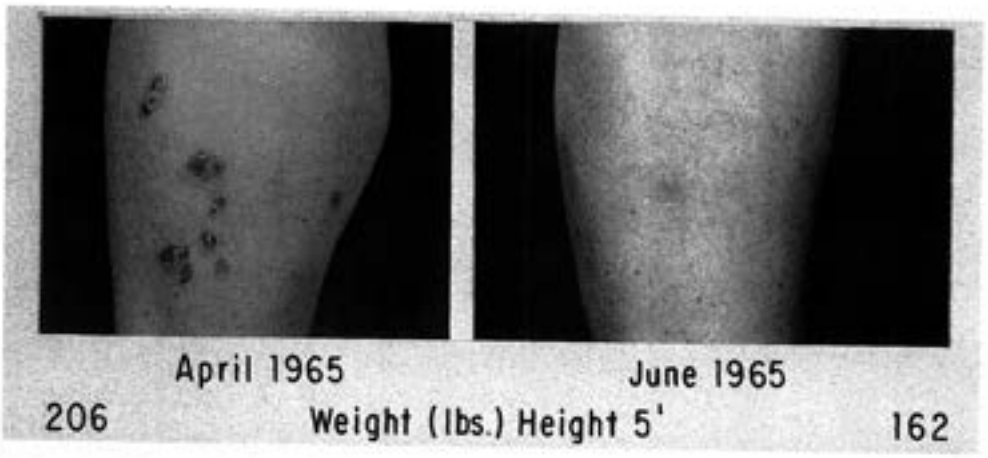
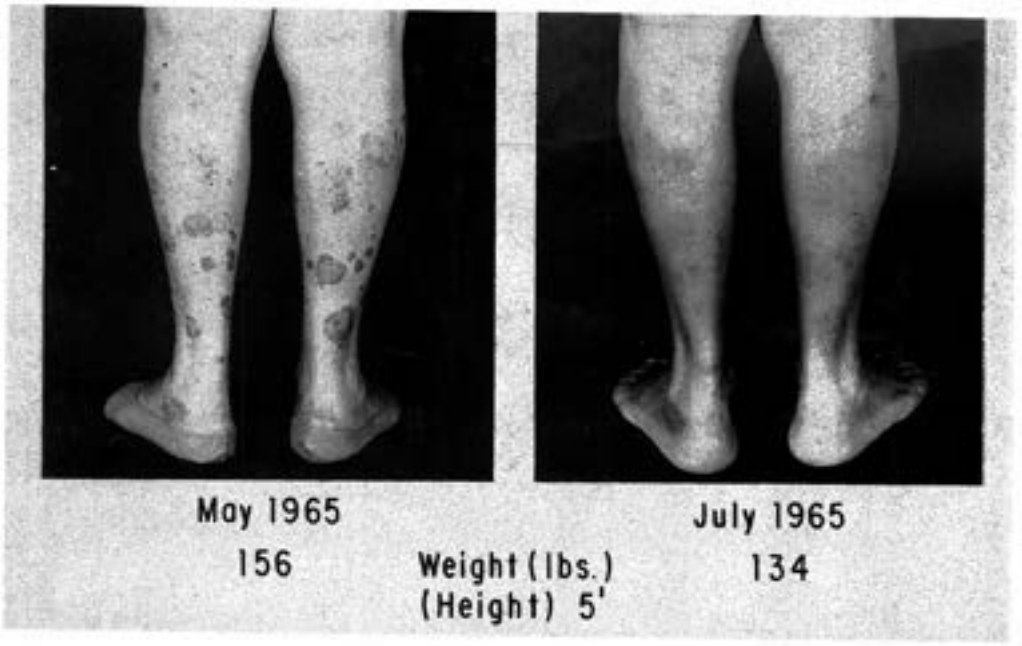
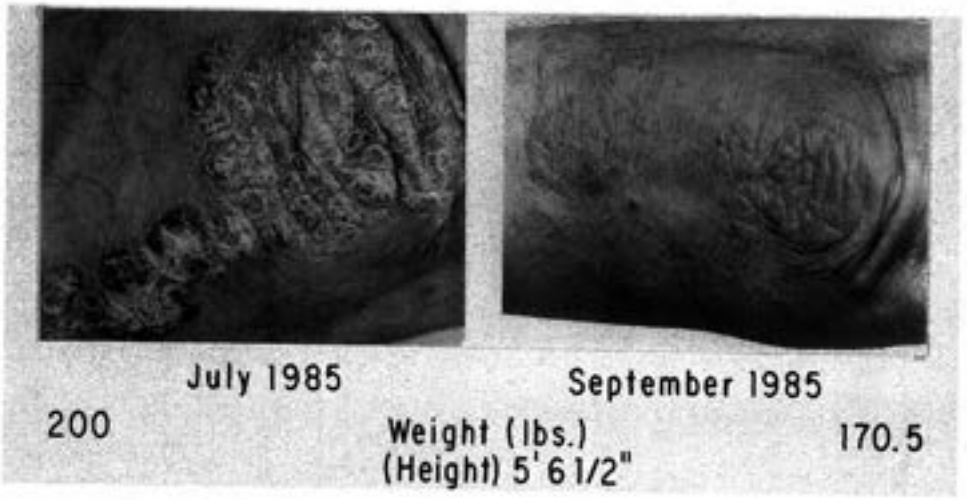
It soon became obvious that patients with psoriasis, being treated with the Rice Diet for any of the above-mentioned problems, showed a dramatic reduction in or disappearance of their skin lesion. Figures 2-5 illustrate these changes in four patients. None of these four patients had any systemic or other additional treatment while under observation here; local steroid treatment was either tapered off or discontinued in the patients who had been using it. Many of the patients whose psoriatic lesions improved during treatment with the Rice Diet had previously been treated unsuccessfully for years with systemic and/or local medications. There was not a single patient seen whose psoriatic lesions became worse on the Rice Diet.

Whether the improvement in the psoriasis is due to an increase of a beneficial substance in the Rice Diet or to a decrease of a harmful one is not known. (We suspect it is the latter.) What is known is easily seen in figures 2-5, which show the improvement in the skin condition.

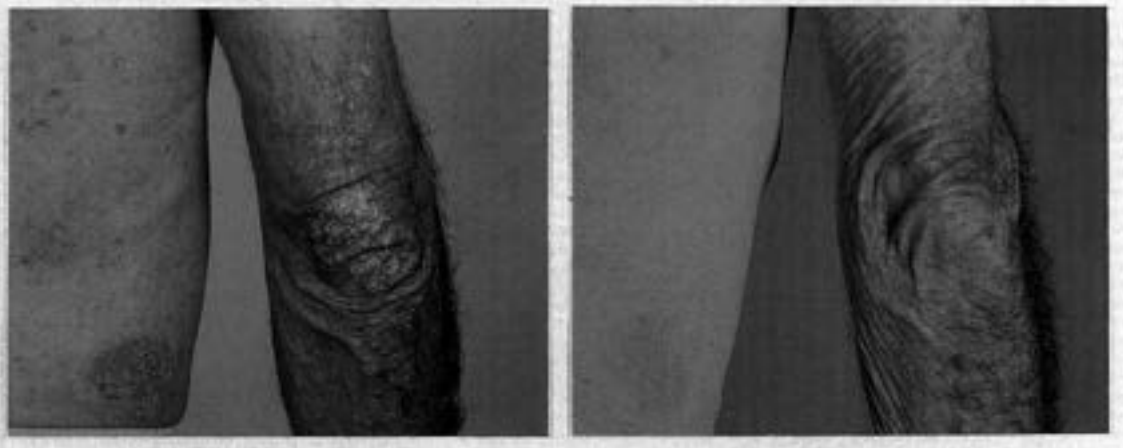



April 1965
June 1965
206
Weight (lbs.) Height 5'
162


May 1965
July 1965
156
Weight (lbs.)
(Height) 5'
134


July 1985
September 1985
200
Weight (lbs.)
(Height) 5' 6 1/2"
170.5

Disappearance of Psoriatic Lesions in 73 Year Old Man Treated by Rice Diet for 8 Weeks



April 18, 1984 June 13, 1984

COMMENT

Claude S. Burton, M.D.

NO one has found a *cure* for the skin condition psoriasis. Though our patients find this discouraging, we explain that with trial and error there is an excellent chance we will find a treatment to *control* the process. With appropriate supervision and treatment not even the hairdresser can detect that my patients in fact have psoriasis.

I don't rely on a single treatment. Different approaches work for different people. Dr. Kempner and Newborg's anecdotal cases convince me that the Rice Diet should be added to the dermatologist's armamentarium, especially if the patient is obese, diabetic, or hypertensive.

I cannot explain how the Rice Diet works in the treatment of psoriasis. Prostaglandin profiles are diet responsive and, based on early prostaglandin studies in psoriasis, a new enthusiasm for dietary therapies is emerging, especially those rich in EPA (eicosapentanenoic acid — an unsaturated fatty acid prostaglandin precursor found in the flesh of many cold water fishes and now available from health food stores as MAX-EPA, thought to be the reason eskimos have such a low incidence of heart disease). Drugs that interfere with folate metabolism and virtually any agent that inhibits DNA or protein synthesis are effective at controlling psoriasis. One can imagine that the Rice Diet might have influences in all of these areas. Certainly, further clinical and laboratory investigations are warranted.

The Kempner diet excels in the treatment of heart and kidney disease, hypertension, diabetes and obesity. All of these illnesses limit choices of therapy for psoriasis and vice versa. For example, beta-blockers often flare psoriasis. Fatty infiltration of the liver in diabetics and obese patients may limit the utility of methotrexate therapy. For psoriasis patients with such comorbid conditions, the Rice Diet might be the best first-line approach.

We hope we will soon learn if all psoriasis patients respond to the Rice Diet and if this approach will be useful for non-obese psoriatics.

From the Divison of Dermatology, Duke University Medical Center, Durham 27710.

Reprinted from pages 253-255 of the May 1986, North Carolina Medical Journal

The Sodium/Diabetes Connection

BULLETIN

OF THE

WALTER KEMPNER FOUNDATION

DURHAM, N.C.
JUNE 1993
VOL. VI NO. 1

THE SODIUM/DIABETES CONNECTION

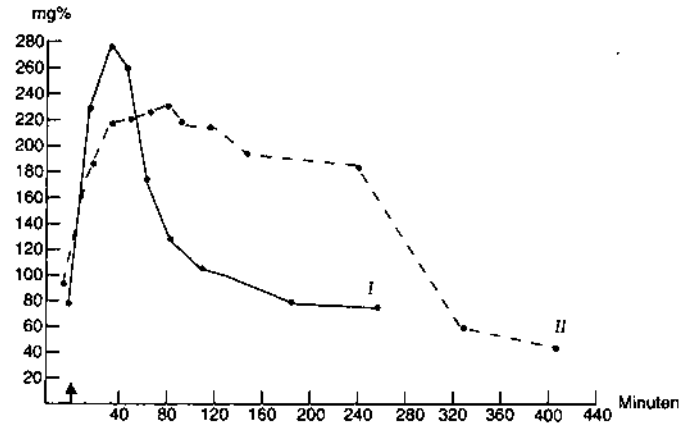
An old story repeats itself every so often. When there are two road signs: one road to the promised land and the second to a lecture about the promised land, 99 out of 100 people follow the sign to the lecture. Something similar is true for diabetic patients. If I tell them to eat the Rice Diet, their next question would be: Could you explain to me why this would improve my disease? There is an old Roman proverb: SENECTUS NATURA LOQUATIOR. Old age by nature is more loquacious. So I will tell you something about an experience which I had many years ago.

In the University Hospital of Heidelberg, where I was an intern in 1926, I did some experiments on dogs and rabbits in which I produced renal diabetes by phlorhizin. A paper of 23 pages was published in 1927 in the "Archiv fuer experimentelle Pathologie und Pharmakologie". It had very little text but the results of more than 600 blood sugar determinations in graphs and tables.

There was no technician and I had to do all the determinations myself in my "spare moments". The time required for taking the blood and the determination was not, as it is now 65 years later, a matter of seconds. (A young professor, whom I blamed a few years ago that he was spending too much money from his government research grant to hospitalize the patients, answered that otherwise he would have to draw all the blood samples himself. The actual determinations were then done by the technicians in the laboratories anyhow.)

The results of my experiments were summarized in the final sentence: "Phlorhizin does not only produce renal and excretory glycosuria but an altered formation and utilization of sugar." Graph 5 illustrates one of the reasons for this conclusion. The blood sugar of this dog under normal conditions had returned to 80 mg. per 100 cc 2 hours after an 100 gm. glucose load. The blood sugar of the same dog after phlorhizin was still elevated to 180 mg per 100 cc of blood even 4 hours after the glucose.

Graph 5



Kurve 5. Hund 4. *I.* 20 Stunden nüchtern: 100 g Glykose. *II.* 20 Stunden nüchtern, 46 Stunden phlorhiziniert (1,0 g): 100 g Glykose.

However, what I would like to tell here is about rabbits 3 and 4 on the 17th, 18th and 19th of August 1926, and what their blood sugars did after injections of *adrenalin*. Table 1 shows that the blood sugars rose from 128 mg./100 cc to 198, from 135 to 243 and from 76 to 173.

EFFECT OF ADRENALIN ON BLOOD SUGAR

Datum und Zeit	Blutzucker in mg%	
17.VIII.1926		17 Stund. nüchtern
11h 20′	128	
11h 30′		1 mg Adrenalin subkutan
11h 50′	129	
12h 25′	168	
12h 50′	196	
1h 20′	198	
2h 10′	170	
3h 00′	145	
4h 00′	134	
5h 00′	104	
6h 30′	95	
18.VIII.1926		63 Stund. Hunger
9h 35′	135	
10h 00′		1 mg Adrenalin
10h 30′	221	
11h 30′	241	
12h 30′	243	
1h 45′	189	
3h 20′	165	
5h 45′	115	
19.VIII.1926		16 Stund. nüchtern
9h 30′	76	
10h 00′		1 mg Adrenalin
11h 00′	144	
12h 00′	173	
1h 00′	173	
2h 00′	136	

Table 1

In plain language: The sugar in the blood increases under the influence of adrenalin. Since adrenalin is normally produced by the adrenal gland, it is obvious that the blood sugar concentration in the body is not only regulated by the insulin from the pancreas, but likewise by the adrenalin from the adrenal gland.

It is often said a high blood sugar is caused by an inefficiency of the pancreas because of too little insulin, but one rarely hears that it is due to a hyperactive adrenal gland producing too much adrenalin. And "thereby hangs a tale": DEPRESSION OF ADRENAL ACTIVITY BY REMOVAL OF SODIUM.

I learned in the Medical School of Heidelberg where I graduated, in the pre-steroid era, that in Addison's Disease, the insufficiency of the adrenal gland caused, for instance, by the gland's destruction due to tuberculosis, one should *give lots and lots of salt* to raise the sinking blood pressure and blood sugar. So I thought to counteract an elevated blood pressure and an elevated blood sugar one should *reduce salt to a minimum.*

This has proven to be useful in both conditions, irrespective of any other substances (derived, for instance, from fat or protein) which it might be possible to eliminate. But the removal of as much salt as possible, and the concomitant restriction of fat and protein, has certainly altered the course of vascular and metabolic disease.

The first time I saw hemorrhages and exudates in the eyeground disappear from the eyegrounds of a patient under diabetes treatment with the Rice Diet was in 1943. The photographs were published 1945 in the North Carolina Medical Journal.

Thirty-three years ago in cases of malignant diabetes, frequently the adrenal and/or pituitary glands, were surgically removed. The following statement was published: (Postgraduate Medicine 24,4,1958). "The Effect of the Rice Diet on Diabetes Mellitus with or without Retinopathy has been explained by Dr. H. Ruestow as due to a reversible inactivation of the pituitary and/or adrenal gland, achieving in a conservative and unbloody way what has been tried by hypophysectomy and adrenalectomy."

One of my patients from Chicago explained to me in a very unpleasant tone when I first met him and told him that his diabetes might disappear if he followed the appropriate diet: "Diabetes does not disappear. You inherit it from your father or grandfather or

some other member of your family," and then he used a rather uncouth word. He turned out to be a rather good and nice patient and could soon do without any insulin or other medication although he had come to Durham taking 120 units of insulin daily.

The most revealing thing I learned from my patients is that it is easier to blame one's parents or grandparents and to have diabetes with all its unpleasant complications and daily insulin injections of more than 100 units, than to resist the divine taste of a high calorie, high protein, high fat and high sodium diet.

What the Fireflies Taught Us More Than 50 Years Ago

WHAT THE FIREFLIES TAUGHT US MORE THAN 50 YEARS AGO

In memory of Dr. Mercedes Gaffron
1908-1993

To Antoine Laurent de Lavoisier we owe one of the most important fundamental biological laws: "Pas de vie sans oxygène" — no life without oxygen. He was born in Paris in 1743. He was highly honored and was called the father of modern chemistry. He was decapitated with the guillotine in 1794, during the French Revolution. His death sentence was signed also by Jacques Louis David, the famous painter of the Napoleonic Era, who had once painted a picture of Lavoisier's family and was a friend of his wife.

No life of any plant, no animal life, no human life without oxygen. And how many diseases are due to a lack of oxygen! "Lavoisier" I have said many times, sitting in front of my fireplace before using the bellows to revive the fire, and to my patients I said: what you call narcolepsy or stroke, I call insufficient oxygen in the brain. What you call heart attack, I call insufficient oxygen in the heart muscle. What you call impotence, I call insufficient oxygen in the testes and their surroundings.

In 1939, I published three papers:

1) "The role of Oxygen Tension in Biological Oxidations" (Cold Spring Harbor Symposia on Quantitative Biology (Vol. VIII.)
2) "Oxygen Tension and the Tubercle Bacillus" (The American Review of Tuberculosis Vol. XL, No. 2)
3) "The Metabolism of Human Myeloblasts and its Sensitivity toward Variations of Oxygen Tension"

For paper #3, (*American Journal of Physiology* Vol. 126) I worked with Dr. Mercedes Gaffron. Before Dr. Gaffron got her medical degree in Munich, she had gotten her PhD degree in Berlin with a strangely titled dissertation "Examinations on the Perception of Movement in Dragonfly Larvae, Flies, and Fish" (Zeitschrift fuer Vergleichende Physiologie, Berlin 1937). Later, she was known for an important book on Rembrandt and was for many years a

Research Associate Professor in the Duke Department of Psychology and then a Research Associate in the Department of Medicine where she worked for many years with patients on the Rice Diet. Through her work with flies, she had become able to catch them as easily as I could turn a page in a book. I asked her to catch fireflies which, 54 years ago, were plentiful here, illuminating the surroundings of Duke Hospital as well as my garden. These fireflies we kept in closed glass vessels.

When we let oxygen-nitrogen mixtures with high oxygen concentrations into these vessels, the flies lit up. When the concentrations were low, the glass remained dark.

Recently a patient, who for over two years had been successfully using quinidine and low flow oxygen at night for nocturnal paroxysmal atrial fibrillation, was admitted to the hospital because of a fracture.

After oxygen had been omitted for a few days, this patient again had an attack of atrial fibrillation while asleep. When oxygen was re-instated, the pulse returned to normal.

Sometimes I even have had the impression that I myself "lit up" through oxygen, because when the air in my laboratory became unbearable (Duke Hospital was airconditioned only after the arrival of Dr. Stead in 1947), I opened a big oxygen tank and I thought I was better able to continue my work.

But something more quantitative I learned from a patient (Reported in the 1955 Bulletin of the Walter Kempner Foundation) who was very short of breath, very obese and had a tendency to fall asleep regardless of what he was doing. His weight on admission was 462.5 lbs. During the first five months on the rice reduction diet he lost 120 pounds. The oxygen pressure in his arterial blood increased from 68 to 85 mmHg and his complaints disappeared.

In 1977, Dr. Barbara Newborg published a paper in the Federation Proceedings (Vol. 36) "On the Effect of Weight Loss on Arterial Oxygen Pressure." Of 105 overweight patients, 87 had an average increase in their arterial oxygen pressure of 14.6 mmHg (from 69.9 mmHg to 84.5 mmHg) after an average weight loss of 51 pounds.

Maybe, the fireflies knew something that was not written in the textbooks of medicine.

W.K.

SCIENTIFIC PUBLICATIONS BY WALTER KEMPNER, MD

Volume II

Radical Dietary Treatment of Vascular and Metabolic Disorders