THE TREATMENT OF COMBINED DIABETES AND NEPHRITIS*

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Several possible etiologic relationships may be thought of between such conditions as diabetes, arteriosclerosis and nephritis. First and probably most important, there is the theory that all of these are due primarily to some infectious or toxic process, and the possibility that the same agency which damages one organ may also produce injury in one or more others. With regard to secondary influences, it is scarcely conceivable that a pure nephritis could cause diabetes. It is conceivable, however, that a primary arteriosclerosis might damage both the kidney and the pancreas. It is barely imaginable that nephritis might cause hypertension, and this lead to arteriosclerosis, which in turn might affect the pancreas. There has been in the past a strong suspicion that diabetes is a cause of arteriosclerosis, and in addition to the known frequency of association, especially in elderly persons with diabetes of many years' standing, evidence may be found in the high incidence of gangrene and the fact that this is almost invariably connected with advanced arteriosclerosis. In severe diabetes there is sometimes a form of albuminuria which clears up under diabetic treatment, and albuminuria and showers of casts are well known accompaniments or precursors of diabetic coma. Apart from such direct irritation, diabetes is a disturbance of nutritive function affecting all cells of the body, so that their power of resistance and repair is subnormal and they are more susceptible to all injuries. Diabetes may thus predispose to renal and vascular disorders by increasing susceptibility to accidental injuries. Positive proof of the foregoing interrelationships is lacking, and the evidence is chiefly statistical. The following statistical observations have a bearing on this point.

In 100 unselected diabetic cases in this institute the blood urea was found below 30 mg. per hundred c.c. in sixty-seven; between 30 and 40 mg. in seventeen; between 40 and 50 in ten, and above 50 in six. These figures are mainly those obtained at admission on undetermined diets, but the series also represents more than a thousand analyses on these patients at different stages of treatment. Renal function tests were performed especially when there was any suspicion of abnormality, and the McLean urea index was found below 80 in fourteen cases. Four of these patients were clinically nephritics; two of them were in the fourth decade and two in the fifth decade of life, and one of each pair had hypertension. In addition, there were twelve cases of hypertension with traces of albuminuria, and seventeen cases with palpably sclerosed peripheral vessels without albumin or hypertension. All of these twenty-nine patients were elderly. The sodium chlorid figures are scarcely capable of brief generalization here because of the uncertainty of normal standards, and will be given in detail elsewhere. The impression may be stated that a large proportion of diabetics show noticeably high plasma chlorid concentrations and chlorid thresholds, which perhaps have some relation to the edema of some cases and the hypertension of others. On the whole, it is doubtful whether diabetics show any higher proportion of clinical nephritis or impairment of nitrogen excretion than other hospital patients at corresponding ages; but some special tendency to retention of chlorids, vascular hypertension and arteriosclerosis may be suspected.

There has also been opportunity for study of twenty-two supposedly nondiabetic cases of renal and vascular disease. Six of these patients had marked nephritis, four of them with hypertension; the other sixteen were under treatment for hypertension alone. The question arises as to the incidence of diabetes among such patients, especially as attention has been given in the literature to the occurrence and interpretation of hyperglycemia in hypertension cases. Clinically, we must be governed by the usual criteria. The carbohydrate-rich diet customary for these patients contributes to bring out any diabetic tendency, but an impermeable kidney may sometimes prevent glycosuria. Transitory causes, special intoxications, etc., are known to affect the blood sugar in different ways; but in general, when a patient can take carbohydrate-rich diet for long or indefinite periods with blood sugar within normal limits he is said to be free from diabetes; and when, on the other hand, high diets are accompanied by hyperglycemia which yields to restriction of carbohydrate and of total calories, such a condition is properly regarded as diabetes, even though it be mild and without glycosuria. Two patients of this series were mildly diabetic in this sense, and in one of them the diagnosis was confirmed by marked hyperglycemia and slight glycosuria after ingestion of 100 gm. of glucose. The other patients of the series had normal blood sugars, and glucose tolerance tests which were performed in several of them gave normal results. It is thus evident that hypertension in itself does not produce hyperglycemia. Hyperglycemia found in such cases may be interpreted as evidence of diabetes the same as in other cases. The proportion of pancreatic changes found at necropsies in cases of hypertension and arteriosclerosis fully accords with this conclusion.

The treatment of combined diabetes and nephritis is conducted according to the usual principles for the two diseases. A special difficulty is sometimes supposed to exist in the combined management, but recent methods have largely obviated the conflict. Diabetic treatment by means of a high protein diet, gluten bread and the like may be inimical to an associated nephritis with impaired nitrogen excretion; but it is readily possible to adjust the protein ration to both diseases. If meats are forbidden in the treatment of hypertension, the diet of a diabetic with hypertension is seriously limited; but with restriction of salt[1] such a patient is able to choose his protein at will. One of the greatest dangers formerly consisted in acidosis in conjunction with nephritis; this is avoided under treatment which keeps acidosis strictly absent.

To illustrate these principles, three cases of different types, each being the worst of its type in this series, have been selected for more detailed presenta-

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1. Allen, F. M.: Arterial Hypertension, J. A. M. A. 74: 652 (March 6) 1920.

tion. The first is a youthful patient with valvular disease, severe diabetes and nephritis, with marked tendency to hypertension and nitrogen retention, but without edema, decompensation or toxic symptoms.

CASE 1.—*History.*—A man, aged 33, Irish-American, unmarried, occupation clerical, was admitted Aug. 17, 1919. His father was well at 72. His mother died at 36 of rheumatism followed by dropsy. He has one brother and one sister in good health. The family history was otherwise negative. Th ough born at full term, he was a weak, undersized incubator baby, and always sickly. He had pneumonia in infancy, and measles, mumps, scarlet fever, diphtheria, chickenpox and whooping cough before the age of 10. He never had tonsillitis or true rheumatism. At 18 he had pain in the chest most of the year, and his physician diagnosed endocarditis. The pain left after about a year, and he worked and enjoyed ordinary health, until at 25 years he had acute gangrenous appendicitis, with uneventful recovery after operation. Gonorrhea in 1913 cleared up under his physician's treatment without complications. Syphilis was denied by name and symptoms. The patient had had mild hay-fever for the last four years. He had always had a huge appetite, very active bowels and apparently good digestion, but had remained thin nevertheless. His life had been nervous and hard working but regular, with no excesses in sweets, alcohol or tobacco.

Present Illness.—In the summer of 1918 he caught cold on vacation and was surprised that he required a week to recover. He returned to work unrefreshed, and by mid-September developed thirst and polyuria. His physician then diagnosed diabetes, and stopped the glycosuria by a twenty-four hour fast. He remained at work on a diet till Feb. 22, 1919, taking an occasional fast-day when sugar returned. A well known New York consultant called by his physician at this time found his condition dangerous on account of the combination of heart disease, diabetes, nephritis and hypertension, and therefore kept him in bed for eleven weeks, part of the time on milk diet. The milk was tolerated at first, but later other low-protein diets had to be substituted to avoid glycosuria. The systolic pressure after this treatment remained as high as 218 mm., and he suffered a slight apoplectic stroke, causing partial paralysis of the left arm and right side of the face, which gradually cleared up completely. The diet meanwhile had been kept very low in protein (from 30 to 50 gm.); but about a month before admission, an increase to 75 gm. had been made for the sake of strength. His tolerance meanwhile was progressively falling, so that instead of the 100 gm. of carbohydrate which he could formerly take in his mixed diet without glycosuria, he could take only 40 gm. For three weeks before admission he was kept strictly in bed on a diet of 75 gm. of protein, 40 gm. of carbohydrate, and 1,250 calories.

Physical Examination.—The patient was 5 feet 8 inches in height, and weighed 115 pounds. He was thin and moderately weak, but still retained fair color and cheerfulness. There was no edema, and no irregularity or demonstrable enlargement of the heart; the rate was 96 per minute; the radial arteries were palpably thickened. There was a strong systolic murmur transmitted to the axilla and all over the precordia. The blood pressure was 194 systolic and 142 diastolic. The knee jerks were lively.

Laboratory Tests.—The urine was free from sugar and acetone, but contained heavy albumin and a few hyaline and granular casts, which persisted throughout treatment. The Wassermann reaction of the blood was negative. The plasma sugar was 0.176 per cent. before breakfast, August 18, the plasma chlorids 648 mg. per hundred c.c., the carbon dioxid capacity of the plasma 61.5 volume per cent., the blood urea 134 mg. per hundred c.c. The elimination of phenolsulphonephthalein was 5 per cent. (1.5 per cent. in the first hour, 3.5 per cent. in the second). The urea index, reckoned according to McLean, was 4.7.

Treatment and Progress.—The patient was received as a bed patient because of his mitral regurgitation and hypertension. Immediately after examination, as there was no cardiac decompensation and it was desired to exclude rest as a factor in relieving the hypertension, he was allowed to be up and about the ward freely, with the consequence that his blood pressures registered 206 to 214 systolic and 160 to 170 diastolic, with increased complaints of headache, dizziness and weakness. Treatment was begun with a salt-free, protein-free diet of 50 gm. of carbohydrate and 1,000 calories. This diet consisted of starch and fat, sometimes as puddings, but generally baked into cookies with a variety of flavors to avoid monotony; and, owing to the skill of the kitchen staff, the diet was as usual taken without difficulty. The progress up to September 1 is shown in Table 1.

TABLE 1.—FINDINGS IN CASE 1

			Urine				Blood				Blood Pressure	
Date, 1919	Weight, Pounds	Fluid Intake, C.c.	Volume, C.c.	Specific Gravity	Total Nitrogen, Gm.	Sodium Chlorid, Gm.	Plasma Sugar, per Cent.	Plasma CO_2 Volume per Cent.	Plasma NaCl, Mg. per 100 C.c.	Urea, Mg. per 100 C.c.	Systolic, Mm.	Diastolic, Mm.
8/18	87¼	600	1,150	—	—	—	0.176	61.5	648	134	214	170
8/19	86	800	1,030	1.010	3.25	0.97	—	—	—	—	172	146
8/20	....	150	585	1.010	6.40	0.94	—	—	—	—	150	125
8/21	84¾	450	485	1.013	2.65	0.59	—	—	—	—	165	135
8/22	....	300	485	1.012	2.84	0.71	—	—	—	—	172	130
8/23	82¾	300	470	1.012	2.47	0.53	—	—	—	—	185	130
8/24	....	700	360	1.014	2.03	0.12	—	—	—	—	189	130
8/25	81¼	5,000	910	1.007	....	0.53	0.208	53.2	616	132	189	130
8/26	....	4,100	1,890	1.004	3.56	1.12	—	—	—	—	170	130
8/27	86½	3,800	2,560	1.006	4.82	1.82	—	—	—	—	146	110
8/28	....	5,100	2,780	1.004	4.19	1.64	—	54.1	494	78	148	130
8/29	87	3,500	2,280	1.005	3.43	0.80	—	—	—	—	208	156
8/30	....	3,500	2,390	1.005	2.90	0.41	0.192	52.2	508	48	202	140
8/31	85½	4,000	2,200	1.003	3.10	0.24	— (fast day) —		—	—	195	140
9/ 1	....	600	1,490	1.004	2.60	0.46	0.134	57.0	476	36	186	132

The salt exclusion and fluid restriction up to August 25 produced a fall in blood pressure and relief of attendant symptoms, though the blood analyses were not bettered except by a slight fall in the concentration of chlorids. The nitrogen excretion was low; also the low urinary chlorids failed to show any chlorid retention in this edema-free patient sufficient to account for his hypertension. The large fluid intake beginning August 25 promptly produced dizziness, weakness, nervousness and general malaise. The increase of urine was slow and inadequate; the rise of weight indicated retention of considerable water in the body without visible edema, and there were also two or three loose bowel movements daily during this period. The blood pressures recorded are representative of several taken at different times each day; the diurnal variation was slight. In contrast to the immediate symptoms mentioned, the change in the blood pressure was slow. August 28, the pulse pressure was surprisingly and somewhat alarmingly small; thereafter the pressures rose. The fall in the blood urea and chlorids may be ascribed partly to the transitory flushing out (less evident in the nitrogen than in the chlorids of the urine), but probably mostly to dilution, though it should be noticed that such dilution did not greatly alter the plasma sugar or bicarbonate. A fast-day, August 31, improved the blood analyses, particularly the unduly high sugar.

September 1 to 9, the fluid intake (including the moisture of the food) was restricted to 600 c.c. daily, and fat was

increased so as to make the diet 50 gm. carbohydrate and 1,500 calories. Subjective symptoms were promptly relieved, and the blood pressure fell slowly to 148 systolic and 115 diastolic. The increase of the protein-free diet was intended to reduce protein catabolism to a minimum, and the urinary nitrogen actually fell by September 9 to the unusually low level of 1.3 gm. Nevertheless, with the diminished fluids, the blood urea had risen on the same date to 63.8 mg. per hundred c.c., while the plasma sugar was 0.181 per cent. and the chlorids 560 mg. per hundred c.c.

After September 9, the diet was changed to 30 gm. of protein, 30 gm. of carbohydrate and 1,200 calories, with one fast-day weekly. On this program the plasma sugar gradually fell to 0.123 per cent., September 27, and 0.105 per cent., October 13, and remained normal thereafter. The systolic blood pressure remained almost constantly below 160 mm., though the patient was up and dressed all day and spent half of every day in light tasks in the hospital or errands outside. On a few occasions of exceptional strain the systolic pressure went up for a few hours between 170 and 190. Several tests were performed with ingestion of salt as high as 10 gm. daily and water as high as 5 liters, but restoration of the hypertension by this means was impossible. The reason may be found perhaps in the improvement of the diabetes, or perhaps in the ready tendency to diarrhea. The phenolsulphonephthalein

TABLE 2.—FINDINGS IN CASE 2

		Diet			Blood			Blood Pressure	
Date, 1919	Weight, Pounds	Protein, Gm.	Carbohydrate, Gm.	Calories	Plasma Sugar, per Cent.	Plasma Chlorids, Mg. per 100 C.c.	Urea, Mg. per 100 C.c.	Systolic, Mm.	Diastolic, Mm.
9/ 4	138	Fasting	..	...	0.349	580	44	220	140
9/ 5	137	Fasting	..	...	—	—	—	204	100
9/ 6	133½	Fasting	..	...	0.176	612	47	148	88
9/ 7	130¼	(whisky)	..	210	—	—	—	152	90
9/ 8	129½	(whisky)	..	588	—	—	—	172	92
9/ 9	128¼	0	20	160	0.125	640	76	156	90
9/10	128	0	30	390	—	—	—	145	88
9/11	127¾	0	40	790	—	—	—	154	90
9/12	—	8.0	50	1,033	0.283	616	60	148	88
9/13	128	8.0	50	1,033	—	—	—	140	100
9/14	128¼	6.5	50	226	—	—	—	152	90
9/15	128½	7.0	50	1,029	0.179	—	—	146	95
9/16	128	7.0	50	1,029	0.214	580	25	162	85
9/17	127¾	30.0	50	1,201	—	—	—	126	80
9/20	128	30.0	50	1,201	0.183	592	28	134	80
9/27	128¼	30.0	50	1,201	0.185	—	33	162	84
10/ 2	127¾	30.0	50	1,201	0.178	616	—	140	85
10/ 3	129	Fasting	..	.....	—	—	—	145	90
10/ 4	126¾	37.5	40	737	0.114	576	21	172	100

elimination was improved at the lower pressures, ranging in several tests from 21 to 27 per cent. in two hours. On one or two days each week the fluid restrictions were relaxed and 30 gm. of magnesium sulphate given for eliminative purposes. With 2 gm. of sodium chlorid in the diet, the final blood analysis, November 24, revealed: plasma sugar, 0.123 per cent.; plasma chlorids, 531 mg. per hundred c.c., and blood urea, 31.3 mg. per hundred c.c. The chief unfavorable feature was that the diastolic pressure was never reduced below 108 and was more often about 115 mm. The patient was dismissed, November 24, on a diet of 30 gm. of protein, 40 gm. of carbohydrate, 2 gm. of salt and 1,300 calories, at a weight of 78 pounds.

At home, various unintentional mistakes occurred with the diet. On visits to the hospital, blood samples were taken during digestion of breakfast. The worst results were: plasma sugar, 0.25 per cent.; plasma chlorids, 623, and blood urea, 112 mg. per hundred c.c., and blood pressure 180 systolic and 130 diastolic. With further experience the results have remained equal to those in the hospital. It has become possible to change the fast-days to days of half or quarter diet. The patient has resumed his former very light clerical occupation, but can work only half time with great effort. He remains entirely well subjectively, except for the existing degree of emaciation, hunger and weakness.

Although in the majority of combined cases the diabetes or the nephritis or both are mild, this case shows that they are sometimes severe. There is no serious conflict in the treatment even here. The diabetes does not interfere with protein restriction for the nephritis, or salt restriction for the hypertension. There is an actual problem in providing the necessary calories. This is solved by undernourishing the patient to the point at which he can tolerate 30 gm. of carbohydrate. Incidentally, the unusually low protein ration raises the tolerance for carbohydrate. With this carbohydrate it is possible to fill up the rest of the diet with fat without acidosis. The relief of the hypertension relieves the heart, and the patient is capable of more exercise and work than before. At the same time the weakness of diabetes and undernutrition seems not to impair the heart but is the greatest safeguard against overtaxing it, and probably without the diabetes the heart trouble would have become worse. The diet is a hard one, because of the close restriction of carbohydrate, protein, total calories and salt. Otherwise the patient is as comfortable as though he had diabetes alone. His actual prognosis also is that of the diabetes or whichever single condition proves most dangerous, without special influence of the complications.

The second patient is a woman past middle life, with moderate diabetes and nephritis, with dangerous hypertension and retinitis, but slight tendency to nitrogen retention, edema or intoxication.

CASE 2.—This patient was No. 16 in the Rockefeller Institute series, and her history up to the summer of 1917 has been given elsewhere.[2] In two admissions to the Rockefeller Institute Hospital she had been observed by the diabetes and nephritis services, and had been dismissed symptom-free and with a good prognosis from the standpoint of diabetes, and unrelieved and with a bad prognosis from the standpoint of nephritis. The last blood pressure recorded in the publication mentioned was 250 systolic, 160 diastolic. Subsequently the patient was somewhat careless in diet and received treatment elsewhere, in the form of dietary restriction for glycosuria and two days of bed rest each week for the hypertension. The hypertension continued and there were increasing symptoms of headache, weakness, dizziness and mental confusion. Finally, dimness of vision due to an actively progressing retinitis forced her to apply for resumption of treatment, and she was admitted to the hospital, Sept. 4, 1919.

This admission was five years after her first diabetic treatment at the Rockefeller Institute. The age was now 52 years. The weight was 138 pounds, about the same as at the former discharge. The physical examination was essentially as before, except that arteriosclerosis seemed more marked in both the radial and the retinal vessels, and the heart slightly more enlarged. Its rhythm was regular, the sounds very loud, with a systolic murmur at the apex as before. There was slight edema, about equal in the face and limbs. The blood pressure was 220 systolic, 140 diastolic.

The laboratory examination revealed moderate sugar and nitroprussid reactions in the urine, slight albumin, a few hyaline casts and no blood cells. In contrast to the former strong Wassermann reactions, this test was now entirely negative in repeated examinations in the laboratory of Dr. Cyrus Field, perhaps in consequence of previous antisyphilitic treatment. The plasma sugar was 0.349 per cent.; plasma chlorids, 580 mg. per hundred c.c.; blood urea, 43.6 mg. per hundred c.c. The carbon dioxid capacity was at first slightly low (53.2 per cent. by volume), but rose quickly to 61.7 and remained normal thereafter. A single determination of the blood creatinin by Dr. Field revealed 4.2 mg. per hundred c.c.

This treatment differed from the previous treatment at the Rockefeller Institute only in the fact that the fasting was absolute, and salt was omitted from the subsequent diet. The blood pressure, which was known to have been greatly elevated for more than five years, was thus reduced very quickly and easily. The retinitis was also halted completely, whether

2. Monograph 11, Rockefeller Institute, 1919.

by relief of the diabetes or the nephritis is undetermined. The patient was discharged, October 23, at a weight of 125 pounds, on a diet of 50 gm. of protein, 30 gm. of carbohydrate and 1,500 calories, with 2 gm. of sodium chlorid. She had received 30 gm. of magnesium sulphate twice a week in the hospital with apparent benefit, and was instructed to continue this purgation at home. No rigidly normal level of blood sugar was demanded, because of the patient's age and her known tendency to break diet.

At subsequent visits she admitted minor indiscretions in both food and salt, but has held to the diet better than usual because of fears for her eyes. The worst analyses, during digestion forenoons or afternoons, have been: plasma sugar, 0.25 per cent.; plasma chlorids, 619 mg. per hundred c.c.; blood urea, 39.6 mg. per hundred c.c. The best have been: plasma sugar, 0.175 per cent.; chlorids, 605 mg. per hundred c.c.; blood urea, 22.6 mg. per hundred c.c. The highest blood pressure, found at the time of the highest plasma chlorid, was 186 systolic and 90 diastolic. The lowest pressure, found at the time of the lowest plasma chlorid, was 152 systolic and 80 diastolic. The symptoms previously associated with the hypertension now remain absent.

This patient will always be as lax in diet as she dares, and the results will therefore never be ideal. Treatment of diabetes and reduction of obesity sometimes suffice by themselves to reduce blood pressure, as illustrated by one striking case (No. 33) in the Rockefeller Institute series. This observation supports the foregoing statistical view that active diabetes creates some tendency to hypertension. The present patient illustrates the fact that a hypertension which is resistant to these measures and to rest treatment sometimes yields readily to salt privation.

The third patient represents mild diabetes under successful control, on which was superimposed a hopelessly severe nephritis, with slight hypertension and edema, but marked nitrogen retention and intoxication.

CASE 3.—*History.*—A man, aged 46, American, unmarried, physicist, was admitted, Nov. 19, 1919. The father died at 70 with diabetes; the mother at 68 of liver disease; a paternal aunt, at 70, of diabetes. One sister of the patient died in childhood; another died following a cesarean section, sugar being found in the urine after this operation. The entire family were obese. The patient had had as the only known illnesses up to the age of 7; whooping cough, two attacks of measles and some severe intestinal disturbance of unknown nature. He had "brain fever" at 8. Up to this time he had been delicate, but then began to gain weight rapidly, so that at 14 he weighed 190 pounds, and from 17 to 37 held a constant weight of 205 pounds. Life insurance was obtained in 1900. The appetite, digestion and general health had been good, and there had been no excesses except in work.

Present Illness.—In 1901, while working under great strain, the patient suffered apparently an acute nervous breakdown. A physician found the classical symptoms of diabetes, with 9 per cent. glycosuria. In a month on Osler's service at the Johns Hopkins Hospital the symptoms cleared up, and for seven years thereafter the patient carried on his full work and ignored all dietary restrictions. In 1908 the symptoms of nervous breakdown returned, and the patient spent six weeks in a well known physical culture institution, where he

TABLE 3.—FINDINGS IN CASE 3

		Diet				Urine					Blood				
Date, 1919	Weight, Pounds	Protein, Gm.	Carbohydrate, Gm.	Calories	Total Fluid, C.c.	Volume, C.c.	Specific Gravity	Albumin (Esbach), Gm. per Liter	Total Nitrogen, Gm.	Sodium Chlorid, Gm.	Plasma Sugar, per Cent.	Plasma Chlorids, Mg. per 100 C.c.	Plasma CO_2 Capacity, Volume per Cent.	Urea, Mg. per 100 C.c.	Notes
11/20	137½	1.0	67	641	—	1,040	1.010	2.0	—	5.50	0.180	659	48.1	105	Salt-free diet begun. 7:30 a.m.: R. B. C., 2,900,000. McLean index, 1.2
11/21	—	0.5	108	1,125	250	820	1.010	1.5	—	7.20	—	—	....	—	9 a.m.: R. B. C., 3,400,000
11/22	135½	0.6	110	1,581	600	700	1.010	1.5	7.4	7.40	—	—	....	—	
11/23	—	0.3	115	1,613	830	540	1.012	1.7	7.5	5.20	—	—	....	—	Magnesium sulphate, 30 gm.
11/24	136¼	0.6	110	1,504	500	570	1.013	2.6	2.4	2.80	—	—	....	—	11 a.m.: R. B. C., 3,300,000
11/25	—	0.9	105	1,568	500	340	1.013	2.0	3.7	2.60	—	—	....	—	
11/26	134	0.6	101	1,554	680	320	1.013	2.5	2.5	2.00	0.192	657	....	92	Magnesium sulphate, 30 gm. 8 a.m.: R. B. C., 3,600,000
11/27	—	0.0	52	894	—	640	1.012	1.5	7.3	4.40	0.153	660	46.2	99	10:15 a.m.: R. B. C., 3,450,000; red cell volume, 22.5%; creatinin, 3.2 mg. per 100 c.c.
11/28	—	3.6	104	1,698	1,500	450	1.011	1.8	3.3	3.30	—	—	....	—	Magnesium sulphate, 30 gm.
11/29	131¾	3.6	101	1,205	500	710	1.010	1.4	6.7	4.90	—	—	50.0	—	7 p.m.: R. B. C., 3,150,000
11/30	—	3.6	104	1,236	2,300	1,150	1.011	2.0	5.1	3.10	0.166	643	....	94	10 a.m.: R. B. C., 3,275,000
12/ 1	131	3.6	104	1,236	2,300	500	1.006	0.8	—	6.70	—	—	....	—	Magnesium sulphate, 30 gm.
12/ 2	—	3.7	98	1,414	4,900	2,100	1.007	0.8	3.5	1.60	—	—	....	—	11 a.m.: R. B. C., 3,500,000
12/ 3	133	6.0	103	1,010	—	1,480	1.007	1.0	2.5	1.70	0.144	591	....	90	
12/ 4	—	3.6	68	1,006	560	740	1.008	1.0	—	0.70	—	—	....	—	12:20 p.m.: R. B. C., 3,130,000; hemoglobin, 53.5%
12/ 5	131¼	16.0	87	1,254	1,550	2,730	1.009	—	4.6	1.00	—	—	....	—	
12/ 6	—	15.0	112	1,268	2,320	670	1.006	—	1.4	0.60	—	—	....	—	
12/ 7	132¾	18.0	99	1,069	2,165	2,410	1.006	1.3	4.8	1.06	—	—	....	—	
12/ 8	—	19.0	115	1,453	1,500	960	1.008	1.0	2.4	0.79	0.133	545	40.4	63	8 p.m.: R. B. C., 3,150,000; hemoglobin, 52.5%; creatinin, 1.5 mg. per 100 c.c.
12/ 9	131¾	12.0	96	1,504	1,300	500	1.010	—	1.8	0.35	—	—	....	—	
12/10	—	8.0	57	829	185	670	—	—	2.3	0.41	—	—	....	—	Magnesium sulphate, 30 gm. 11 a.m.: R. B. C., 3,560,000
12/11	—	15.0	87	794	560	670	—	—	2.2	0.38	—	—	....	—	
12/12	—	15.0	87	1,151	650	1,210	1.021	—	4.0	0.63	—	—	....	—	
12/13	120	15.0	87	1,151	650	560	1.035	—	2.3	0.39	—	—	....	—	
12/14	—	8.8	105	850	1,000	780	1.010	1.6	3.0	0.51	—	—	....	—	
12/15	120	8.8	105	850	1,000	650	1.016	1.1	2.5	0.31	0.184	559	57.6	112	McLean index, 1.9
12/16	—	16.0	112	1,126	750	470	1.010	1.2	1.8	0.27	—	—	....	—	5:30 p.m.: R. B. C., 2,600,000
12/17	120	26.0	89	1,514	600	820	1.009	1.0	3.6	0.60	—	—	....	—	6 p.m.: R. B. C., 2,500,000
12/18	—	25.0	100	1,784	650	250	1.012	0.5	1.3	0.15	—	—	....	—	
12/19	—	25.0	100	1,784	650	490	1.016	1.3	2.6	0.09	—	—	....	—	
12/20	—	25.0	100	1,584	700	520	1.020	—	2.2	0.20	—	—	....	—	
12/21	120	25.0	100	1,584	750	580	1.010	0	2.4	0.34	0.111	518	....	124	8:30 a.m.: R. B. C., 3,100,000; hemoglobin, 55%
12/22	—	27.0	122	1,764	800	840	1.011	—	4.1	0.60	—	—	....	—	3 p.m.: R. B. .C, 3,300,000
12/23	120	27.0	122	1,764	800	720	1.011	1.1	2.9	0.40	—	—	....	—	
12/24	—	24.5	101	1,128	680	390	1.011	1.0	1.6	0.15	—	—	....	—	
12/25	—	36.0	99	1,489	850	800	1.010	1.0	3.5	0.31	—	—	....	—	7:30 p.m.: R. B. C., 3,450,000; hemoglobin, 55%
12/26	120	24.5	101	1,128	800	570	1.010	—	2.4	0.11	0.149	555	51.9	104	8:30 a.m.: R. B. C., 3,300,000; red cell volume, 25%; hemoglobin, 55%; creatinin, 9.1 mg. per 100 c.c.

went through violent exercise without restriction of diet. He then felt well, and remained so for eighteen months, when another breakdown sent him to his physician, who placed him on a lax diabetic diet. He had lost 13 pounds at the athletic institution, and under the diet treatment lost further in weight and tolerance. In January, 1917, acetonuria began, also a sore on the little toe of the right foot, which gradually spread instead of healing.

He was admitted to the Rockefeller Institute Hospital, March 23, 1917, for diabetes and diabetic gangrene. All symptoms cleared up very easily, and a diet of 75 gm. protein, 100 gm. carbohydrate and 1,750 calories was quickly tolerated without glycosuria. The fasting plasma sugar on two occasions was 0.143 and 0.150 per cent. April 28, 1917, he was dismissed on a diet of 100 gm. protein, 50 gm. carbohydrate and 2,000 calories. The weight on admission and discharge was 162 pounds. Unfortunately, the examinations and records of the hospital period were incomplete, because Dr. Fitz, who had sole charge of the case, was called into military service about this time. Evidently no renal function tests were made, but as diabetes was the only diagnosis and no mention of albuminuria or other signs was set down, there is a strong inference that no obvious nephritis existed at that time.

The patient adhered to his diet with the exception of increasing protein somewhat, and remained free from glycosuria. In April, 1918, a hemorrhage in the left retina practically obliterated vision. Later hemorrhages occurred in both eyes, so that they have been of little use since June, 1919. There has also been an increasing development of headaches, nausea and occasional vomiting, weakness, dyspnea and palpitation on exertion, mental depression, and slight general edema, and recently pain and ulceration of the right great toe.

Physical Examination.—The patient's height was 5 feet 10 inches, and weight, 138 pounds. He was pale, weak and nearly blind, with slight edema, which was about equal in the face and limbs. The oculist reported high grade myopia, retinitis, and old hemorrhages in the vitreous in both eyes, and detached retina in the left eye. Dental caries and pyorrhea were marked. The heart was not enlarged, but there was a short systolic apical murmur. The blood pressure was 190 systolic and 100 diastolic. There was palpable thickening of the radial and other arteries. The knee jerks were diminished. The right great toe was tender, and a small ulcer at its tip oozed thin fluid,

Laboratory Examination.—The urine was negative for sugar and acetone, but contained abundant albumin and casts, which persisted unchanged throughout treatment. The Wassermann reaction of the blood was negative. Other data are given in Table 3.

The diet consisted of starch, fat and a little fresh fruit, with negligible protein and salt content. The edema cleared up and the skin became wrinkled; nevertheless the loss of weight up to November 24 was small in proportion to the chlorid excreted. The blood pressure, November 20, was 198 systolic and 100 diastolic, and by November 25 had fallen to 145 systolic and 70 diastolic. There was a question at first whether the low erythrocyte count represented entirely anemia or partly hydremia, but only a slight increase occurred under the salt privation and low fluid intake. Also with this program up to November 27, there was no important change in the plasmic chlorid or blood urea concentration. Next an attempt was made at "flushing out" by forcing fluids, but the patient could take relatively little on account of nausea. Any success of "flushing out," as judged by the nitrogen and chlorid excretion, is questionable. The body weight rose slightly while actual tissue was presumably being lost, but the blood count was not greatly altered. Under these conditions, December 8, there was found a general fall of urea, creatinin, chlorid and bicarbonate in the blood. There is no reason to assume a retention of acid as the cause of the fall in plasma bicarbonate; on the contrary, the evidence indicates a retention of fluid, in the tissues rather than in the blood, and the distribution of the dissolved substances through this fluid. More direct proof of this explanation will be presented elsewhere. At the same time the patient's condition became alarming because of vomiting, nausea, profound weakness, depression, fainting spells, blood pressure 90 systolic and 50 diastolic, hiccup, and muscular twitchings. This onset of "uremia" was apparently due to the simple excess of water. Accordingly, the fluid ingestion was sharply diminished after December 9, and for a few days was even less than shown, because partly lost by vomiting. The weight fell rapidly, and the blood analysis, December 15, revealed a rise in urea, chlorid and bicarbonate. The threatening symptoms cleared up, and the blood pressure resumed its average of about 140 systolic and 70 diastolic. Thereafter fluids were given in moderation, guided chiefly by the patient's comfort, for fear of too great retention of waste product. Nevertheless, the blood creatinin by December 26 had risen to 9.1 mg. per hundred c.c.

During the foregoing period, protein had been gradually introduced into the diet as shown. After January 1, 2 gm., after January 12, 4 gm., and after January 20, 8 gm. of salt were given daily. These quantities were disposed of without rise of weight or blood pressure, and the impression was that they were definitely beneficial in facilitating fluid ingestion and general diuresis. In this way they may have aided in reducing the blood creatinin, which at the last analysis was 3.4 mg. per hundred c.c. Various other therapeutic measures were tried. Increase of diet up to 65 gm. of protein, 165 gm. of carbohydrate and 2,000 calories failed to strengthen the patient, but ended with the following blood picture: plasma sugar, 0.217 per cent; plasma chlorids, 548 mg. per hundred c.c.; blood urea, 281 mg. per c.c.; red cell count, 1,800,000. Subsequent to December 26, the plasma carbon dioxid capacity never fell below 57.2 volume per cent.; there were no clinical symptoms of acidosis, and sodium bicarbonate administration produced no perceptible benefit. Neither digitan nor theocin seemed of any value for diuresis. Magnesium sulphate purgation failed to modify the blood analyses, and was abandoned because any possible eliminative action seemed to be overbalanced by the weakness and depression produced. Sweating by means of either the electric light cabinet or hot packs likewise seemed undesirably weakening without affecting the blood analyses.

The patient was discharged, Jan. 29, 1920, on a diet of 40 gm. protein, 100 gm. carbohydrate and 1,500 calories, at a weight of approximately 110 pounds. The final blood examination, Jan. 28, revealed: plasma sugar, 0.142 per cent.; carbon dioxid capacity, 57.6 volume per cent.; plasma chlorid, 588 mg. per hundred c.c.; blood urea, 135 mg. per hundred c.c.; red cell count, 1,960,000. The condition appeared hopeless, though some subjective improvement occurred toward the close. In February, a message was received that edema was returning, and the salt ration was therefore ordered reduced from 8 to 4 gm., and later to 2 gm. On the strict diet at home there has been gradual improvement beyond all expectations, so that the patient at present (July, 1920) performs his full daily duties in an occupation not requiring eyesight. The original intention was to report this as a completely hopeless case. The ultimate prognosis remains unchanged, but the treatment seems to have warded off acute dangers and restored comfort and working power for a considerable period.

With the ability to tolerate 100 gm. of carbohydrate, the mild diabetes introduced no difficulty in the treatment of this case. There was evidently harm in too much and too little of both salt and water, and a proper ration of both was necessary for the best diuresis and avoidance of intoxication. The reason for the development of such a severe nephritis in this case is unknown. With earlier thorough treatment there is a chance that the progress might have been arrested, or, whatever the success in other respects, the blindness could probably have been prevented.

CONCLUSION

It may be said that the majority of cases of combined diabetes and nephritis offer much hope when treated with the necessary thoroughness. By the

employment of such measures from the earliest stages, many of the distressing later consequences will be avoided.

ABSTRACT OF DISCUSSION

DR. GEORGE NORRIS, Philadelphia: Many years ago a patient came under my care who had had a severe and progressive diabetes for sixteen or seventeen years. This was before the days when we made blood analyses and when doctors were apt to be more careless about diets than they are at present, and when the subject was little understood. The patient, becoming discouraged with the treatment, decided to work out his problem for himself, which he did in an unusually scientific manner. He found that if he restricted his diet sufficiently and took enough violent exercise to produce copious perspiration every day, he could keep sugar-free. He often made careful tests of the urine several times daily. This went on for years. He finally came to see me, not for the diabetes, which he could control; but for symptoms of angina pectoris. He had an arteriosclerosis which was quite marked and considerable nephritis. His problem was this: If he took his exercise and was sugar-free he had symptoms of angina pectoris; if he omitted the exercise he was free from symptoms of angina but had sugar and diacetic acid in the urine. He decided to continue the exercise and be sugar-free, and died of angina pectoris a few months later.

DR. LEONARD G. ROWNTREE, Minneapolis: What is the relative value of the level of blood creatinin and of the McLean urea index in arriving at the status of renal function, and what influence has diet on each of them? In a group of diabetics studied by my resident, Dr. Beard, at the University Hospital, the salt intake was determined, the patients being permitted to use it at will. Many patients took as high as 20 gm., and one as high as 40 gm. of salt a day. Obviously, diabetics like salt. Even on a markedly restricted diet some of these patients put on weight and some developed edema. Should there be any limit to salt restriction in diabetes or in diabetes complicated by nephritis? We carried on some experiments on cardiorenal cases in Baltimore in which we restricted the salt intake over rather long periods. Subsequently we administered salt and found it retained, apparently without any harm to the patient. The retention seemed to indicate a body need for salt and possibly too great a restriction.

DR. FREDERICK M. ALLEN, New York: We have used chiefly the phenolsulphonephthalein, the McLean urea index and the chlorid threshold as tests of renal function, but I am not able to express an opinion concerning their significance. Creatinin did vary considerably in the last case I mentioned. The organic changes in the kidney are doubtless unalterable by functional treatment, but some disturbances, such as vascular hypertension or renal congestion, may sometimes be relieved and thus some improvement of kidney function be accomplished. The restriction of salt in diabetics is a doubtful question. Diabetics tend toward excess in all flavors and condiments. One patient stated that she ate nearly a teacupful of salt daily. No harm has been demonstrated, except in cases with edema or hypertension, but the plasma chlorids are frequently high, and on general principles we try to keep them within moderate limits. Salt restriction apparently has no bad effects in patients with high chlorid thresholds and persistently high plasma chlorids. These patients may not require the traditional 2 gm. of salt per day. Salt privation in normal persons or in patients with low thresholds causes the plasma chlorids to fall very low; the patients complain chiefly of weakness, and the proper salt ration must be determined by trial for such individuals.

Childhood Infection and Tuberculosis.—The general acceptance of the doctrine of childhood infection, as the cause of later tuberculous disease, has made child-welfare work, and all that it means in the protection of the child and the development of the child, a definite part of a broad antituberculosis program and has likewise made a knowledge of tuberculosis essential in the training of the child-welfare worker. —George T. Palmer, *Am. Rev. Tuberc.* **3**:271 (July), 1919.

A CONSIDERATION OF THE GASTRIC TEST MEAL FROM EXPERIMENTAL DATA

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Gastric analysis resolves itself into an analysis of gastric function or functional analysis and etiologic or specific analysis. These two conceptions must be sharply differentiated, before we rationally approach this subject. The time has now come for us definitely to define the meaning of gastric analysis. This demands that before we lay down the foundation stones for the interpretation of gastric analysis we have an exact conception of the nature and limitations of the gastric response in health. The literature is full of the results of gastric analyses in widely diversified clinical conditions. But the important point, and the one around which the results of all such analyses must revolve, is the knowledge of just what exactly constitutes normal and pathologic gastric function. For instance, we read that hyperacidity occurs in a certain percentage of gallbladder cases, a certain percentage of chronic appendicitis cases and a certain percentage of ulcer cases; yet no one has clearly defined exactly what constitutes hyperacidity. In our laboratories, with the collaboration of a number of chemists,[1] we were able to demonstrate that 42 per cent. of 842 complete gastric curves with all varieties of foods gave an acidity of 100 or over. Furthermore, we were able to demonstrate that while the average total acidity for beef and beef products was 120, for eggs the average total acidity was 80, and for vegetables it was 70. In other words, we were able to demonstrate clinical hyperacidity as estimated by titration findings as an absolutely normal phenomenon with some 40 per cent. of normal men; and animal proteins give persistently high acidities easily classified from clinical standards as equivalent to those encountered pathologically. These contributions emphasize the one important fact that we have failed to base our clinical interpretations on the knowledge of normal limitations in acidity. The conclusion was forced on us that there were several normal types, one clearly belonging to this group, and individuals who do belong to this group show characteristically with every variety of foodstuff a hypersecretory response. Another conclusion was that there are normal fast and slow stomachs, just as there are morphologically steer horn and J stomachs as normal variations under the roentgen ray. It is equally clear that the gastric response varies with the type of the meal, and there is more or less specificity in the response to various foods.

Again, in the consideration of low acidities, it is clear that, with the exception of certain foods, this phenomenon is not a normal one, and from our clinical studies it is equally apparent that the study of low acid curves reveals a variety of mechanisms, all of

1. Bergeim: Am. J. Physiol. **45**: 1 (Dec.) 1917. Bergeim, Evvard, Rehfuss and Hawk: Ibid. **48**: 411 (May) 1919. Fishback, Smith, Bergeim, Lichtenthaeler, Rehfuss and Hawk: Ibid. **49**: 174 (July) 1919. Smith, Fishback, Bergeim, Rehfuss and Hawk: Ibid. **49**: 204 (July) 1919. Fishback, Smith, Bergeim, Rehfuss and Hawk: Ibid. **49**: 222 (July) 1919. Miller, Fowler, Bergeim, Rehfuss and Hawk: Ibid. **49**: 254 (July) 1919. Miller, Fowler, Bergeim, Rehfuss and Hawk: Ibid. **51**: (March) 1920.