

## ON THE CHARACTER OF PROTEIN METABOLISM IN CHRONIC NEPHRITIS.<sup>1</sup>

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The study of the character of protein metabolism in chronic diseases of the kidneys thus far failed to bring to light any specific peculiarities due to the disease, nor did it bring the conviction that the nitrogenous metabolism in these conditions had a normal course.<sup>2</sup> The reason for the failure in obtaining the desired information lay in the insufficiency of the secretory function of the diseased organs. Thus, even on a diet constant in its nitrogen content the nitrogen output in nephritis varied from day to day so that v. Noorden characterized it as "bizarre." The contradictory views on the character of protein metabolism reached by individual observers is due in a great measure to this peculiarity of the eliminating capacity of the diseased kidneys. True, in many instances the conditions of the experiment were not selected with sufficient care to allow of a conclusive answer to the query. Thus, for a long time the question was debated whether or not the quantity of protein intake influenced the character of the nitrogenous metabolism. The experiments planned for the solution of this problem consisted in the following. Observations were made on the nitrogen output of patients placed on high and low protein intake. The first period

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<sup>2</sup> Fleischer, *Deutsches Arch. f. klin. Med.*, 1881, xxix, 129. Hirschfeld, *Grundzüge der Krankenernährung*, Berlin, 1891, p. 46. P. Müller, *Ueber Stickstoffaufnahme und Stickstoffausscheidung bei chronisches Nephritis*, Dissertation, Berlin, 1891. v. Noorden and Ritter, *Zeit. f. klin. Med.*, Suppl., 1891, xix, 197. Kornblum, *Virchows Arch.*, 1892, cxxvii, 409. Mann, *Zeit. f. klin. Med.*, 1892, xx, 105. Köhler, *Deutsches Arch. f. klin. Med.*, 1900, lxxv, 542. Butler and French, *Guy's Hospital Reports*, 1902, lvi, 49. v. Noorden, *Sammlung klinischer Abhandlungen*, Berlin, 1902. Rzetkowski, *Zeit. f. klin. Med.*, 1902, xlvi, 178. Mohr, *ibid.*, 1904, li, 331.

was one with low nitrogen intake; this was immediately followed by one containing a higher nitrogen intake, which was again succeeded by one with a low content of nitrogen. The conclusions reached by several authors (P. Müller, Rzetkowski, Beetles and French) were that a retention always followed a high nitrogen intake, the decrease in the intake was followed by either a loss in the output, or by an approximate equilibrium. On the basis of these experiments a diet of low protein content was recommended for patients suffering from chronic disease of the kidneys. True as the conclusion might have been, it did not necessarily follow from the recorded experiments, for the reason that a nitrogen retention following an increase in protein intake is a physiological phenomenon, and does not necessarily indicate impaired secretory function of the kidney.

More promising of results was a plan of experimentation recommended by Falta.<sup>3</sup> The patient, according to that plan, was placed in a condition of nitrogenous equilibrium on a standard diet. To this diet on the day of experiment at one time an additional quantity of protein was administered and the rate of elimination of the additional nitrogen was observed. On normal individuals, this method lead to very important conclusions; applied to a patient with chronic disease of the kidneys, it remained in the hands of Falta without definite results.

To us, it seemed probable that the failures of Falta and of other observers were due principally to the fact that in selecting the standard diet, not sufficient attention was given to one of the most important factors, namely, to the eliminating capacity of the kidneys for nitrogenous substances. *A priori*, this capacity should vary from one patient to another, and for the same patient with the condition of his kidneys. Thus, in a study of the character of protein catabolism in course of nephritis, the diet of the patient should be adjusted in such a manner that its nitrogen content does not exceed the eliminating efficiency of the kidneys for nitrogenous substances. The first step in an investigation based on that principle naturally consists in establishing the eliminating efficiency of the kidneys. This is easily determined by placing the patient on a

<sup>3</sup>*Deutsches Arch. f. klin. Med.*, 1904, lxxxix, 231; 1906, lxxxvi, 517.

low protein diet and by adding to it varying quantities of urea. The highest daily nitrogen output under these conditions indicates the eliminating efficiency of the kidneys.

The choice of the urea in preference to any other nitrogenous substance is based on the consideration that normally exogenous protein is converted nearly completely into urea, and normally a rise in nitrogen output following an increased protein intake is occasioned almost exclusively by the increase in the urea content of the urine. After the efficiency of the kidney is established, the patient should be placed in a state of nitrogenous equilibrium, on a diet with a nitrogen content somewhat below the value of the eliminating efficiency of his kidneys. The low protein intake may be maintained with impunity for a considerable length of time, as was well demonstrated by many investigations of recent years, and particularly by Chittenden<sup>4</sup> and his co-workers and by Folin.<sup>5</sup>

But even on a low protein diet, it is of importance to avoid overtaxing the kidneys at any one period of the day. This is best attainable by dividing the meals in such a manner that every intake has the same nitrogen value, and that the meals are distributed between equal intervals. Of course, it is important to observe that the daily food contains a total of calories equivalent to about forty calories per kilo weight of the patient.

The present work represents the results of experiments on a patient with chronic interstitial nephritis, performed according to the plan just outlined. The observations were continued over a period of four months.

The conditions of the experiment were the following. In order not to overtax the function of the kidneys, and in order to maintain them on an approximately equal plane of activity during all hours of the day, the patient was placed on a diet containing about 6 grams of nitrogen, the daily ration being divided into five portions, each one containing an equal amount of nitrogen. The food was given every three hours, beginning at 6 A. M. and ending at 6 P. M.; the urine was collected before each meal. On this regime the output of nitrogen by the urine was practically uniform during the entire

<sup>4</sup> *Physiological Economy in Nutrition*, New York, 1904.

<sup>5</sup> *American Jour. of Physiol.*, 1905, xiii, 66.

day. This was regarded as the standard output and served for comparison with the output on the days when the patient received, besides the diet, some one additional substance. The substances employed were urea (this was given to test the capacity of elimination), glyocol, l-alanin, d-l-alanin, asparagin and eggs. The additional food stuff or chemical was added to the first early morning meal and the nitrogen output was followed during that day in three hour intervals, and the following days in twenty-four-hour periods until the output fell to its normal level, when a subsequent experiment was made. The intake of liquids was uniform from day to day.

*History of the Patient.*—John Baptist, M., age 59; occupation, clerk; nativity, Germany; married, no children; family history negative as regards tuberculosis, rheumatism or lues. Patient had rheumatism 25 years ago, urethritis years ago. Smoked and used alcohol (beer and wine) excessively. Served in German Army three years, taking part in the Franco-Prussian War. Patient attributes his illness to exposure at that time.

Patient had first attack of acute rheumatism 25 years ago. All joints of the body were involved. He had fever and sweats and was sick for about five months. Almost every winter since, he gets an attack. In 1886, he was in Mount Sinai and German Hospitals. The joints swell, and were very painful. Attacks, as a rule, lasted from four to five months. Was not short of breath. Bowels always regular. Appetite fair. Present complaints: stiffness and weakness of arms and legs. Since 1904 he has had melæma, passing blood daily for weeks; at such times he grew very weak and suffered from dizziness. He had a second attack a year later, and a year after, a third.

Patient is of average height, weighs 160 pounds, is well nourished. Musculature good; panniculus abundant. Can walk without assistance. Scars on dorsum of left wrist and on right leg, remains of an old burn. Pupils equal, react to all reflexes. Arcus senilis. Chest of good type. Breathing normal, respiration 18 p. m. Heart, no abnormal sounds are heard. Pulse is Corrigan in quality, marked locomotion of pulse seen in both arms; 80 p.m., regular. Marked arterial sclerosis of vessels. Abdomen is normal; liver felt at free border of ribs, spleen not made out. Genitalia and rectum are normal. Gross motor power is good in upper extremities, also fair in lower. Reflexes are normal. The knee joints are enlarged, especially the right, and there appears slight swelling to inner side. Dilated veins on legs; other joints are normal. Some limitation of flexion in knee joints. Extension to full limit in knee joints painful, especially on right leg.

*Special Status February 5, 1908.*—Marked facial erythema. Pressure over this area does not cause complete blanching, and the redness immediately returns on removal of pressure. The ears show irregular areas of redness and white, and in several places are seen the small, white patches—the result of previous tophi. The erythema is found all around the neck and the anterior part of the chest, as well as in small macular patches over the shoulders and back.

Heart, outline normal. At the base, the aortic sounds are blowing in character, and the second sound is moderately accentuated. The arterial walls are markedly sclerosed, the pulse is of high tension.

The upper extremities show areas of mottling or intervals of white. The hands are cold and cyanotic. The lower extremities are somewhat livid. The reflexes are all exaggerated.

*Special Observation.*

Measurements of Blood Pressure.

Oct. 28, 1908	Systolic pressure	Right 195	Left 195	
	Diastolic pressure	Right 110	Left 105	
Oct. 30, 1908	Systolic pressure	Right 190	Left 188	
	Diastolic pressure	Right 100	Left 100	10.15 A. M.
	Systolic pressure	Right 216	Left 206	
	Diastolic pressure	Right 115	Left 104	
Nov. 2, 1908	Systolic pressure	Right 215	Left 205	
	Diastolic pressure	Right 105	Left 92	12.00 M.
Nov. 4, 1908	Systolic pressure	Right 220	Left 215	
	Diastolic pressure	Right 100	Left 105	
	Systolic pressure	Right 216	Left 202	
	Diastolic pressure	Right 104	Left 102	
Nov. 6, 1908	Systolic pressure	Right 215	Left 202	
	Diastolic pressure	Right 105	Left 100	10.00 A. M.
	Circumference in front of ankle = 10" on each side.			
Nov. 7, 1908	Systolic pressure	Right 210	Left 205	
	Diastolic pressure	Right 100	Left 105	9.30 A. M.
	Systolic pressure	Right 208	Left 214	
	Diastolic pressure	Right 105	Left 110	12.00 M.
	Systolic pressure	Right 220	Left 210	
	Diastolic pressure	Right 112	Left 110	2.00 P. M.
	Systolic pressure	Right 220	Left 210	
	Diastolic pressure	Right 112	Left 140	4.30 P. M.
	Systolic pressure	Right 218	Left 208	
	Diastolic pressure	Right 110	Left 105	7.00 P. M.
	Systolic pressure	Right 215	Left 210	
	Diastolic pressure	Right 115	Left 110	9.50 P. M.
Nov. 10, 1908	Systolic pressure	Right 212	Left 205	
	Diastolic pressure	Right 110	Left 140	10.00 A. M.
	Systolic pressure	Right 210	Left 205	
	Diastolic pressure	Right 110	Left 110	2.00 P. M.
	Systolic pressure	Right 207	Left 215	
	Diastolic pressure	Right 112	Left 115	4.00 P. M.
	Systolic pressure	Right 210	Left 195	
	Diastolic pressure	Right 120	Left 110	7.35 P. M.
Nov. 11, 1908	Systolic pressure	Right 202	Left 200	
	Diastolic pressure	Right 105	Left 100	10.00 A. M.
	Systolic pressure	Right 198	Left 198	

	Diastolic pressure	.....	Right 105	Left 105	2.00 P. M.
	Systolic pressure	.....	Right 166	Left 212	
	Diastolic pressure	.....	Right 110	Left 116	8.00 P. M.
Nov. 14, 1908	Systolic pressure	.....	Right 168	Left 160	
	Diastolic pressure	.....	Right 105	Left 105	10.00 A. M.
	Systolic pressure	.....	Right 198	Left 204	
	Diastolic pressure	.....	Right 108	Left 105	2.30 P. M.
	Systolic pressure	.....	Right 146	Left 134	
	Diastolic pressure	.....	Right 108	Left 106	8.00 P. M.
	Systolic pressure	.....	Right 225	Left 225	
	Diastolic pressure	.....	Right 120	Left 125	2.15 P. M.
Nov. 21, 1908	Systolic pressure	.....	Right 225	Left 220	
	Diastolic pressure	.....	Right 115	Left 118	11.00 A. M.
	Systolic pressure	.....	Right 198	Left 198	
	Diastolic pressure	.....	Right 120	Left 120	6.00 P. M.
	Systolic pressure	.....	Right 165	Left 170	
	Diastolic pressure	.....	Right 110	Left 115	9.00 P. M.
Nov. 24, 1908	Systolic pressure	.....	Right 218	Left 214	
	Diastolic pressure	.....	Right 110	Left 112	11.30 A. M.
	Systolic pressure	.....	Right 218	Left 210	
	Diastolic pressure	.....	Right 115	Left 120	4.30 P. M.
	Systolic pressure	.....	Right 192	Left 185	
	Diastolic pressure	.....	Right 120	Left 115	9.35 P. M.

*Blood Examinations.*

May 10, 1908.—H.b., 10 per cent.; H.b. index, 0.3; R.B.C., 1,512,000; W.B.C., 6,600. Differential W.B.C. count—B., 0; N., 75; E., 2; S.L., 8; L.L., 8; L.M., 3; Tr., 4. Nuclear count—1, 70; 2, 23; 3, 7.

May 15, 1908.—H.b., 21 per cent.; H.b. index, 0.65; R.B.C., 1,920,000; W.B.C., 8,400. Differential W.B.C. count—B., 1; N., 72; E., 1; S.L., 10; L.L., 3; L.M., 1; Tr., 12. Nuclear count—1, 71; 2, 28; 3, 1.

May 17, 1908.—H.b., 25 per cent.; H.b. index, 0.62; R.B.C., 2,088,000; W.B.C., 12,000. Differential W.B.C. count—B., 0; N., 68; E., 1; S.L., 9; L.L., 8; L.M., 4; Tr., 10. Nuclear count—1, 61; 2, 31; 3, 6; 4, 2.

May 20, 1908.—H.b., 21 per cent.; H.b. index, 0.50; R.B.C., 2,224,000; W.B.C., 8,400. Differential W. B. C. count—B., 0; N., 77; E., 4; S.L., 15; L.L., 2; L.M., 0; Tr., 2. Nuclear count—1, 67; 2, 33. Abnormalities in R.B.C.—3 nucleated red. Moderate polychromatophilia and poikilocytosis.

June 6, 1908.—H.b., 23 per cent.; H.b. index, 0; R.B.C., 2,920,000; W.B.C., 7,300. Differential W.B.C. count—B., 0; N., 69; E., 5; S.L., 8; L.L., 9; L.M., 2; Tr., 7. Nuclear count—1, 60; 2, 33; 3, 4; 4, 3.

June 22, 1908.—H.b., 30 per cent.; H.b. index, 0.5; R.B.C., 3,100,000; W.B.C., 6,200. Differential W.B.C. count—B., 1; N., 68; E., 4; S.L., 8; L.L., 6; L.M., 4; Tr., 9. Nuclear count—1, 49; 2, 50; 3, 1. Abnormalities in R.B.C. Poikilocytosis.

July 17, 1908.—H.b., 50 per cent.; H.b. index, 1; R.B.C., 3,232,000; W.B.C., 7,200. Differential W.B.C. count—B., 1; N., 69; E., 2; S.L., 8; L.L., 7; L.M., 3; Tr., 10. Nuclear count—1, 37; 2, 49; 3, 11; 4, 3.

February 2, 1909.—H.b., 100 per cent.; H.b. index, 0; R.B.C., 4,408,000; W.B.C. 9,200. Differential W.B.C. count—B., 0; N., 74; E., 1; S.L., 7; L.L., 10; L.M., 2; Tr., 6.

*Urine*.—Light colored, clear, normal odor.

*Diagnosis*.—Arthritis urica and Nephritis chronica interstitialis.

*Diet*.—The diet was composed of eggs, milk, cream, butter, bread, potatoes, farina, oatmeal, rice, cocoa, postum coffee, applebutter, peach butter and fruit. The nitrogen content and the calorific value of the daily intake are recorded in Table I.

The meals are given at 6 A.M., 9 A.M., 12 M., 3 P.M. and 6 P.M. The nitrogen content of each meal was uniform until January 7. However, it was observed that under such conditions the nitrogen output of the first three hour period was slightly lower than the average daily output, while that of the fourth was somewhat above it. The nitrogen content of the individual meals was therefore arranged so that the proportion of first meal to the following was as 1.5:1.0 and that of the fourth to the following as 0.5 to 1. Thus, for instance:

5.30 A. M.	8.30 A. M.	11 30 A. M.	2.30 P. M.	5.30 P. M.
Nitrogen gms. 1.95	1.30	1.30	0.65	1.40

#### METHODS OF ANALYSIS.

The urine was collected in three-hour samples from 6 A. M. to 9 P. M., and one sample for the night. All urines were preserved by means of toluol. Total nitrogen was determined by the usual Kjeldahl-Gunning method; ammonia, by the method of Folin-Shafer; urea, by the method of Benedict and Gephart.<sup>6</sup> This method consists in the following: five cubic centimeters of the urine and an equal volume of ten per cent. solution of hydrochloric acid are heated in an autoclave at 175° C. and the solution then rendered slightly alkaline by means of a ten per cent. solution of caustic soda. Uric acid estimations were made by the Leube-Salkowsky method; creatine and creatinine, by the method of Folin; mineral analysis, by the usual methods.

#### ANALYSIS OF RESULTS.

*Urea Experiments*.—Urea was given to the patient principally as a control to the experiments with other substances, for the rate of its elimination is regulated only by the rate of absorption and by the eliminating capacity of the kidney. In fact, the rate of elimination of this substance may be regarded as a measure of the elimi-

<sup>6</sup> *Jour. of the American Chem. Soc.*, 1908, xxx, 1760.

nating capacity of the organ. Six experiments were performed with this substance. In an early period of the experiment, urea was twice given in quantities of three grams (1.41 gram of nitrogen), and twice 6.0 grams (2.82 grams of nitrogen). It was noted that when the smaller dose was given it was removed completely in 48 hours. The days of the administration of a higher dose was noted by a marked increase in the nitrogen output, but the excessive nitrogen was not removed completely by the urine, and the output had that irregular character noted by so many observers.

The results of these experiments are briefly summarized in the following tables:

*November 4*

	T. N.	Urea N.
Intake Urea 3 g.....	5.96	4.44
On standard diet for that period .....	5.20	3.90
	<u>0.76</u>	<u>0.54</u>

*November 5.*

	T. N.	Urea N.
Intake Urea 3 g.....	6.21	4.62
On standard diet for that period .....	5.20	3.90
	<u>1.01</u>	<u>0.72</u>

In this experiment the elimination slightly exceeded the intake of urea, perhaps owing to some diuresis.

*November 7.*

	T. N.	Urea N.
Intake Urea 3 g.....	5.95	4.79
On standard diet for that period .....	5.20	3.90
	<u>0.75</u>	<u>0.89</u>

*December 9.*

	T. N.	Urea N.
Intake 6 g. Urea.....	6.16	4.67
On standard diet for that period .....	4.96	3.56
	<u>1.20</u>	<u>1.11</u>

The following days, no increase above the standard, elimination somewhat irregular.

Experiment of December 16 had the same course as that of December 9.

	<i>January 22.</i>		<i>January 23.</i>		<i>January 24.</i>	
	T. N.	Urea N.	T. N.	Urea N.	T. N.	Urea N.
Intake Urea 3 g. (1.41 g. N.).....	6.15	4.80	5.24	3.95	5.66	4.14
On standard diet for that period ....	<u>5.28</u>	<u>3.90</u>	<u>5.28</u>	<u>3.90</u>	<u>5.28</u>	<u>3.90</u>
	0.87	0.90	-0.04	0.05	0.38	0.24

Thus, on the basis of these experiments, one may regard a diet containing more than 8 grams of nitrogen as one which is apt to overtax the eliminating capacity of the kidney of our patient. A review of the experiments with other substances shows that the patient's nitrogen output rarely exceeded 6.50 grams per day, even when the diet contained nearly 9.0 grams of nitrogen.

*Glycin Experiments.*—Several experiments were performed with this substance. Also here the administration of a large quantity of the substance was followed by a retention and an irregular elimination of the excessive nitrogen intake, while after administration of moderate quantities of the substance, the excessive nitrogen was removed from the organism in forty-eight hours. Thus:

	December 3.		December 4.		December 5.		December 6.	
	T. N.	Urea N.						
Intake 20 g. Glycin (3.7 g. N.)...	5.82	4.07	5.56	4.13	5.89	4.19	5.14	3.90
On standard diet for that period ..	<u>4.96</u>	<u>3.56</u>	<u>4.96</u>	<u>3.56</u>	<u>4.96</u>	<u>3.56</u>	<u>4.96</u>	<u>3.56</u>
	0.76	0.51	0.60	0.57	0.93	0.63	0.18	0.34

In these four days, the patient removed 2.53 grams of which 2.05 grams were in form of urea, thus only about 70 per cent. of the nitrogen intake was removed by the urine.

In the second experiment, only 1.25 grams of nitrogen in form of glycin were given to the patient.

	January 11.		January 12.	
	T. N.	Urea N.	T. N.	Urea N.
Intake 7 g. of Glycin.....	5.67	4.27	6.23	4.66
On standard diet for that period .....	<u>5.28</u>	<u>3.91</u>	<u>5.28</u>	<u>3.91</u>
	0.39	0.36	0.95	0.75

Thus in the second experiment all the excessive nitrogen was removed by the urine in forty-eight hours.

There is a lack of information regarding the rate of elimination of the nitrogen after administration of glycin to normal man. Dogs generally remove in twenty-four hours all the nitrogen added in form of glycin to a standard diet.<sup>7</sup> The highest elimination occurs between the sixth and ninth hour after administration. In our patient, no special regularity of the nitrogen elimination during the

<sup>7</sup> Levene and Kober, *American Jour. of Physiol.*, 1909, xxiii, 324.

different periods of the day could be noted, even when only a moderate quantity of glycin was given.

*The Form in which the Excessive Nitrogen is Removed from the Body.*—There is not sufficient information as to the form in which the excessive nitrogen is removed by man after addition of glycin to a standard diet. In a dog all the nitrogen ingested in form of glycin is removed in form of urea. In our experiments only 80 per cent. of excreted nitrogen had appeared in form of urea.

*Alanin experiments.*—Two experiments were performed with that substance, d-l-alanin was given in one instance, l-alanin in the other. The results of the first experiments only were followed for more than one day.

After the first administration there was noted a retention and a rather irregular nitrogen output. In two days only about 40 per cent. of the excessive intake was removed from the organism. The rise was most marked between the ninth and twelfth hours of the first day. However, the intake was high, and no experiment was performed with a lower intake of alanin.

There is insufficient information regarding the rate of elimination of the excessive nitrogen after feeding the substance to a normal man. A dog removes all the nitrogen taken in the form of alanin in the course of twenty-four hours.

*Asparagin Experiments.*—Two experiments were performed with this substance. In one experiment a large quantity of asparagin containing 3.2 grams of nitrogen was given, in the other, a moderate quantity equivalent to 1.5 grams of nitrogen. The elimination of excessive nitrogen following the administration of this substance was as good as that following urea. Also here the rate of elimination was the highest after the administration of a moderate quantity of asparagin. Thus:

	January 17.		January 18.		January 19.	
	T. N.	Urea N.	T. N.	Urea N.	T. N.	Urea N.
Intake 15 g. of asparagin (3.2 g. of N.)..	6.81	5.31	6.30	4.77	6.03	4.48
On standard diet for that period .....	5.28	3.91	5.28	3.91	5.28	3.91
	1.53	1.40	1.02	0.86	0.75	0.57
	January 29.		January 30.		January 31.	
	T. N.	Urea N.	T. N.	Urea N.	T. N.	Urea N.
Intake 7 g. of asparagin (1.5 g. of N.)..	6.38	4.67	5.58	4.06	5.60	4.17
On standard diet for that period.....	5.28	3.91	5.28	3.81	5.28	3.91
	1.10	0.76	0.30	0.25	0.32	0.26

The highest increase in the output was noted in the first experiment between the ninth and the twelfth hour, and between the sixth and the ninth hour in the second experiment. During the first twenty-four hours after the administration of the high dose of asparagin, the patient removed 50 per cent. of the excessive nitrogen intake; during the same period after administration of the small dose, the patient removed 70 per cent. of the nitrogen intake. Even after administration of urea, a large quantity of not more than 50 per cent. of the excessive nitrogen intake was removed in the first twenty-four hours. In the experiment with asparagin 86 per cent. of the excessive nitrogen was removed in the form of urea. Again, on this point there is lack of information regarding the behavior of the substance in normal man, while a normal dog removes all excessive nitrogen in form of urea.

*Egg Experiments.*—Four experiments were performed with this diet. The results briefly are as follows:

	<i>February 2.</i>		<i>February 3.</i>		<i>February 4.</i>	
	T. N.	Urea N.	T. N.	Urea N.	T. N.	Urea N.
Intake 1.5 g. N.....	5.63	4.08	5.45	3.98	5.46	4.11
On standard diet for that period ..	<u>5.28</u>	<u>3.90</u>	<u>5.28</u>	<u>3.90</u>	<u>5.28</u>	<u>3.90</u>
	0.35	0.18	0.17	0.08	0.18	0.21

	<i>February 5.</i>		<i>February 6.</i>		<i>February 7.</i>		<i>February 8.</i>	
	T. N.	Urea N.						
Intake 2 g. N.....	5.68	4.26	5.97	4.45	5.54	4.31	5.88	4.44
On standard diet for that period ..	<u>5.28</u>	<u>3.90</u>	<u>5.28</u>	<u>3.90</u>	<u>5.38</u>	<u>3.90</u>	<u>5.28</u>	<u>3.90</u>
	0.40	0.36	0.69	0.55	0.16	0.41	0.60	0.54

	<i>February 9.</i>		<i>February 10.</i>		<i>February 11.</i>	
	T. N.	Urea N.	T. N.	Urea N.	T. N.	Urea N.
Intake 1.5 g. N.....	6.02	4.54	6.00	4.49	5.92	4.34
On standard diet for that period ..	<u>5.28</u>	<u>3.90</u>	<u>5.28</u>	<u>3.90</u>	<u>5.28</u>	<u>3.90</u>
	0.74	0.64	0.72	0.59	0.64	0.44

	<i>February 12.</i>		<i>February 13.</i>	
	T. N.	Urea N.	T. N.	Urea N.
Intake 1.5 g. N.....	6.12	4.50	5.73	4.24
On standard diet for that period ....	<u>5.28</u>	<u>3.90</u>	<u>5.28</u>	<u>3.90</u>
	0.84	0.60	0.45	0.34

Thus, in the first experiment the patient removed 45 per cent. of the excessive nitrogen intake; in the second, he removed nearly 100

per cent. of the intake in course of four days; in the third, about 140 per cent. in course of three days; and in the fourth, 100 per cent. in the course of two days.

Comparing the rate of elimination of the first period with that in normal man as studied by Falta, one finds the elimination lowered to half the normal rate. This low elimination can scarcely be interpreted by the deficient eliminating capacity of the kidneys, since the rise in the nitrogen output by the patient, after administration of urea and of aminoacids, was much higher than in the experiments with eggs. One would, therefore, be justified to conclude that in the first period of excessive protein feeding there was a retarded conversion of protein into aminoacids and into urea.

Of the excessive nitrogen during the first period, 70 per cent. was removed in form of urea; during the second, 83 per cent. In normal man, calculating from the tables of Folin<sup>8</sup> in his work on the influence of the nitrogen intake on the composition of the urine, one finds that there was removed from 88 to 100 per cent. of the excessive nitrogen in form of urea. In normal dogs,<sup>9</sup> the nitrogen removed in excess over that on a standard diet is always removed in the form of urea exclusively. Thus, the course of nitrogen metabolism in our patient was not completely normal, even when he was placed under conditions which prevented a retention of the end products of nitrogenous metabolism. The abnormality was expressed in a low rate of elimination of total nitrogen by the urine after administration of protein, and in a lower proportion of urea to total nitrogen of the urine, as compared with the same in normal man. On the basis of this, it seems probable that in chronic nephritis not only the eliminating capacity of the kidneys is lowered, but that also the process of protein catabolism is retarded and is incomplete. The low figures of the creatine output may be regarded as indicating the same condition.

#### CONCLUSION.

1. For the study of the character of nitrogen metabolism in nephritis the nitrogen intake of the patient needs to be regulated in such a manner that it should not exceed the nitrogen value which the diseased kidneys are capable of eliminating.

<sup>8</sup> *American Jour. of Physiol.*, 1905, xiii, 66.

<sup>9</sup> Levene and Kober, *American Jour. of Physiol.*, 1909, xxiii, 324.

2. The eliminating capacity of the kidneys can be established in the following manner: the patient is placed on a diet containing a low proportion of protein (equivalent to about 5 grams of nitrogen) and a sufficient supply of calories. To this diet from day to day varying quantities of urea are added and the nitrogen output for every twenty-four hours is estimated. The highest nitrogen output under this condition is regarded as the maximum of the eliminating capacity of the kidneys for nitrogenous substances.

3. In the observations recorded in this communication the nitrogen output of the patient on the standard diet remained at 5.5 grams per day. The addition to the diet of 1.5 to 3 grams of nitrogen in form of urea caused a rise in the intake not exceeding 6.25 grams. On the basis of this, the diet was regulated so as not to exceed a nitrogen intake of 7 grams.

4. Comparing the rate of elimination of nitrogen after the administration of glycin, alanin, and asparagin with that after the administration of urea, there was noted a slower rate after the administration of the first two acids, and an equal rate after the administration of asparagin (probably owing to the presence of an acid amid group in the molecule).

5. After the administration of excessive protein in addition to the standard diet, there was noted a much lower rate of nitrogen elimination than was to be expected in a normal man, on the basis of the work of Falta.

6. Of the total nitrogen removed in excess over that on the standard diet in our patient, 80 per cent. was in the form of urea, while in normal man, as calculated from the tables of Folin, one finds the proportion of urea to vary between 90 and 100 per cent., while in a normal dog the proportion is always 100 per cent.

7. On the basis of these observations it was concluded that in our patient the rate of conversion of protein into simple nitrogenous substances and into urea is below the normal.

8. The patient remained for four months in a condition of nitrogenous equilibrium, and otherwise in good health, on a diet containing about 6.5 grams of nitrogen and 3,000 calories, which were reduced to 2,500 calories to prevent constant gain in weight.

9. From this it seems suggestive that also for dietetic-therapeutic purposes it may be of importance to establish the eliminating efficiency of the kidneys for nitrogenous substances.

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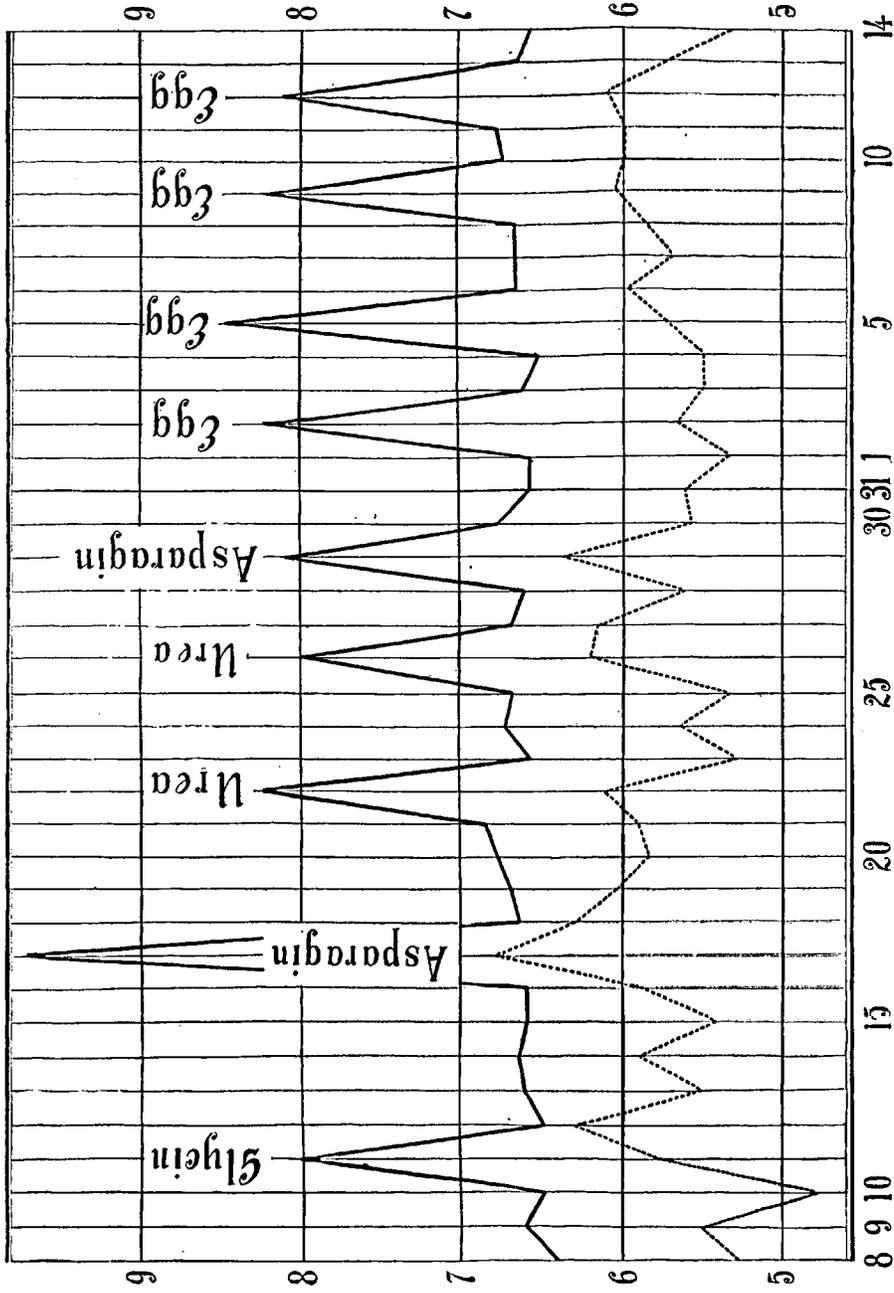


CHART I. The curve shows the relation of nitrogen output to the intake. The abscissa indicates the dates; the ordinate, nitrogen in grams. The continued line indicates the intake; the dotted line, the output.