

A STUDY OF A CASE OF DIABETES MELLITUS TREATED BY THE ALLEN METHOD

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THE following case of diabetes mellitus is reported to record an observation on the efficacy of the fasting treatment in a case of maximum severity.

Case history. J. R. J., belonging to the American Engineers, was admitted to the hospital on June 23, 1918, with the following history. He was a white American soldier, 22 years old, born in North Carolina, and had been in the army about three months. As far as could be made out his family history was negative for diabetes. Several members of his family, however, were said to suffer from 'kidney trouble'.

In 1913 (five years before entry) the patient had an operation for empyema from which he made an uneventful recovery. Except for several other minor operations he had been well in civil life and remembered no serious illness. He had done clerical work. A year previously (1917) he was refused life insurance 'on account of his kidneys' and was advised to avoid 'sweets and acids'. Five months later he reapplied for insurance and was accepted. As soon as he arrived in France (approximately June 3, 1918, three weeks before entry) he developed acutely great thirst, great appetite, and shortly afterwards increasing weakness and polyuria. Since the onset of his illness he had lost, he thought, about three stone in weight. A week before entry (June 16) he reported to his medical officer for these symptoms, and in addition on account of dizziness, headache, and shortness of breath on exertion. A specimen of urine was found to contain sugar and the man was sent to hospital with the diagnosis of diabetes mellitus.

Physical examination showed a well-developed and poorly-nourished individual with marked loss of subcutaneous fat. He seemed stuporous, but could be roused. His breath smelt strongly of acetone, and he was breathing deeply with slight 'air hunger'. His tongue was dry and furred, with throat, tonsils, and teeth not remarkable. The skin was notably dry over the entire body with a tendency to scale.

The chest was flat, with prominent clavicles. The cardiac impulse was in the fifth space nipple line. No enlargement was made out by percussion. The action was regular, not rapid (64), the sounds of good quality, and no murmurs were heard. The blood-pressure was 100 systolic, 80 diastolic. Both chests expanded equally, and were resonant throughout. No areas of consolidation were made out. No râles were heard. An X-ray plate showed no evidence of pulmonary tuberculosis. The abdomen was soft throughout. No masses or areas of tenderness were discovered by palpation. The genitals and reflexes were normal. A casual specimen of urine contained much sugar, a trace of albumin, a heavy ferric chloride reaction, and had a specific gravity of 1.036. The Wassermann reaction was negative.

From this history and these physical findings, the case appeared to be one of acute diabetes with considerable acidosis occurring in a young man without a diabetic family history, without physical or X-ray signs of tuberculosis, and without any evidence of syphilis. It was determined to follow in as much detail as possible the fasting treatment described by Allen (1).

Outline of Treatment.

According to Allen's views the best-established and most generally accepted theory of diabetes is that it results from deficiency of the internal secretion of the pancreas. As a result there is first a weakened function of carbohydrate metabolism, next a weakened function of protein metabolism, and finally, in severe cases, an imperfect metabolism of fat. For treatment, Allen has turned to experimental diabetes. When about nine-tenths of a dog's pancreas is removed, the resulting condition may appear as a progressively fatal disease. If an attempt is made to keep the dog fat and to satisfy his large appetite, he goes steadily downhill for several months and dies in extreme cachexia. On the other hand, the glycosuria can be stopped by fasting, after which the animal can be placed on a low diet insufficient to cause the reappearance of sugar in the urine, but which will support life almost indefinitely. Such an animal is thin, but strong and lively, with no cachexia and no sign of downward tendency.

Allen's treatment for patients is analogous. The first step is to fast the individual till glycosuria ceases. When the fasting patient has been sugar free for twenty-four or forty-eight hours he is fed cautiously. Usually the first food given after the fast is carbohydrate in the form of green vegetables, and this is increased in regular amounts day by day until a trace of glycosuria appears. The purpose of such a programme is to learn the carbohydrate tolerance and to clear up the last traces of acidosis. After this period protein is added until the patient shows glycosuria or reaches a safe protein ration. Fat is somewhat less urgently needed and can be added as conditions seem to indicate.

In subsequent treatment the attempt to put weight on the patient according to the time-honoured traditions of diabetic treatment is discarded. The most severe diabetic may be thin and weak because he cannot metabolize enough food to be strong or well-nourished, but as long as his weakened pancreas is not overtaxed, and as long as he remains aglycosuric, with a normal blood-sugar concentration, he seems able to retain such weight and strength as he has for at least a considerable period of time. Any attempt to build him up with any kind or quantity of food beyond that which he is able to metabolize perfectly, however, seems to hasten a fatal result. Therefore his diet is restricted to his disease and he is kept sugar free with disregard for his body weight or appearance.

On the whole, the main features wherein the outlined treatment differs from the previously established methods may be summarized under three headings. The first two represent differences merely of degree, in that the treatment is more radical than the old; namely, first an initial fast sufficient to clear up glycosuria in any case and usually one or two days longer; second, a subsequent diet to keep glycosuria and acidosis permanently absent, with as many interspersed fast-days as may be necessary for this purpose. The third feature represents differences not in degree but in kind, and is diametrically opposed to the prevalent teachings; it opposes the idea that the diabetic should be kept at the highest possible level of weight and strength and that gain in weight is synonymous with improvement; it substitutes for this the plan of keeping the severest diabetics intentionally and permanently at a sufficiently low level of weight and metabolism in the belief that return of symptoms and downward progress is thus prevented. Whatever the ultimate outcome of a given case, two conclusions seem justified by present knowledge. The treatment removes glycosuria and acidosis

more quickly and surely than has been the practice heretofore, and patients do better when glycosuria and acidosis are removed than when they are allowed to continue.

Details of Treatment.

In the present case, the above outline of treatment was followed conscientiously. At entry the patient was put to bed, giving an enema and a dose of castor oil. He was then fasted for seven days, or until he was aglycosuric for twenty-four hours, without further medication. During this time he was encouraged to drink plenty of water, was given weak tea three times a day without milk or sugar, and was allowed 1,000 c.c. of thin soup a day made from one Oxo cube. After the urine was sugar free for twenty-four hours, the patient's carbohydrate tolerance was tested by vegetables, and finally a mixed diet well within the limits of tolerance was constructed to contain enough protein to satisfy protein destruction, enough carbohydrate to prevent the development of any serious acidosis, and enough calories of food to maintain reasonable comfort. Such a course, to be without danger, demanded careful laboratory work by accurate methods so that the data obtained were reliable, and by sufficiently simple methods so that they could be carried out in a hospital such as the one existing.

A diet kitchen was established in charge of one Sister who was given exclusive care of the case. The necessary equipment consisted in a pair of scales weighing to half a gramme, a measuring cylinder, weighing dishes, and a standard table of food analyses such as Atwater and Bryant's (2).

Being summer, it was possible to buy a variety of fresh vegetables at slight expense. The Sister went to market each day and bought vegetables for the day following. Their carbohydrate, protein, and fat content were estimated from food tables, the quantities necessary for any specified diet were worked out by arithmetic, tabulated, and subsequently weighed and cooked. In this way a 'prescription diet' was ordered and accurately filled each day without undue labour or expense. The fast was broken with 10 gm. of carbohydrate, and 10 gm. were added to this initial diet each day.

Finally the patient was able to tolerate 150 gm. of carbohydrate without glycosuria. To make this diet, 315 gm. of tomatoes, 382 gm. of asparagus, 100 gm. of cauliflower, 150 gm. of cucumber, 150 gm. of spinach, 256 gm. of string beans, 112 gm. of potato, and 19 gm. of bread were used, making in all a total of 2,684 gm. of bulk. The patient ate this large amount willingly.

By this time all benefit which could be derived from a nearly pure carbohydrate diet seemed gained, and the patient was given a mixed diet containing 75 gm. of protein, 50 gm. of carbohydrate, and 1,750 calories. This diet was made from 400 gm. of tomatoes a day, 300 gm. of asparagus, 100 gm. of cabbage, 177 gm. of spinach, 55 gm. of potato, 128 gm. of cucumber, 4 eggs, 100 gm. of lamb, 97 gm. of bacon, 15 c.c. of olive oil, and 18.5 gm. of butter. The patient was kept on this for a week, gaining strength rapidly, excreting no sugar, and with normal blood-sugar concentration. He was then evacuated after a total of thirty-three days of observation.

Certain laboratory facts were essential to follow the patient's progress. It was necessary to determine the amount of sugar excreted during the period of glycosuria and to discover the least possible reoccurrence. It was important to estimate the blood-sugar concentration from time to time as maximum tolerance is not obtained and improvement does not usually occur while the blood-sugar is appreciably above normal. Since fasting was undertaken to remove acidosis as well as glycosuria this phase of the disease was studied. Finally the case showed remarkable disturbances in protein metabolism, and thus an index of nitrogen excretion was of clinical significance.

The various methods employed were simple, accurate, and required few special laboratory instruments or reagents. The urine was collected in wide-necked glass bottles by the patient himself, and was separated into four specimens each day, the first containing the urine excreted between seven in the morning and twelve noon, the second from twelve noon until seven in the evening, the third from seven in the evening until midnight, and the fourth from midnight until seven in the morning. This was done to detect traces of sugar. On two occasions a questionable trace, which was missed in a mixed specimen, appeared in one of the four specimens. It was important to detect such a trace as it was proposed to keep the patient's urine absolutely sugar free.

The specimens were measured and tested for sugar separately by Benedict's (3) qualitative test. The total twenty-four hour urine was recorded and a mixed specimen obtained for further analysis. As a routine, the specific gravity was estimated, the sugar, when present, by fermentation, aceto-acetic acid qualitatively by the ferric chloride reaction, and the urea and ammonia nitrogen by the method of Van Slyke and Cullen (4). Thus, from such simple urinalysis, sugar excretion was followed, nitrogen excretion was indicated by the accurate determination of the urea and ammonia nitrogen which represents between 80 and 90 per cent. of the total, acetone body excretion was studied qualitatively by the ferric chloride test and more quantitatively by the excretion of ammonia. The patient was bled frequently with a fine needle for observation on blood-sugar and acidosis. The blood was oxalated to prevent clotting, centrifugalized, and the plasma used for analysis. The plasma sugar was estimated by the colorimetric method of Meyers and Bailey (5). The combining power of the plasma for CO_2 was used to determine the degree of acidosis and was found by Van Slyke's (6) method. For convenience, this finding was translated into the corresponding CO_2 tension of the alveolar air—an estimation which Beddard, Pembrey, and Spriggs (7) have found of great importance in the prognosis of diabetic acidosis. The influence of fasting, of a carbohydrate diet, and of a mixed diet upon the case is shown by the following tables.

The Effect of Fasting on Glycosuria and Glycaemia.

The effect of the fast on the urinary sugar and blood-sugar is shown in Table I.

TABLE I.

Day.	Urine Amount.	Specific Gravity.	Sugar.	Blood-Sugar.
	c.c.		Grm.	%
1	2400	1034	116.0	0.58
2	1600	1035	77.3	0.27
3	2450	1023	67.2	0.27
4	3200	1014	51.5	0.27
5	2700	1012	24.9	0.25
6	3850	1007	Traces	0.24
7	3650	1006	None	0.17

As can be seen, the excretion of sugar diminished day by day as the fast continued, dropping rapidly at the beginning and end. The blood-sugar curve is more striking and demonstrates the importance of the determination. On the first day it was high and dropped suddenly. Then for five days it remained practically constant. When the patient became sugar free it was still 0.17 per cent., which is nearly double the normal. Had the patient been fed immediately upon even a low mixed diet, it is almost a certainty that he would have excreted sugar and would have had to fast again. As it was, he was given 10 gm. of carbohydrate and 60 calories, which was essentially another fast-day. This had

a beneficial moral effect upon the patient, as he knew he might expect an increase on the following day, and gave the blood-sugar a chance to become more nearly normal.

The Effect of Fasting on Acidosis and Acid Excretion.

This is shown in Table II.

TABLE II.

Day.	Urine Amount.	Specific Gravity.	Ammonia Nitrogen.	Ammonia Nitrogen Ammonia Nitrogen and Urea Nitrogen.	Ferric Chloride Reaction.	Alveolar CO ₂ Tension.
	c.c.		gram.	%		mm.
1	2400	1034	6.98	37.4	+++	20.0
2	1600	1035	2.94	20.4	+++	22.8
3	2450	1023	3.26	17.5	++	32.4
4	3200	1014	2.49	15.4	+	42.0
5	2700	1012	1.88	13.3	+	44.2
6	3850	1007	1.82	11.7	Trace	44.8
7	3650	1006	1.37	8.3	Trace	

Here, again, the effect of fasting was very striking. At entry the alveolar CO₂ tension was 20 mm., a point close to the danger mark. With fasting it rose steadily, so that on the fourth day it was within normal limits, and there was no longer a question of death by coma. During the first twenty-four hours nearly 7 gm. of ammonia nitrogen was excreted. This dropped consistently to 1.37 gm. on the last fast-day. The ratio between the ammonia nitrogen and the ammonia and urea nitrogen was equally improved. At first the ammonia represented 37 per cent. of the nitrogen so estimated, but fell by fasting to 8 per cent. six days later.

The two foregoing tables demonstrate that the patient at entry had a high blood-sugar concentration, was excreting a large amount of sugar, had developed a serious degree of acidosis, and was excreting large amounts of acetone bodies as indicated by ammonia excretion. As final proof of the severity of the case, the nitrogen excretion during the fast is offered. This is shown in Table III.

The Effect of Fasting on Nitrogen Excretion in relation to Sugar Excretion.

TABLE III.

Day.	Urine Amount.	Specific Gravity.	Sugar.	Nitrogen.*	D = N Ratio.
	c.c.		Grm.	Grm.	
1	2400	1034	116.0	19.25	6.02 = 1
2	1600	1035	77.3	17.32	4.45 = 1
3	2450	1023	67.2	18.40	3.65 = 1
4	3200	1014	51.5	19.38	2.66 = 1
5	2700	1012	24.9	18.62	1.33 = 1
6	3850	1007	Traces	18.60	
7	3650	1006	None	19.72	

* This is estimated from the urea and ammonia nitrogen, which together were assumed to represent 83 per cent. of the total nitrogen.

While the data in the foregoing table are not absolutely correct, nevertheless certain justifiable and interesting conclusions may be drawn. In the first

place, the diabetes had progressed sufficiently to upset protein metabolism to a marked degree. It is difficult to explain the large amount of nitrogen excreted at the end of a seven-day fast in any other way. Secondly, the $D = N$ ratio on the third day of the fast was approximately $3.65 = 1$. It is reasonable to believe from this evidence that, even after three days of fasting, the case was still extremely severe and almost, if not entirely, a 'total diabetic'.

The subsequent progress of the case was as follows :

The Effect of Increasing Amounts of Carbohydrate and of a Mixed Diet upon Glycosuria and Glycaemia.

TABLE IV.

Day.	Protein.	Fat.	Carbo- hydrate.	Calories.	Urine Amount. c.c.	Specific Gravity.	Sugar. gram.	Blood- Sugar. %
6		Fasting			3850	1007	Trace	0.24
8	2.9	1.0	10	61	2875	1006	0	0.17
12	21.6	5.1	50	341	3870	1005	0	0.09
15	30.4	7.8	80	525	4630	1006	0	0.10
18	39.0	9.5	100	658	3925	1009	0	0.08
24	44.2	12.5	150	911	5250	1008	0	0.10
27	75.0	132.7	50	1750	2900	1012	0	0.08
33	75.0	132.7	50	1750	2220	1018	0	0.07

The urine remained consistently free from sugar. The blood-sugar on the carbohydrate diet continued to fall, and after reaching normal remained within normal limits despite the change in diet at the end. On the twenty-fourth day, when the patient was receiving 150 gm. carbohydrate, a more careful test was made in regard to the effect of so much food upon the blood-sugar. The patient was bled before breakfast and two hours and a half after each meal, when the post-absorptive hyperglycaemia might be expected to have reached its highest figure. The result of this test is shown in Table V.

TABLE V.

Time.	Protein.	Fat.	Carbohydrate.	Calories.	Blood-Sugar %.	Urine.
7 a.m.					0.10	Sugar test negative in all four speci- mens for the 24 hours of that day
8 a.m.	14.1	3.8	45.0	278		
10.30 a.m.					0.12	
12.00 noon	16.0	5.0	52.5	326		
2.30 p.m.					0.09	
5.00 p.m.	14.1	3.7	52.5	307		
7.30 p.m.					0.12	
Total	44.2	12.5	150.0	911		

There was a slight rise in blood-sugar after breakfast and supper, but so insignificant as to justify the belief that the patient was still well within his tolerance.

The Effect of Increasing Amounts of Carbohydrate and of a Mixed Diet upon Acidosis and Acid Excretion.

TABLE VI.

Day.	Protein.	Fat.	Carbo- hydrate.	Calories.	Urine Amount.	Specific Gravity.	Ammonia Nitrogen.	Ammonia Nitrogen and Urea Nitrogen.	Ferric Chloride Reaction.	Alveolar CO ₂ Tension.
					c.c.		gram.	%		mm.
6	Fast				3850	1007	1.82	11.7	Trace	44.8
8	2.9	1.0	10	61	2875	1006	1.12	9.7	Neg.	51.0
12	21.6	5.1	50	341	3870	1005	0.49	7.7	Neg.	53.8
15	30.4	7.8	80	525	4630	1006	0.50	6.3	Neg.	49.6
18	39.0	9.5	100	658	3925	1009	0.26	3.6	Neg.	
24	44.2	12.5	150	911	5250	1008	0.32	3.4	Neg.	53.8
27	75.0	132.7	50	1750	2900	1012	0.39	3.9	Neg.	47.6
33	75.0	132.7	50	1750	2220	1018	0.71	5.7	Neg.	45.5

As might be foreseen, the ammonia nitrogen excretion dropped quickly with a carbohydrate diet to about 0.30 gram. in twenty-four hours. At the same time the ratio between ammonia nitrogen and ammonia plus urea nitrogen fell to about 4 per cent. The ferric chloride reaction disappeared and remained negative. The alveolar CO₂ tension rose, proving that all acidosis had cleared up. When the carbohydrate was cut down, and the fat markedly increased, there was an immediate slight but definite acidosis. The alveolar CO₂ tension fell from 53.8 mm. to 45.5, the ammonia nitrogen rose to 0.71 gram., and the ammonia nitrogen ratio increased to 5.7 per cent. If it had not been necessary to evacuate the case, even such a mild reaction could have been overcome by further manipulation of the diet. The diet seemed safe, however, from this observation and that of the blood-sugar, and nothing further was attempted.

The Effect of Increasing Amounts of Carbohydrate and of a Mixed Diet upon Nitrogen Excretion.

TABLE VII.

Day.	Protein.	Fat.	Carbo- hydrate.	Calories.	Urine Amount.	Specific Gravity.	Nitrogen.*
					c.c.		gram.
6	Fasting				3850	1007	18.60
8	2.9	1.0	10	61	2875	1006	14.50
12	21.6	5.1	50	341	3870	1005	7.56
15	30.4	7.8	80	525	4630	1006	9.66
18	39.0	9.5	100	658	3925	1009	8.76
24	44.2	12.5	150	911	5250	1008	11.31
27	75.0	132.7	50	1750	2900	1012	12.10
33	75.0	132.7	50	1750	2220	1018	15.12

* This is estimated from the urea and ammonia nitrogen, which together were assumed to represent 83 per cent. of the total nitrogen.

Here the sparing effect of carbohydrate upon protein metabolism is well illustrated. As soon as the fast was broken, the nitrogen excretion diminished strikingly. As the carbohydrate diet increased, and with it the protein intake

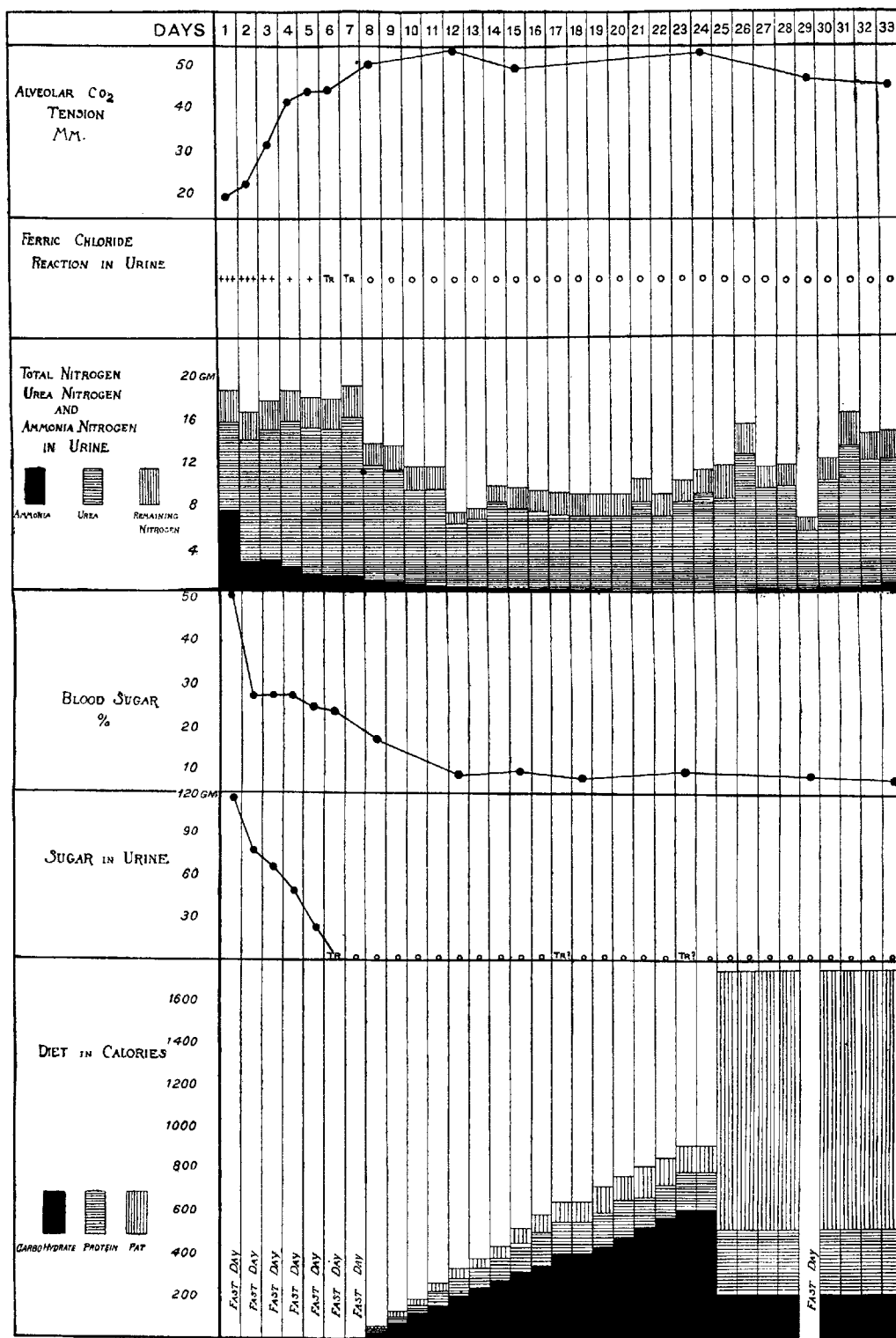


CHART.*

* The total nitrogen is estimated from the urea and the ammonia nitrogen, which together were assumed to represent 83 per cent. of the total.

to a certain extent, nitrogen excretion rose. On the last day, the patient excreted approximately 15 gm. of nitrogen upon a diet theoretically containing 12 gm. Whether this observation is absolutely true or not, it is a sufficiently marked change. After fasting seven days there was still a nitrogen loss of about 19.0 gm. per twenty-four hours, or of about 120 gm. of body protein. After his course of treatment the patient was discharged in a condition approaching nitrogen equilibrium. A graphic chart of the daily observations upon the case is added to show whatever findings have not been recorded in the tables.

Summary.

This paper reports observations upon a case of diabetes mellitus. At entry to hospital the patient had a blood-sugar concentration of 0.58 per cent. and an acidosis sufficient to lower his alveolar CO_2 tension to 20 mm. During the first twenty-four hours in hospital he excreted 116 gm. of glucose and 6.98 gm. of ammonia nitrogen. These facts show that the patient was critically ill. On the third day of a carbohydrate-free diet the patient's urine showed a D = N ratio of approximately $3.65 = 1$, and afforded additional evidence that the case was one of maximum severity. The patient was treated according to the method proposed by Allen, and illustrates its value in a favourable case. A seven days' fast was necessary to render the patient's urine free from sugar. At the end of this period the blood-sugar had fallen to 0.17 per cent., the alveolar CO_2 tension had risen to 44.8 mm., the ammonia nitrogen excretion had fallen to 1.37 gm., and the patient's condition was much improved.

After the urine was sugar free, the carbohydrate tolerance was tested by a systematic daily increase in as pure a carbohydrate diet as was possible to be obtained in the form of green vegetables. The patient tolerated 150 gm. of carbohydrate by this method without becoming glycosuric. During this time the blood-sugar fell to normal, and was not found materially increased on the last day of the test, when repeated bleedings were made to determine the degree of post-absorptive hyperglycaemia. During the period of carbohydrate feeding, the alveolar CO_2 tension remained high, and the ammonia nitrogen excretion dropped to about 0.30 gm. in twenty-four hours, showing that all acidosis had disappeared. The carbohydrate-sparing effect on protein metabolism was demonstrated. The nitrogen excretion dropped from about 19 gm. in twenty-four hours on the last day of the fast, to about 7.5 gm. when protein intake was low. As the vegetable protein intake increased considerably the urinary nitrogen increased somewhat.

After thirty-three days' observation the patient was discharged from hospital in good condition with normal blood-sugar concentration, with trivial acidosis, and approximately in nitrogen equilibrium upon a mixed diet within his tolerance, yet ample for his bodily needs.

REFERENCES.

1. Allen, *Boston Medical and Surgical Journal*, 1915, clxxii. 241; *American Journal of Medical Science*, 1915, cl. 480; *ibid.*, 1917, cliii. 313.
2. Atwater and Bryant, *United States Department of Agriculture*, 1906, Bulletin 28.
3. Benedict, *Journal American Medical Association*, 1911, 1193.
4. Van Slyke and Cullen, *Journal Biological Chemistry*, 1914, xix. 211.
5. Meyers and Bailey, *ibid.*, 1916, xxiv. 149.
6. Van Slyke, *ibid.*, 1917, xxx. 347.
7. Beddard, Pembrey, and Spriggs, *Lancet*, 1903, i. 1366.