DIABETES MELLITUS IN CHILDREN

REPORT OF TWO CASES WITH A STUDY OF THE URINARY NITROGEN *

P. C. JEANS, M.D.
ST. LOUIS

Frequency.—From time to time reported cases of diabetes in childhood have been collected, the first such collection having been made by Kulz in 1878, and the last by Morse¹ in 1913. There are now on record more than 1,000 cases, in which an equal distribution between boys and girls and an incidence increasing with the age are observed. Though over 100 cases in children under 1 year of age have been reported, there is nothing in the majority to show that the sugar was glucose, and it is quite probable that many of these were cases of lactosuria. Knox,² in going over the literature in 1911, could find but 16 cases which he regards as true diabetes. In Morse's collection there are 200 children under 5 years of age, which, considering the time period covered by the survey, makes the disease at this early age almost a rarity. It has been estimated that among diabetics of all ages, the childhood incidence is about 2 per cent.

Prognosis.—The prognosis in children has been regarded by all writers on the subject as grave, no matter how mild in the beginning or how gradual in development. Among the collected cases there are twenty-six patients reported as recovered, but the proof of recovery is satisfactory in less than ten, one third of the cases having been followed but three months or less. On the basis of ten recoveries in one thousand cases there has been a mortality of 99 per cent.

*The Allen Treatment.*³—No one can say what is now the ultimate prognosis of diabetes in childhood under the new régime which more than vaguely promises a long life of good health if not a permanent cure. There are no case reports of children under this new régime to show even its immediate effects. Since the publication of Allen's work there have come under our observation two cases of diabetes mellitus in childhood which will be reported in detail.

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* From the Department of Pediatrics, Washington University Medical School, and St. Louis Children's Hospital.

1. Morse, J. L.: Boston Med. and Surg. Jour., 1913, **168**, 530.

2. Knox, J. H. Mason, Jr.: Bull. Johns Hopkins Hosp., 1913, **24**, 274.

3. Allen, F. M.: Studies Concerning Glycosuria and Diabetes, Harvard Univ. Press, Cambridge, Mass., 1913; *ibid.*, Jour. Am. Med. Assn., 1914, **58**, 539; *ibid.*, Boston Med. and Surg. Jour., 1915, **172**, 241; *ibid.*, Am. Jour. Med. Sc., 1915, **150**, 480; *ibid.*, Boston Med. and Surg. Jour., 1915, **173**, 743.

REPORT OF CASES

CASE 1.—The patient was a girl 2 years of age.

Family History.—The father, mother and one older child are all in good health and there is no history of diabetes in the family.

Past History.—The patient was born spontaneously at term, was breast fed, and developed normally both mentally and physically. There has been no illness except as is mentioned below.

Present Illness.—The patient first came under observation Dec. 30, 1914, for frequency of urination, which had been present for three weeks following an intestinal disturbance. She received treatment for this condition for one month, with improvement. During this month of observation she gained in weight from 11.15 to 11.94 kg. and three urine examinations showed nothing abnormal. She again came under observation May 11, 1915, with the history of having had measles during the latter part of March, with which she had been very ill for three weeks. The urine was not excessive or troublesome before the measles, but did become so immediately afterward. At this time the mother noticed that the diapers were sticky, and a few days later sugar was found in the urine by the family physician. The polyuria was associated with greatly increased thirst, demanding water numerous times during the night. Sleep was broken and restless. When obtained on May 11, the urine caused abundant reduction of Fehling's solution and fermented with yeast. The child was admitted to the St. Louis Children's Hospital May 22, 1915, at which time the general physical examination revealed nothing of importance. She was exceedingly well nourished and did not appear ill, though she was irritable and had general malaise. The Wassermann reaction was negative. Her weight on admission to the hospital was 11.6 kg. and her age was 26 months.

Progress.—On the regular hospital diet the patient excreted 46 gm. of sugar in twenty-four hours. With the institution of fast she became sugar-free in the first twenty-four hours and at the same time her increased thirst disappeared and the amount of urine decreased abruptly from 1,500 c.c. daily to 700 c.c., and later to much less than this. She slept well at night and her general disposition improved. With a gradual increase in the diet over a period of three weeks, she showed glycosuria on a diet having a value of 870 calories and including 22 gm. of carbohydrate. Following another fast day she remained sugar-free on various diets (Table 1) until she was discharged from the hospital, Nov. 24, 1915. The successful handling of several of these diets indicates an increase in her tolerance. Her diet at home was practically a constant one and she remained sugar-free and in good health for a month, when she returned with an acute bronchitis and a slight glycosuria. The bronchitis was rather severe and there was considerable fever for three days. On readmission to the hospital, Dec. 17, 1915, she received, by mistake, a diet slightly in excess of the previous allowance, and yet the urine became sugar-free, with improvement of the acute infection. She was discharged December 24 with a lower diet. The urine was examined almost daily and sugar was found on March 8 and March 14, 1916. She had been having a carbohydrate free diet one day each week. The patient was readmitted to the hospital March 15, 1916, when she was again fasted and discharged with a lower diet. She remained sugar-free and free from complaints until Nov. 7, 1916, when, associated with a slight indigestion and a coryza, she again had a small amount of sugar in the urine. She is now sugar-free and in good health. Her weight in November, 1916, was 13.6 kg.

Discussion of Case 1.—The criteria of the condition of a diabetic are the amount of sugar in the urine and blood and the degree of acidosis. The degree of acidosis may be measured in a variety of ways, but the common methods, and the ones used in these cases, are the

amounts of acetone bodies excreted in the urine and the urinary ammonia coefficient. At no time was the acidosis of such a degree as to give distinct clinical manifestations, though during all observation periods the amount of acetone bodies in the urine was definitely increased above the normal. During the last period the amounts were strikingly less than before. Following each fasting period there occurred a marked increase in the acetone bodies, which made but a short curve, quickly returning to a lower level as food was allowed. This increase was rather to be expected, but the decrease which occurred in every instance on the day of fast seemed unusual and is in distinct contrast to the behavior of the normal child. This phenomenon might be the object of considerable speculation, though the most plausible explanation would seem to be the sudden withdrawal of protein with its acetone body precursors, together with the availability of stored glycogen in sufficient amounts to protect the normal combustion of fats. As the stored glycogen decreases, there occurs an increase in acetone bodies, as in any other patient. The more acetone body formation is studied the more complicated does the question become, and whether or not this phenomenon is to be explained in this way, the fact itself is of interest.

The ammonia followed the acetone curve fairly closely, though it seemed somewhat delayed in excretion. At all times the ammonia coefficient was found increased over that found in normal children. During the last period the ammonia, as well as the acetone bodies, was lower than in previous periods, which is encouraging in the prognosis for this patient.

The values given in the accompanying tables for blood sugar are lower than other published observations, probably due to the method employed. The method followed was that of Shaffer,⁴ who, in his paper, discusses the difference in results by his method and by previously published methods. Whatever criticism may be directed against any method in current use as being an absolute measure of blood sugar, still leaves that method of value in determining comparative results. To determine the normal value by this method a number of presumably normal children from 2 to 3 years of age were selected and blood samples were taken after a night of fast and before breakfast. The normal values thus obtained varied closely in the neighborhood of 0.05 per cent. If the sample was taken later in the day, after food had been given, the values were higher. The figures in the accompanying tables represent the morning fasting values.

Relatively few observations have been made of the blood sugar in this patient, but there is a sufficient number to show that there has

4. Shaffer, P. A.: *Jour. Biol. Chem.*, 1914, **19**, 285.

TABLE 1.—DATA

Date, 1915	Diet				Calories		Weight, Kilos
	Fat	Protein	Carbo- hydrate	Alcohol	Total	Per Kilo	
May 25*.....	..	..	..	..		..	
27.....	65	34	27	0	855	73	11.66
28.....	65	34	27	0	855	73	
31.....	87	42	30	0	1,110	97	11.38
June 1.....	87	42	30	0	1,110	97	
2.....	0	0	0	25	175	15	
3.....	21	5	0	0	215	20	
4.....	43	14	4	7	520	47	
5.....	41	19	13	9	575	53	10.83
7.....	54	25	13	9	720	68	10.63
9.....	54	25	13	9	720	68	10.60
11.....	54	25	13	9	720	66	10.91
12.....	54	25	13	9	720	65	11.06
15.....	64	32	13	9	840	73	10.86
18.....	68	35	13	4	890	81	10.89
21.....	72	39	22	0	870	73	11.14
23.....	0	0	0	25	175	16	11.14
24.....	17	4	0	16	235	26	10.99
26.....	51	21	13	13	705	67	10.52
28.....	55	20	16	11	735	71	10.40
30.....	66	25	13	11	850	80	10.69
July 2.....	76	32	13	9	950	89	10.66
5.....	76	32	13	9	950	87	10.89
9.....	76	32	13	9	950	88	10.86
16.....	76	32	13	9	950	88	10.77
20.....	76	32	13	9	950	85	11.14
23.....	76	32	13	9	950	85	11.25
27.....	76	32	13	9	950	87	10.97
Aug. 5.....	76	32	13	9	950	87	11.00
7.....	80	35	13	4	995	90	11.05
12.....	84	39	22	4	1,060	93	11.43
Sept. 8.....	84	39	22	4	1,060	91	11.66
20.....	84	39	22	4	1,060	89	11.96
28.....	76	29	27	4	965	81	11.99
Oct. 9.....	76	29	27	4	965	80	12.04
11†.....	80	35	18	0	970	85	11.43
21.....	80	35	18	0	970	81	11.99
29.....	80	35	18	0	970	80	12.07

* Hospital diet.

† The heading "Acetone" includes diacetic acid. Beta-oxybutyric acid is recorded as acetone.

‡ Oct. 10, 1915, was a fast day.

OF CASE 1

Blood Sugar, r Cent.	Urine				Urinary Nitrogen				
	Amount, C.c.	Sugar, Gm.	Acetone,† Mg.	B. oxy- butyric, Mg.	Total N, Gm.	Ammonia N, Mg.	Creatinin N, Mg.	Creatin N, Mg.	Uric Acid N, Mg.
.....	1,020	46							
.....	1,480	14	...		5.01	1,080	55	..	49
.....	1,490	14	...		5.40	980	53		
.....	1,300	23	487	1,157	5.41	820	46	39	63
.....	1,485	27	438	1,276	4.48	850	47	45	88
.....	700	0	...		2.49	300	36	..	40
.....	715	0	240	1,024	1.93	300	28	38	25
.....	765	0	360	1,590	2.63	500	37	38	53
0.045	880	0	310	1,440	3.26	600	36	46	45
.....	935	0	140	430	3.34	600	34	39	38
.....	715	0	120	140	2.24	300	25	35	43
.....	705	0	200	230	3.21	410	32	42	51
.....	555	0	60	140	1.85	200	27	29	38
.....	555	0	160	620	2.36	360	28	35	41
0.067	580	0	160	670	4.10	670	38	42	65
0.068	675	1	287	590	4.59	370	52	57	59
.....	875	0	87	160	2.52	480	47	49	50
0.080	625	0	350	2,300	2.72	510	41	72	29
.....	520	0	320	1,320	2.14	620	34	38	60
0.047	735	0	220	770	2.68	770	41	39	49
.....	545	0	106	300	1.88	354	31	32	35
.....	495	0	131	463	3.09	390	31	41	45
.....	605	0	188	658	2.84	418	27	48	45
.....	510	0	125	378	2.91	304	..	..	44
.....	375	0	454	1,040	2.65		43	55	54
.....	525	0	131	361	3.05	367	32	49	41
.....	410	0	227	439	2.20	340	25	34	21
.....	390	0	226	480	2.60	557	36	39	31
.....	660	0	545	1,240	3.20	702	33	38	32
.....	550	0	...		2.54	495	34	..	38
.....	525	0	131	400	2.40	327	31	..	35
.....	400	0	180	870	2.63	567	41	32	
.....	500	0	110	423	3.01	387	37	52	33
.....	610	0	137	200	3.77	423	49	67	47
0.061	330	0	201	975	2.40	293	35	46	40
.....	460	0	722	2,400	4.09	968	46	79	68
.....	295	0	94	280	2.95	300	28	41	32
.....	350	0	222	890	2.25	287	32	49	37

TABLE 1.—DATA OF

Date, 1915	Diet				Calories		Weight, Kilos
	Fat	Protein	Carbo- hydrate	Alcohol	Total	Per Kilo	
Nov. 19.....	80	35	18	0	970	78	12.48
Dec. 18.....	84	39	22	26	1,235	..	
20.....	84	39	22	26	1,235	100	12.39
21.....	0	0	0	25	175	14	12.24
23.....	84	34	13	0	980	80	12.28
1916							
Mar. 16.....	80	35	18	0	965	73	13.14
17.....	0	0	0	25	175	..	
18.....	65	20	20	0	765	..	
19.....	65	20	20	0	765	59	13.05
21.....	65	20	30	0	810	62	13.14
22.....	65	20	40	0	850	65	13.14
23.....	65	20	50	0	890	68	13.17
24.....	65	20	60	0	930	70	13.22
25.....	0	0	0	25	175	13	13.25
26.....	35	13	10	0	420	..	
27.....	65	20	20	0	770	59	12.94

TABLE 2.—DATA

Date, 1915	Diet				Calories		Weight, Kilos
	Fat	Protein	Carbo- hydrate	Alcohol	Total	Per Kilo	
Nov. 25*.....	..	..	..	..		..	
27.....	69	38	31	0	925	56	16.14
28.....	69	38	31	0	925	..	
Dec. 1.....	77	45	40	0	1,065	67	15.91
2.....	81	48	45	0	1,135	71	15.91
3.....	81	48	55	0	1,175	73	16.19
4.....	81	48	65	0	1,215	74	16.39
5.....	81	48	75	0	1,255	76	
6.....	0	0	0	24	170	10	16.00
7.....	13	3	0	6	175	11	15.70
8.....	55	20	16	9	675	44	15.43
10.....	66	26	13	9	835	53	15.67
12.....	76	32	13	9	955	61	15.64
14.....	80	36	18	0	965	61	15.75
17.....	84	39	22	0	1,065	66	15.72
20.....	84	41	22	0	1,040	67	15.61

* Hospital diet.

† The heading "Acetone" includes diacetic acid. Beta-oxybutyric acid is recorded as acetone.

‡ The blood sugar is charted opposite the diet which it represents. The determination was made the following.

CASE 1—(Continued)

Food gar., Cent.	Urine				Urinary Nitrogen					
	Amount, C.c.	Sugar, Gm.	Acetone, [†] Mg.	B.-oxy- butyric, Mg.	Total N, Gm.	Am- monia N, Mg.	Creat- inin N, Mg.	Creatin N, Mg.	Uric Acid N, Mg.	Urea N, Gm.
.054	430	0	267	895	3.37	537	44	60	31	
....	345	2	400	1,350						
....	340	0	272	650	3.88	467	40	57	50	
.089	375	0	160	574	2.14	234	39	45	34	
....	250	0	557	884	2.92	610	32	50	64	
.071	850	0	520	2,090	4.55	589	48	72	28	3.35
....	500	0	95	234	2.49	413	41	64	47	1.53
.041	345	0	46	1,610	3.82	700	43	73	46	2.45
....	300	0	353	1,160	3.31	667	39	52	52	1.92
....	325	0	85	103	3.07	431	44	53	77	2.01
....	210	0	70	149	2.48	266	45	53	58	1.73
....	355	0	50	55	2.24	200	43	58	58	1.52
....	380	0	52	50	2.27	194	45	55	54	
.060	315	0	24	35	1.73	156	41	46	41	
....	345	0	98	214	2.76	251	50	67	58	
....	525	0	180	440	2.50	309	42	49	43	

IF CASE 2

Food gar., Cent.	Urine				Urinary Nitrogen				
	Amount, C.c.	Sugar, Gm.	Acetone, [†] Mg.	B.-oxy- butyric, Mg.	Total N, Gm.	Ammonia N, Mg.	Creatinin N, Mg.	Creatin N, Mg.	Uric Acid N, Mg.
....	810	40	255	846	6.30	494	126	208	93
....	535	0	410	1,720	5.92	571	81	130	84
.057	660	0	235	709	6.76	870	84	117	131
.053	705	0	220	16	5.92	422	77	55	95
....	665	0	145	88	5.99	396	70	61	108
.062	565	0	80	71	6.06	349	86	55	99
.074	860	0	70	55	6.80	379	98	59	102
.063	605	1	45	22	4.78	277	59	61	82
.084	805	0	280	66	5.03	251	86	47	90
.085	430	0	219	900	4.21	255	48	95	48
.059	455	0	420	2,400	4.44	454	67	87	72
.049	500	0	154	242		293	65	..	60
....	650	0	205	431	4.41	474	57	50	58
.058	655	0	108	270	4.03	377	71	32	64
.052	490	0	81	157	5.88	471	..	27	77
.050	350	0	153	272	3.60	235	64	29	33

been at no time after starting treatment a very marked hyperglycemia. It is generally stated that the blood sugar of normal individuals does not decrease appreciably below the normal level with a short fast, and such also has been our experience. It is stated, also, that a high blood sugar in diabetes is not lowered as quickly as in normal subjects, though a subnormal drop in blood sugar following fast is very noticeable in this patient.

At the beginning of observation this patient had an average body weight for her age, 11.6 kg. During the first year of observation there was a gain of 1.4 kg., and during the first six months of the second year there has been a gain of 0.6 kg. There has been a considerable increase in her body length, and it is evident that her growth has been at the expense of her stores of body fat. She is now below the average weight for her age.

Summary of Case 1.—A moderately severe case of diabetes mellitus in a 2-year-old girl, coming under observation early and remaining under observation one and one-half years, was made sugar-free by an initial fast, and remained sugar-free throughout the observation period except for five occasions. One of these was due to intentional over-feeding, and another was the result of an acute infection. The other three occasions were transient and occurred only on the days mentioned. There has been complete relief of the subjective symptoms and the polyuria, and there is considerable evidence that her tolerance has increased. At no time was the evidence of acidosis sufficient to draw any especial attention to it. Though she is by no means cured, there seems to be no good reason why she should not have a long life, free from diabetic symptoms.

CASE 2.—The patient was a boy aged 3 years.

Family History.—The father and mother and the child of the first pregnancy are in good health. A Wassermann reaction on the mother was negative. The second and fourth pregnancies resulted in miscarriage. The fifth pregnancy resulted in a premature birth at six and one-half months, the child of which died of bronchopneumonia at 9 months.

Past History.—The patient was the child of the third pregnancy and was delivered by means of forceps at term. He was normal at birth and continued so for several months. From the age of 6 months he was frequently brought to the Children's Hospital dispensary for various minor ailments. During infancy he was an overfed, condensed milk baby, fat, but having recurring attacks of diarrhea, with one of which at 21 months he had two convulsions. Condensed milk was continued both with this baby and the succeeding one, contrary to all advice, which illustrates the parental attitude to our instruction. The patient cut his teeth, walked and talked at the usual age. There was an acute bronchitis at 18 months and again at 2 years. Aug. 16, 1915, he became ill with measles, which ran a mild course.

Present Illness.—He was admitted to the Children's Hospital, Nov. 25, 1915, having had polyuria and increased thirst for two weeks. These symptoms were associated with loss of appetite, slight loss of weight and a definite bread hunger. There were no other complaints.

Examination.—The patient was well nourished and apparently in good health. There were several features that suggested dyspituitarism. The hands were spade-like and the skin was dry. The fingers were of the shape seen in acromegals. The hands and feet were large and the stature was somewhat above the normal. Roentgenograms of the sella turcica and of the feet and hands showed no abnormalities.

Progress.—On the regular hospital diet the patient excreted 40 gm. of sugar in twenty-four hours. On restricted diet without fast he became sugar-free in the first twenty-four hours, and with a gradual increase in the diet he again had glycosuria when the diet reached the value of 76 calories per kilogram and included 75 gm. of carbohydrate. Following a fast he became sugar-free and remained so on his subsequent diet until April 3, 1916, a period of four months. After this time the parents refused to keep him under supervision and the dietary restrictions were largely removed. He is said to have remained in good health until June 1, 1916, when he became ill. June 2 he was admitted to the Children's Hospital in coma. At this time he had deep, pauseless respirations at the rate of 52 per minute, his temperature was 102.4 F., and there were râles at the bases of both lungs. Following the intravenous administration of 150 c.c. of 4 per cent. sodium bicarbonate solution, the respiratory rate decreased to 36, the patient recognized his mother and held simple conversation. Four hours later he was again comatose and the respiratory rate was 70. Following intravenous administration of sodium bicarbonate he became more quiet at once, and at no time later did he show air-hunger breathing. The urine for twenty-four hours, from June 2 to 3, measured 100 c.c., and showed much albumin and many casts. There was no sugar. The ammonia nitrogen was 24 per cent. of the total nitrogen. The urine for twenty hours from June 3 to 4 measured 465 c.c. and showed much albumin and many casts. There was 1.2 gm. sugar and the ammonia nitrogen was 12 per cent. of the total nitrogen. Examination of the blood on June 3 showed, per 100 c.c., 103 mg. of nonprotein nitrogen, 38 mg. of acetone and diacetic acid and 75 mg. of beta-oxybutyric acid (as acetone). The blood sugar was 0.3 per cent. The blood on June 4 showed, per 100 c.c., 41 mg. acetone and diacetic acid and 107 mg. beta-oxybutyric acid (as acetone). The blood sugar was 0.4 per cent. The white cell count on June 3 was 60,000, of which 70 per cent. were polymorphonuclear cells. Death occurred on June 4, being preceded by several clonic convulsions. A necropsy was refused.

Discussion of Case 2.—When this patient first came under observation there was some question as to whether the case was one of true diabetes or a transient glycosuria. Though he had a high tolerance for carbohydrate, there was considerable evidence in favor of the diagnosis of diabetes. There was at all periods except one a distinct tendency toward acidosis, as shown by the laboratory findings. In the twenty-four-hour period which makes the exception he received 75 gm. of carbohydrate and showed a glycosuria. He showed a hyperglycemia while receiving from 55 to 75 gm. of carbohydrate in twenty-four hours, and a fairly marked subnormal drop in blood sugar following fast. The twenty-four-hour amount of urine was not excessive, but he was removed from the regular hospital diet and routine so quickly after admission that this point was not well determined. There was a definite polyuria before admission. The thirst and polyuria quickly disappeared under treatment, but the bread hunger remained.

The marked increase in the acetone bodies on the day of fast differs

from Case 1 and corresponds to the normal child. Otherwise the figures for the acetone bodies and for ammonia are similar in kind though not in degree to those of Case 1.

Up to April, 1916, at which time his visits ceased, the prognosis seemed good. As Allen states, there are two factors which determine the success of treatment, the scientific and the human factor. In Case 1 the human factor is found at its best, while in Case 2 this factor was apparently the point of failure, this being by far the milder of the two cases. The scientific factor was the same in both instances.

Aside from possible pneumonia, there is evidence that the death of this patient was due to two factors, acidosis and uremia. When observed in April the urine was free from albumin, but previous to his death both the urine and the blood showed evidence of a nephritis with retention of nonprotein nitrogen. The alkali therapy relieved the acidosis to some extent, but had little effect on prolonging his life.

Summary of Case 2.—A mild case of diabetes in a 3-year-old boy coming under observation two weeks after the onset of symptoms. Merely lowering the diet was sufficient to make the urine sugar-free. There was relief of the polyuria and subjective symptoms, except bread hunger, by regulation of the diet. He remained sugar-free and in good health during the four months of observation. Following this the dietary restrictions were broken and death occurred six and one half months after the onset from acidosis and uremia.

Diet.—In spite of Allen's statement that we should be governed by no theoretical standards of calories or protein, but rather by the individual tolerance for each individual food, it is well to have in mind the theoretical considerations that go to make up a well-balanced diet. If the patient's tolerance permits, it would seem better for him to have a well-balanced than a badly balanced diet, and the younger the patient the more important does this become. The protein needs of a child are about 1.5 gm. per kilogram, and this amount constitutes from 9 to 13 per cent. of the total calories. As to the proportion of fat and carbohydrate that should make up the diet, there are no absolute data. Though the diet of a thriving child varies within rather wide limits in different individuals, one, the food value of which beside the protein is equally distributed between the fats and carbohydrates, makes a very good average. Fats and carbohydrates are of almost equal importance as protein spacers. It seems likely that in the young, growing child the body needs are best supplied by having the food value of the fats somewhat greater than that of the carbohydrates, even as much as 25 per cent. greater. In preparing a restricted or minimum diet for a child there should be at least the minimum requirement of protein, 1.5 gm. per kilogram, the fats should be about 50 per cent. and the

carbohydrates about 40 per cent. of the total calories. In many diabetic children this amount of carbohydrate would not be well tolerated, and for this reason it should be decreased and the fat increased sufficiently to meet the needs of the individual patient.

Body Weight.—The question of diet has a very intimate relation to that of body weight. Allen's statement that any increase in body weight that is attended with glycosuria or an increase in the acetone bodies should be checked holds true for children as well as for adults, but apparently little attention is paid to the fact that children are expected to grow. This growth must ultimately involve increase in weight, and it would seem necessary to allow a reasonable increase in weight in any child who remained sugar-free and acetone-free.

NITROGEN DISTRIBUTION IN THE URINE

A study of the urinary nitrogen was made in the two cases of this report, extending over a period of ten months in Case 1, and of one month in Case 2. The total nitrogen, creatin, creatinin, uric acid and ammonia were determined, and in Case 1 the urea was determined during one period.

Creatin and Creatinin.—For the determinations of this report the revised Folin⁵ method was employed. No attempt was made to remove the acetone bodies, since in but few, if any, specimens were these substances present in amounts sufficient to interfere with the determination.⁶ The diet was at all times such as is usually termed creatin-free and creatinin-free, and consisted of milk, eggs, butter, cream, and, for most of the periods, vegetables.

Since it has been shown that on a creatin-free and creatinin-free diet the excretion of creatin and creatinin is unaffected by the variety or amount of exogenous protein, except as sugar may be obtained from the protein,⁷ a diabetic who is sugar-free and therefore utilizing all of the carbohydrate of the diet might be considered as a normal individual as far as creatin and creatinin excretion is concerned, provided sufficient carbohydrate is fed. There is considerable evidence that, in regard to the excretion of these substances, these patients behaved as normal children. At periods in which relatively large amounts of carbohydrate were allowed and apparently utilized, the creatin and creatinin coefficient was not different from that obtained during periods of lower carbohydrate intake. In Case 1 a slightly higher coefficient was obtained in the later than in the earlier periods, probably because

5. Folin, O.: Jour. Biol. Chem., 1914, **17**, 469.

6. Greenwald, I.: Jour. Biol. Chem., 1912-1913, **14**, 87. Graham, G., and Poulton, E. P.: Proc. Roy. Soc., Series B, 1914, **87**, 205.

7. Benedict, S. R., and Osterberg, E.: Jour. Biol. Chem., 1914, **18**, 195.

of the relative decrease in adipose and increase in muscular tissue. Taking 12 kg. as the mean weight for the year in Case 1, the average creatin value as 0.048 gm. and the average creatinin value as 0.037 gm., the coefficient is found to be 4 for creatin, 3.1 for creatinin and 7.1 for their sum. In Case 2 is found a coefficient of 3.2 for creatin, 4.6 for creatinin and 7.8 for their sum. This difference in the total coefficients can easily be accounted for by the relatively larger amount of adipose tissue in Case 1. Several normal children⁸ of about the same age while having a creatin-free and creatinin-free diet were found to have a total coefficient of from 7.0 to 7.7, with one exception, which gave a coefficient of 10.

The coefficients of the total creatin and creatinin nitrogen in these patients is practically the same as is found in adults for creatinin nitrogen,⁹ a fact not especially surprising. In adults there is a constant daily and even hourly excretion of creatinin for each individual, though varying somewhat in different individuals. One might expect to find this same constancy for children, if not in creatinin, perhaps in the sum of creatin and creatinin. This has never been shown and does not appear in these patients, though the variations in the amounts of these substances found is not remarkable. Every effort was made to obtain exact twenty-four hour specimens.

Uric Acid.—For all periods up to March 17 there was in the diet of Case 1 a small and fairly constant amount of vegetables, consisting largely of spinach and cauliflower, boiled with three changes of water. Otherwise the diet was purin-free. For the last period vegetables were omitted and the diet consisted of cream, eggs and butter. Benedict's modification of Folin's method of determination was employed.¹⁰ At no time was the uric acid excretion very constant nor was there any constant relation to the total nitrogen. However, the variations were within fairly narrow limits. The average daily excretion of uric acid nitrogen for the periods containing some vegetables was 0.043 gm., and for the period of purin-free diet it was 0.050 gm. In Case 2 there were much higher uric acid values, but these can easily be interpreted as partly exogenous. The patient was removed from a generous diet on admission to the hospital and the uric acid excretion during observation, though irregular, showed a decided tendency to decrease. In a small group of normal children⁸ from 18 to 24 months of age, whose previous diet had always been low in purins, the average values for uric acid nitrogen on a purin-free diet was found to vary from 0.051

8. These figures were taken from the determinations made by Veeder and Johnston, which are not yet published.

9. Shaffer, P. A.: *Am. Jour. Physiol.*, 1908, **23**, 1.

10. Benedict, S. R., and Hitchcock, E. H.: *Jour. Biol. Chem.*, 1915, **20**, 619.

to 0.055 gm. Children older than this who have been accustomed to meat and other purin-containing foods gave even higher values during short interval observations.

The figures here presented show that the uric acid excretion in the two diabetic patients is practically the same as is found in normal children of the same age under similar dietary conditions, and further show the surprising fact that a child of 12 kg. excretes as much uric acid as an adult.¹¹

Urea.—In Case 1 urea nitrogen was determined in the last period, the findings not being remarkable in any way. The amounts found varied from 58 to 74 per cent. of the total nitrogen and showed an inverse proportion to the amounts of ammonia present. In the normal child the ammonia nitrogen varies in the neighborhood of 4 to 6 per cent. of the total nitrogen, and the urea 80 per cent. or more. The increased ammonia values during this period account adequately for the decreased urea.

11. Raiziss, Dubin and Ringer: Jour. Biol. Chem., 1914, **19**, 473.