RENAL GLYCOSURIA *

SOLOMON STROUSE, M.D.

CHICAGO

III

The diagnosis of renal glycosuria is based on the syndrome of (1) glycosuria without hyperglycemia, (2) glucose excretion almost entirely independent of carbohydrate intake, and (3) absence of diabetic symptoms. To these data should be added, I think, a fourth, namely, that such patients do not subsequently develop diabetes mellitus or show a disturbance of carbohydrate metabolism similar to that found in diabetes mellitus. Not many reported cases have been observed long enough to answer either of the latter two questions. Garrod's¹ case was observed six years, Goto's² five years. Allen, Wishart and Smith³ have recently recorded three cases of renal glycosuria, and have discussed the unsatisfactory nature of this interesting anomaly. It is the purpose of this paper to place on record four cases, patients who have been under observation for from two to eight years since the onset of the disease and on two of whom late metabolic studies were possible.

Glycosuria without hyperglycemia is certainly no longer sufficient evidence on which to base a diagnosis of renal glycosuria, as this combination may be found in patients with mild but true diabetes mellitus. Early cases of diabetes mellitus, those, for instance, discovered in life insurance examination, not infrequently show an excretion of glucose not dependent entirely on carbohydrate intake. In such cases the discovery of glycosuria may precede the onset of typical diabetic symptoms. Study of the cases reported in the literature as renal glycosuria forces the belief that probably not all cases belong to the same class (Strouse and Beifeld⁴). The ultimate outcome or late development in only a few cases is on record. The blood sugar response to ingested glucose has been reported rarely, and the reported results are not entirely uniform. Lewis and Mosenthal⁵ record one case with a normal blood sugar curve. Allen, Wishart and Smith³ say that the low blood sugar values "after large starch or sugar ingestion

*From the Medical Clinic and the Nelson Morris Memorial Institute for Medical Research of the Michael Reese Hospital.

1. Garrod, A. E.: *Brit. M. J.* **2**:850, 1913.

2. Goto, K.: *Arch. Int. Med.* **22**:96 (July) 1918.

3. Allen, F. M.; Wishart, M. B., and Smith, L. M.: *Arch. Int. Med.* **24**:523 (Oct.) 1919.

4. Strouse, S., and Beifeld, A. H.: *J. A. M. A.* **62**:1301 (April 25) 1914.

5. Lewis, D. S., and Mosenthal, H. O.: *Johns Hopkins Hosp. Bull.* **27**:133, 1916.

stand in contrast not only to the conditions in diabetes, but also to the hyperglycemia of normal persons after feeding." Yet Paullen's patient⁶ showed a blood sugar response to ingested glucose distinctly of the abnormal "metabolic" type. Janney⁷ has called attention to the abnormal hyperglycemic curve in Paullen's case. The cases which form the basis of this report shed some light both on the blood sugar reaction and on the clinical course.

REPORT OF CASES

CASE 1.—This man was first seen in December, 1912. He was then 23 years old. He was refused life insurance in November on account of sugar in his urine, which was his reason for consulting us. He had no complaints, no increased appetite, polydipsia or polyuria, and had not lost weight.

Past History.—Five years before he had possibly had typhoid fever. He denied syphilis. He was always a "high liver" and had eaten of rich foods plentifully. He had used alcohol moderately, smoked cigarets freely, and was of a nervous, excitable temperament. About one year before he was in a sleighing accident and was thrown to the street, landing on his head. Unconsciousness lasted only a few minutes, when he arose and drove an automobile home. He had intense headaches for three or five days at that time. He was examined by a competent physician who found no evidence of skull fracture. The urine had been examined shortly before and shortly after the accident but no sugar had been found.

Family History.—There is no diabetes in the family, but all members belong to the high strung, neurotic type.

Examination.—Physical examination (1912) was very thoroughly made and was completely negative. The Wassermann test was negative.

COMMENT

Without going into details on the course of the study made at that time, which has been previously reported⁴ it can be said in brief: (1) that he had a glycosuria practically independent of carbohydrate intake; (2) that it was possible to render him sugar free only one time, for a period of a few days; (3) acidosis and clinical signs of acid intoxication developed on carbohydrate withdrawal more quickly than in the normal; (4) restriction of protein intake did not reduce the glycosuria, and (5) the blood sugar both during starvation and after a full meal was normal. (The original blood sugar determinations were from Von Noorden's clinic.) Early in 1913 the patient decided to try to force the issue. If diabetes were present he wanted to know it at once. Consequently he ate anything and everything that he wished and has continued to do so up to the present. He has been under constant observation. At no time has urinary sugar disappeared, and at no time was a hyperglycemia demonstrated in a single examination. In May, 1919, practically seven years after

6. Paullen, J. E.: J. A. M. A. **75**:214 (July 14) 1920.

7. Janney, N. W.: J. A. M. A. **75**:217 (July 14) 1920.

the onset, the patient put himself under closer observation. His history during the past years was that of a perfectly normal man. He had grown stout, had been under no dietary restrictions whatever, and had shown no symptoms of diabetes mellitus. *His urine contained more sugar.* He had been for the past few months indulging in sweets and had been drinking more freely of alcoholic beverages, as he had been acting as official taster of syrups and alcoholic drinks in a big hotel. On May 15, 1919, he was given 100 gm. glucose in 200 c.c. of lemonade, with the results shown in Table 1.

TABLE 1.—SUGAR CURVE OF MR. B. AFTER INGESTION OF GLUCOSE

Time	Blood Sugar, Gm. per Cent.	Urine Sugar, per Cent.	Urine Sugar, Gm. per Hour	Urine Quantity, C.c.
8:45 a.m.	0.142	3.0		120
9:00 a.m. (100 gm. glucose)				
10:00 a.m.	0.27	0	0	0
10:15 a.m.		2.8	1.4	75
10:30 a.m.	0.31	0	0	0
11:00 a.m.	0.33	0	0	0
11:30 a.m.	0.36	3.0	2.16	87

TABLE 2.—SUGAR CURVE OF MR. B., AFTER INGESTION OF GLUCOSE, JUNE 6, 1919

Time	Blood Sugar, Gm. per Cent.	Urine Sugar, per Cent.	Urine Sugar, Gm. per Hour	Urine Quantity, C.c.
8:30 a.m.	0.09	0.75		28
8:35 a.m. (100 gm. glucose)				
9:05 a.m.	0.10	1.0	0.48	24
9:45 a.m.		2.7	2.88	80
10:05 a.m.	0.14	0	0	0
10:35 a.m.	0.10	3.8	4.56	90

This result was extremely surprising. The hyperglycemic curve was definitely diabetic in type (see last article) and the sugar excreted was high. Up to a short time before this test, the amount of sugar excreted had always been so small that quantitative determination by ordinary clinical procedures had been impossible (the new Benedict⁸ method was not employed). This sugar gave typical tests for glucose. May 19, 1919, a blood sugar curve taken at 12 noon was 0.05. It was considered possible that the high carbohydrate feeding in the past few months had broken down his tolerance and that the patient had become diabetic. He was requested to refrain from this excessive carbohydrate and alcohol intake but to make no other restrictions in his diet. He returned for a subsequent alimentary test on June 6, 1919, when he was again given 100 gm. glucose in 300 c.c. lemonade.

8. Benedict, S. R.: J. Biol. Chem. **34**:195, 1918.

This test, as far as the blood sugar curve is concerned, is definitely normal except for the delay in reaching its maximum., May 19, 1919, a Mosenthal test meal was given. The meal consisted of 1,760 c.c. fluid—13 gm. nitrogen, 11 gm. salt, 81.25 gm. protein and 162 gm. carbohydrate. The results are shown in Table 3.

TABLE 3.—REACTION OF MR. B. AFTER MOSENTHAL TEST MEAL

Time	Quantity Urine, C.c.	Specific Gravity	Sugar, Gm.	Sodium Chlorid, Gm.	Total Nitrogen, Gm.	Urea Nitrogen, Gm.
8-10 a.m.	285	1.018	1.48			
10-12 a.m.	75	1.025	0.50			
12- 2 p.m.	215	1.022	2.41			
2- 4 p.m.	190	1.025	2.41	13.71	8.44	2.51
4- 6 p.m.	145	1.027	0.61			
6- 8 p.m.	145	1.026	0.84			
Total, day.....	1,055		8.25	13.71	8.44	2.51
8 p.m. to 8 a.m.	350	1.029	2.97	3.57	4.45	1.97
Total.....	1,405		11.22	17.28	12.89	4.48

This reaction to the Mosenthal test meal is not altogether normal. An excess of sodium chlorid and of nitrogen is excreted, and the urea nitrogen is low. There is no fixation and no retention of total nitrogen. May 20, 1919, the phenolsulphonaphthalein test showed in the first hour 23 per cent., and in the second hour 9 per cent., a depression of excretion. As in Allen's three recent cases, the sub-normal phthalein excretion is the only indication of any renal retention. Although in our case the test for renal function was done seven years after onset, there seems to be no depression of renal function.

This patient was not seen again until the summer of 1920. July 20, 1920, he was given 100 gm. glucose in 300 c.c. lemonade, with the results shown in Table 4.

TABLE 4.—SUGAR CURVE OF MR. B., JULY 20, 1920, AFTER INGESTING GLUCOSE

Time	Blood Sugar, Gm. per Cent.	Urine Sugar, per Cent.	Urine Sugar, Gm. per Hour	Urine Quantity, C.c.
9:00 a.m.	0.10	0.41		90
9:10 a.m. (100 gm. glucose)				
9:40 a.m.	0.20	0.81	0.55	50
10:10 a.m.	0.156	1.39	1.388	50
11:10 a.m.	0.142	1.31	1.64	125
12:10 p.m.	0.117	1.91	1.81	95

This reaction, when compared with the reactions discussed in the previous paper, will be seen to be abnormal in type. The maximum rise to 0.20 is higher than seen in our normal controls, although unlike the typical metabolic curves the height is reached in the half hour. However, the maintenance of the level of 0.156 in the hour and the slow drop are strongly suggestive of a metabolic type.

CASE 2.—A young man, 13 years of age, was first seen in May, 1916. Sugar had been found in his urine accidentally at that time in the course of a routine urine examination in preparation for tonsillectomy. He had had several attacks of acute tonsillitis and the usual infectious diseases of childhood. He had no symptoms of diabetes. His family history was completely negative.

Physical Examination.—He was an unusually robust young chap, and except for the presence of sugar in the urine the physical examination was completely negative. At the time he was first seen he had been on a carbohydrate free diet for three weeks. Despite the presence of a small amount of urinary sugar his blood sugar was only 0.05.

He was not treated for diabetes but was told to lead a normal life, only omitting sugar and food containing sugar. From this time, May, 1916, to June, 1918, he was watched constantly. Growth and development had been normal; the trace of sugar, too small to measure quantitatively by usual clinical procedures, was constantly present. Several blood sugars were done during this period; these were normal or subnormal.

COMMENT

No symptoms of diabetes have arisen. In June, 1918, he became sugar free and was accepted as a first class life insurance risk. He also was accepted in the Reserve Officers' Training Camp. Since that time he has eaten freely of everything, including candy, sweet drinks and pastries. May 23, 1919, a sugar tolerance test was made; 100 gm. glucose in 300 c.c. lemonade was given (Table 5).

TABLE 5.—SUGAR CURVE OF C. F. AFTER INGESTING GLUCOSE

Time	Blood Sugar, Gm. per Cent.	Urine Sugar	Quantity Urine, C.c.
8:30 a.m.	0.08	0	..
8:35 a.m. (100 gm. glucose) ..			
9:05 a.m.	0.14	0	82
9:35 a.m.	0.05	0	53
10:05 a.m.	0.05	0	52
11:05 a.m.	0.15	Trace	40

This reaction is perfectly normal, except for the peculiar, unexplained rise of the blood sugar and the glycosuria at the two and one-half hour period. The absence of urinary sugar following the ingestion of 100 gm. of glucose three years after the onset of the disease is a striking feature. Between the date of this test and July, 1920, this young man continued to show perfect development, and during this period had his tonsils removed. He continued to be free of symptoms of diabetes although glycosuria was present more or less constantly. July 18, 1920, he was given 125 gm. glucose in 300 c.c. lemonade (Table 6).

It will be seen from Table 6 that the starvation level of 0.13 is rather higher than it should be even for a normal, and that the height of the blood sugar curve is reached in one-half hour, attaining a height of 0.19 with a slow descent to normal. The quantity of sugar in

the urine is small. This reaction, especially for 125 gm. glucose, cannot be considered pathologic; but it is like the reaction in Case 1, suggestive of a metabolic disturbance. As discussed in the previous paper, there is no specific value in the study of alimentary hyperglycemia nor is there a definitely specific variation from normal. Neither one of the tolerance tests made in 1920 on these two cases, however, can be classified as completely within normal bounds.

TABLE 6.—SUGAR CURVE OF C. F., JULY 18, 1920, AFTER INGESTING GLUCOSE

Time	Blood Sugar, Gm. per Cent.	Urine Sugar, per Cent.	Urine Sugar, Gm. per Hour	Urine Quantity, C.c.
9:10 a.m.	0.13	0.31		55
9:30 a.m. (125 gm. glucose)				
9:50 a.m.	0.19	0.31	0.12	30
10:20 a.m.	0.17	0.38	0.19	25
11:20 a.m.	0.14	0.41	0.12	30
12:20 p.m.	0.13	0.45	0.13	30

CASES 3 AND 4.—It is impossible to report extensive investigations on these two patients, but they are added to this report as a matter of record, and because in one the onset was characterized by diabetic symptoms. The patients were twins, aged 11 years, first seen in January, 1918. A few weeks previously the little girl complained of irritation of the genitalia and increased thirst. Urinalysis made by her physician at that time showed sugar. The mother, having recognized that in the past both children had had the same diseases at the same time, had the boy's urine examined and was told sugar was present there, too. Both had normal deliveries with uneventful childhood.

Past History.—Both had chickenpox at the age of 5, measles at 6, and whooping cough at 8. The boy had had several attacks of acute tonsillitis and had had his tonsils removed in 1911. The girl had never had trouble with her throat. Both were heavy eaters, the boy specializing in potatoes and bread while the girl went to extremes on candy, jelly and pastries. There is no history of diabetes in the family history.

Physical Examination.—Examination at the time of the first observation showed two very healthy looking youngsters, both inclined to adiposity. Otherwise the physical examination was negative. The blood and stools were negative. The urine of both children showed a reducing substance in small amounts, which the chemical laboratory reported as glucose.

Owing to the history of increased thirst and genital irritation, these patients were considered diabetics, despite the fact that the only blood sugar made was 0.069 on each one. There seemed to be a relationship between carbohydrate intake and glucose excretion, and it had been exceedingly difficult to render these youngsters sugar free without their developing an acidosis. They were passing on an average of from 1.5 to 3 gm. sugar daily, and after the first week this amount remained fairly constant despite efforts to eliminate the sugar entirely. On semistarvation the sugar excretion rose 100 per cent., to 8 gm., and the quick onset of signs of acidosis made it inadvisable to continue treatment. Both these patients were considered at the time to

be mild diabetics of the familial type, although the low blood sugar and the difficulty of rendering them sugar free should have made us regard them as renal glycosurias even at that time. From January to April, 1918, sugar was constantly present in small amounts, but by that time the youngsters had started a revolution and eaten about what they pleased except sugar. In May, 1918, the blood sugar was 0.08 gm. per cent. No symptoms suggestive of diabetes had arisen. The children had both gained in weight and showed normal physical and mental development. At that time they began to eat everything, including sugar, candy, sweet drinks and pastries. They were not seen often, but in February, 1919, the urine of the boy became sugar free, and early in May, 1919, the girl's urine became sugar free. Both children then left the city and subsequent observation has been impossible. In July, 1920, the mother informed us that both children were perfectly normal in every way but the specimens of urine of both still contained sugar.

SUMMARY

Four cases of renal glycosuria are presented. Two patients have been under observation two years, one patient almost five years, and one patient for eight years. All four still show glycosuria. None shows symptoms of diabetes mellitus. In one, tests for renal function seven years after onset showed no depression of renal function except in regard to phthalein excretion. The two who have been observed the longest show at the end of four and eight years, respectively, a utilization of glucose that cannot be considered strictly normal, one at the end of seven years' observation showing a distinctly pathologic alimentary hyperglycemia. This may indicate the beginning of metabolic disturbance. This study emphasizes the importance of long and continued observation of all patients with this most interesting anomaly.