STUDIES ON ALIMENTARY HYPERGLYCEMIA AND GLYCOSURIA *

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In 1647 Thomas Willis recognized the presence of sugar by its sweet taste in the urine of diabetics. This sugar was identified as glucose by Chevreul in 1815. That diabetic blood also contained sugar was first recognized by Dobson in 1775, and his observation was confirmed the following year by Cullen.[1]

In 1831 Tiedemann and Gmelin[2] showed that sugar was normally present in the blood after meals, and that it originated in the digestion of starchy food in the intestine. Up to this time sugar had been considered a pathologic product in the blood and urine of diabetics. The fact that sugar is present in the blood of an animal on a carbohydrate-free diet was first demonstrated by Claude Bernard in 1848. Eight years later, Chauveau asserted that sugar was a constant constituent of the blood, that its presence was not dependent on the diet, and that in the fasting state the sugar value remained constant. The dependence of glycosuria on hyperglycemia was recognized at this time following the work of MacGregor, Rollo and Ambrosini, and tests for the assimilation limit for glucose and starch were instituted by C. Schmidt, v. Becker, Schiff, Lehmann, Frerichs and others, the urine being tested for sugar. This assimilation-limit for glucose has been found to be not at all constant, varying in different individuals and in the same individual, being greatly lowered by starvation as shown by Hofmeister.[3] The method usually employed was to give from 50 to 200 gm. of glucose to an individual of average weight, and to test the urine at intervals for the presence of sugar. The normal values given by different authors vary from 50 to 200 gm. In many cases the urine was examined at intervals varying from one to twenty-four hours after the ingestion of the sugar, and this, with inaccurate methods of sugar determination, largely explains the discrepancies. Other sources of error are the state of health, nutrition and body weight of the patient. The advent of practical methods of blood analysis directed the attention of investigators to tests of alimentary hyperglycemia and the determination of the patient's toler-

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1. Bernard, Claude: Compt. rend de l'acad. d. sc., 1876, p. 1405
2 Tiedemann and Gmelin: Die Verdaung nach Versuchen, Heidelberg, 1831.
3. Hofmeister: Arch. f. exper. Path. u. Pharmakol. **26**:355, 1891.

ance for glucose in this way. Results of such tests have been published by Liefmann and Stern,[4] Boudouin,[5] Frank,[6] Wacker,[7] Tachau,[8] Jacobson,[9] Bergmark,[10] Hopkins,[11] Cummings and Piness,[12] Hamman and Hirschman,[13] Denis and Aub[14] and others. In many of these tests the estimations were made one and two hours after the ingestion of glucose, and the results compared with the preformed sugar value. In other cases the test was more elaborate, the blood being examined at frequent intervals for a period of from four to six hours. These observers seem to agree that in a normal person, following the ingestion of sugar, the blood sugar reaches its greatest concentration in from one-half to one hour, and that the normal value is again reached

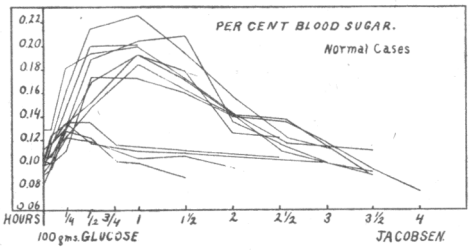

Chart 1

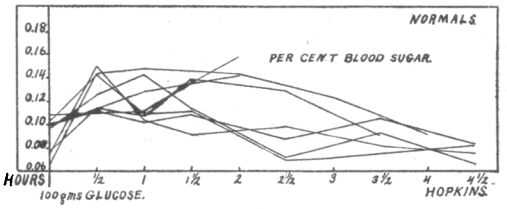

Chart 2

in from two to three hours' time. There is no agreement as to the height of the hyperglycemia. Great variations are to be expected. Aside from the inaccuracies of the various methods we have the uncertain factors of intestinal absorption, state of nutrition, weight of the subject, glycogenetic and glycolytic powers, renal permeability, and glycolysis in the intestine and in the withdrawn blood before the test

4. Liefmann and Stern: Biochem. Ztschr. **1**:299, 1906.
5. Boudouin: Thése de Paris, 1908.
6. Frank: Ztschr. f. physiol. Chem. **70**:291, 1910.
7. Wacker: Ztschr. f. physiol. Chem. **67**:197, 1910.
8. Tachau: Arch. f. klin. Med. **104**:437, 1911.
9. Jacobsen: Biochem. Ztschr. **56**:471, 1913.
10. Bergmark: Jahrb. f. Kinderh. **80**:373, 1914.
11. Hopkins, A. H.: Am. J. M. Sc. **149**:254, 1915.
12. Cumings and Piness: Arch. Int. Med. **19**:777, 1917.
13. Hamman and Hirschman: Arch. Int. Med. **20**:761, 1917.
14. Denis and Aub: Arch. Int. Med. **20**:964, 1917.

is carried out. Illustrating these agreements and variations, composite charts (Charts 1, 2 and 3) made from figures published by Jacobsen,[9] Hopkins,[11] and Hamman and Hirschman[13] are given.

A combination of blood and urine analyses following the ingestion of glucose has been found more instructive. In the fourteen normal cases reported by Jacobsen[9] (Chart 1) sugar was found in the urine in all those whose blood sugar reached a value of 0.174 per cent.; in those below 0.16 per cent. sugar was not found in the urine. Jacobsen's work shows the fallacy of blood analyses at one-hour intervals, as in many normal cases following the ingestion of 100 gm. of glucose, hyperglycemia had already passed off by the end of the first hour.

Bailey[15] reported a normal case on whom frequent blood and urine sugar tests were made following the ingestion of 75 gm. of glucose. The type of blood sugar curve was similar to those of Jacobsen[9] and, as in his cases, the kidneys actively excreted sugar after a concentration of 0.167 per cent. had been reached in the blood.

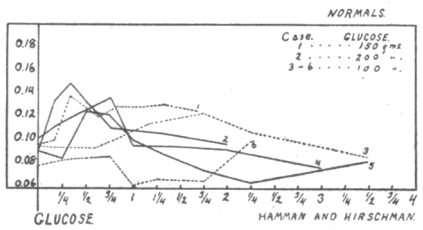

Chart 3

Hamman and Hirschman[13] carried out similar tests on six normal persons, using from 100 to 200 gm. of glucose. In three of their cases the blood sugar curve was of a similar type to those of Jacobsen; the others were very irregular (Chart 3). In these cases active renal excretion of sugar began at blood sugar concentrations varying from 0.124 to 0.255 per cent., giving an average of 0.17 per cent.

An important observation on all of these tests is the marked disproportion between the greatest blood sugar concentration and the amount of sugar ingested, allowances being made for differences in body weight. This disproportion is seen in the work of individual authors and makes one think that sugar tolerance tests based on blood sugar estimations are really tests of intestinal absorption.

15. Bailey, C. V.: Proc. Soc. Exper. Biol and Med. **13**:153, 1916.

TESTS OF ALIMENTARY HYPERGLYCEMIA AND GLYCOSURIA

Stimulated by the works of Bang,[16] Jacobsen,[9] and Hopkins,[11] the present work was undertaken in an attempt to show the relation of glycosuria to hyperglycemia as found in health and as influenced by disease. It was hoped that in such tests interesting observations could be made on variations in blood volume, on the rate of sugar increase in corpuscles as compared to that in the plasma, and on the influence of urine excretion on glycosuria.

METHOD OF PROCEDURE

The subjects partook of a light meal at 5:30 on the afternoon preceding the tests. On the following morning the experiment was begun before anything had been eaten or drunk. The bladder was emptied and later a specimen of urine was passed on which was determined the rate of urinary excretion and the presence or absence of sugar. A specimen of blood was obtained at this time by venipuncture. Following this a certain amount of glucose in a known volume of weak tea was given by mouth and blood and urine specimens obtained at frequent intervals for a period of six or seven hours. In some cases fluid was given during this period. The subject was kept quiet in a reclining posture throughout. Urine sugar tests were made qualitatively by Benedict's method;[17] quantitatively by Benedict's or Myers'[18] methods and by means of the polariscope. In some cases the sugar was determined to be glucose by the character of its osazone.

Blood sugar was estimated by a modification of the Lewis and Benedict[19] method.

Hemoglobin tests were made with the Hellige colorimeter.

Plasma volume was determined by centrifuging the blood in graduated tubes. Chlorids in the urine were estimated by the Volhard-Harvey method. Sugar estimations were made on unwashed corpuscles from which the plasma and upper layers of cells had been pipetted off leaving a known volume of cells in the centrifuge tube.

The data from these last estimations unfortunately do not give one a correct idea of the relative glucose increase in corpuscles and plasma, as by this method a half hour elapsed before the plasma and corpuscles were separated. This gave time for absorption by the corpuscles and a more even distribution of the glucose. The data are, however, of value in showing the distribution of glucose in blood, in which the glucose concentration is not changing. Gradwohl and Blavis,[20] who, by the way, were student and technician, respectively, in the laboratory where this work was being done, have published results similar to these now reported.

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16. Bang, I.: Der Blutzucker, Wiesbaden, 1913.
17. Benedict, S. R.: J. Biol. Chem. **5**:485, 1909; **9**:57, 1911.
18. Myers, V. C.: Proc. Soc. Exper. Biol. and Med. **13**:178. 1916.
19. Myers, V. C., and Bailey, C. V.: J. Biol. Chem. **24**:147, 1915.
20. Gradwohl and Blavis: J. Lab. & Clin. M. **2**:416, 1916-1917.

Alimentary Glucose Test in a Normal Person

CASE 1.—S. S., male, aged 18, was admitted to hospital for observation as a suspected case of pulmonary tuberculosis. Aside from being poorly nourished, nothing abnormal was found on physical examination. His morning blood sugar on two occasions was 0.1 and 0.11 per cent. On the morning of May 15, 1916, he was tested with 75 gm. of glucose. The results are shown in Chart 4 and Table 1. The patient was quite nervous at the beginning of the test, and this probably accounts for the preformed sugar being higher than on previous occasions. The urine sugar was slightly lower than the synchronous blood sugar. Following the administration of the glucose, the blood and urine sugar increased at the same rate up to a concentration of 0.167 per cent., when the urine sugar increased rapidly to 0.89 per cent., although the blood sugar at this time had reached only 0.22 per cent. The blood sugar curve is of the same type as found in normals by Jacobsen and others. The urine sugar value returned to normal more slowly than the blood sugar. Following the ingestion of glucose the blood volume (as shown by the estimation of hemoglobin) increased 7 per cent. during the first half hour, returning to normal in one and one-half hours, although the blood sugar at this time was concentrated. Epstein[21] has frequently referred to this volume increase. The rate of urinary excretion decreased notwithstanding the fact that 400 c.c. of fluid were taken with the glucose. Not before the blood sugar had reached its highest level and was on the decline, did the rate of urinary excretion increase.

TABLE 1 (CASE 1, S. S., 5/15/16).—ALIMENTARY GLUCOSE TEST IN A NORMAL PERSON

Time		Blood					Urine				Fluid Intake, C.c.
				Sugar				Sugar			
								Myers Method		Benedict's Method, Qualitative	
A. M.	Hr.	Hemoglobin, Units	Plasma, per Cent.	In Whole Blood, per Cent.	In Plasma, per Cent.	In Corpuscles, per Cent.	C.c. per Hour	Per Cent.	Gm. per Hour		
9:10	...	80	45.5	0.12	0.118	0.121	36.0	0.099	0.035	0	
9:15	75 gm. glucose			.....	.....	.....	....	.....	....	....	400
9:30	¼	77	44.5	0.153	0.127	0.132	28.2	0.171	0.048	0	
9:50	½+	73	46.3	0.172	0.19	0.154					
10:10											
10:15	1	77	46.0	0.22	0.225	0.193	31.2	0.891	0.28	++++	
10:40	1½—	80	45.3	0.216	0.22	0.211					
11:00											
11:15	2	78	47.0	0.158	0.147	0.147	31.8	0.405	0.129	+++	
11:30											
11:45	2½	79	46.0	0.147	0.147	0.147	16.8	0.315	0.053	++	
12:00 M.											
P. M.											
12:15	3	78	47.0	0.134	0.113	0.124	22.8	0.27	0.06	+	
1:00	3¾	78	46.5	0.135	0.121	0.124					
1:45	4½	76	45.5	0.129	0.121	0.113	21.0	0.252	0.053	+	
2:00											
2:15	5	77	42.0	0.129	0.126	0.113	22.8	0.162	0.037	0	
3:15	6	78	40.0	0.087	0.085	0.091					

This experiment seems to indicate that a normal person, when uninfluenced by food or fluid intake, has reducing substances present in equal concentration in both blood and urine. Following the inges-

21. Epstein, A. A.: Studies on Hyperglycemia in Relation to Glycosuria, New York, 1916.

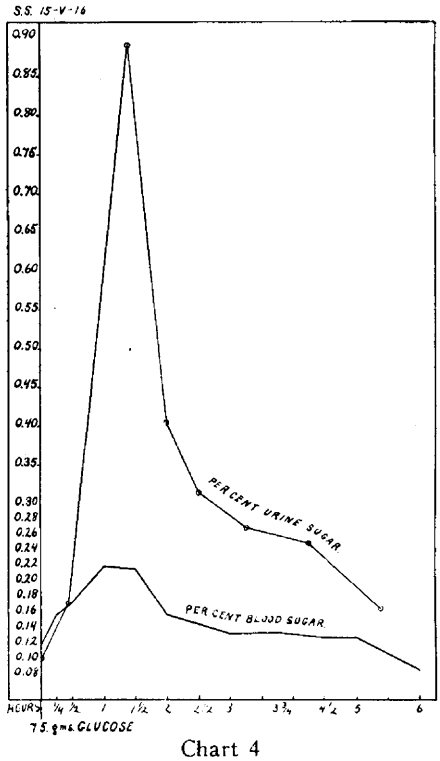

Chart 4

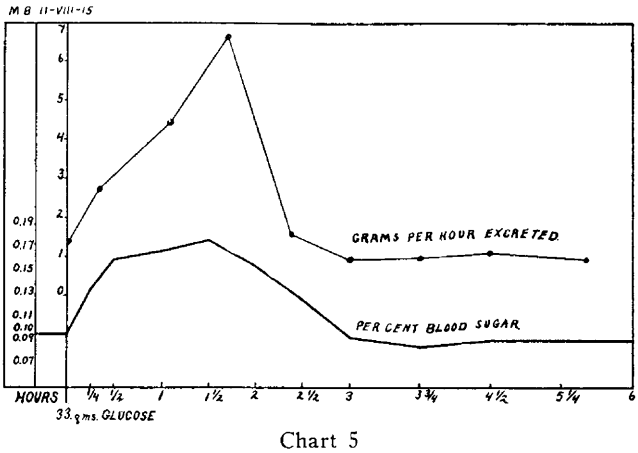

Chart 5

tion of glucose, urine sugar parallels that of the blood up to the latter's concentration of 0.16 to 0.17 per cent. As the blood sugar increases beyond this point the kidneys actively excrete sugar. This excessive excretion decreases as the hyperglycemia passes off. There seems to be an attempt to control the blood sugar concentration by an increase in blood volume. This is partly brought about by a decrease in urinary excretion.

A comparison of the hyperglycemic curves in plasma and corpuscles indicates a more rapid rise in plasma than corpuscles. (This difference, however, is probably much greater than the figures show. As before stated, a half hour elapsed before plasma and corpuscles were separated, giving time for an even distribution of the glucose.)

The findings in this case emphasize the necessity of adopting Benedict's term "glycuresis" [22] to indicate active excretion of sugar in contradistinction to the amount found in the urine during the fasting state.

TABLE 2 (CASE 2, M. B., 8/11/15).—ALIMENTARY GLUCOSE TEST IN A CASE OF RENAL DIABETES

Time		Blood Sugar, per Cent.	Urine				Fluid Intake, C.c.
			C.c. per Hour	Chlorids, Gm. per Hour	Sugar		
A. M.	Hr.				Per Cent.	Gm. per Hour	
9:15	...	0.098	60.0	0.046	3.12	2.0	
9:45	33 gm. glucose		44.0	.....	2.94	1.29	225
10:00	¼	0.135					
10:20	½	0.159	58.0	0.1056	4.83	2.83	225
10:30							
10:45	1	0.168	....	.....	....	.....	225
11:00	1¼	0.172	66.0	0.145	6.66	4.398	
11:10							
11:15	1½	0.176					
11:45	2	0.156	97.0	0.218	6.75	6.7	225
P. M.							
12:15	2½	0.105					
			159.0	0.254	1.04	1.65	
12:25							
12:45	3	0.093					
			94.0	0.169	0.952	0.897	
1:00							
1:25	3½	0.086					
1:45	4	0.088	150.0	0.21	0.657	0.986	225
2:00							
2:15	4½	0.092					
			90.0	0.14	1.2190	1.097	
3:00	5¼	0.092	.....	.....	.....	.....	225
3:45	6	0.092	84.0	0.134	1.086	0.912	

Alimentary Glucose Test in a Case of "Renal Diabetes" [23]

CASE 2.—M. B., female, aged 31, had persistent glycosuria for at least ten years, resisting repeated attempts at treatment; no symptoms of diabetes. For many years her only complaint had been lack of reserve energy. Restriction of diet caused extreme weakness and rapid loss of weight. Her urine showed

22. Benedict, S. R., and Osterberg, E.: J. Biol. Chem. **34**:258, 1918.

23. For further discussion of renal diabetes see Bailey, C. N.: Am. J. M. Sc. **157**:221, 1919.

a trace of protein and a few hyaline and granular casts. Blood pressure: systolic, 110; diastolic, 65.

On the morning of Aug. 5, 1915, her blood sugar was 0.09 per cent., the synchronous urine sugar being 1 per cent. Two days later, with a blood sugar of 0.11 per cent., the urine contained 1.6 per cent. sugar. August 11, she was tested with 33 gm. of glucose. The results are shown in Chart 5 and Table 2. (At this time the patient was four months' pregnant.)

One sees that the patient excreted sugar at the rate of 2 gm. per hour, although at this time her blood sugar was normal. The blood sugar curve is slightly delayed and prolonged. The excretion of sugar was excessive throughout. This being most marked at the 1½-hour period when sugar was being excreted at the rate of 6.7 gm. per hour, although the blood sugar was at about the concentration where normal kidneys become permeable.

The test was repeated fourteen months later. At this time the percentage of glucose in her daily urine had greatly increased, being 7.4 per cent. on Oct. 15, 1916, 6.94 per cent. on the 16th and 9.2 per cent. on the 17th. The glucose test was repeated October 13. The results are shown in Chart 6 and Table 3.

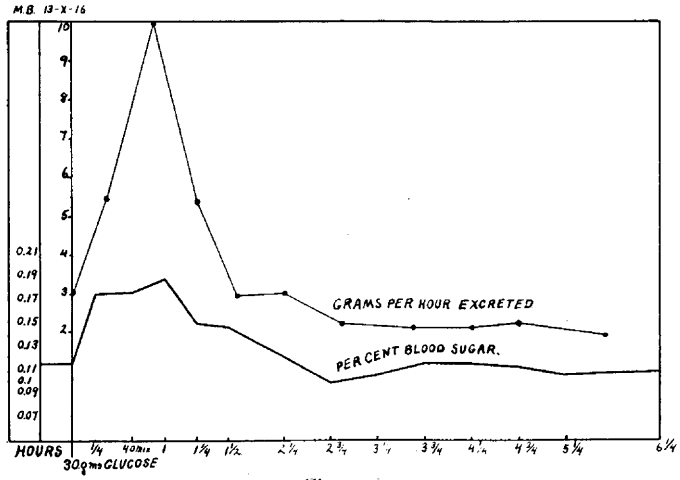

Chart 6

In this test the blood sugar value was within normal limits, but sugar was being excreted at 2.98 gm. per hour. The blood sugar curve is of the normal type. With a blood sugar of 0.189 per cent., sugar was being excreted at the rate of 9.9 gm. per hour. If we compare this test with the previous one (made when the patient was four months pregnant) we find that the blood sugar in the fasting state had increased in value. This, however, is explained by the first test having been made after three days' fasting, which lowers the value. The latter test was made after a ten-hour fast.

The excretory power of the kidneys had increased and the more rapid rise in blood sugar probably indicates an increased absorptive power of the intestines. In the first test the slight delay and prolongation of hyperglycemia is possibly due to slight embarrasment of the kidneys at that time.

In Table 3, the estimation of hemoglobin indicates a 6 per cent. increase in blood volume during the development of the hyperglycemia. The volume returned to normal with the blood sugar. The rate of urinary excretion fell off rapidly on the ingestion of glucose, notwithstanding the large fluid intake, and did not increase until the hyperglycemia had developed.

TABLE 3 (CASE 2, M. B., 10/13/16).—RESULTS OF SECOND GLUCOSE TEST

Time		Blood		Urine			Fluid Intake, C.c.
		Hemoglobin, Units	Sugar, per Cent.	C.c. per Hour	Sugar		
A. M.	Hr.				Per Cent.	Gm. per Hour	
9:15	...	67	0.116	63.0	8.3	2.98	
9:30	30 gm. glucose		.....	....	...	....	400
9:45	¼	62	0.177				
				36.0	11.9	5.35	
10:10	¾	61	0.177				
10:30	1	62	0.189				
				45.0	3.0	9.9	
10:40							
10:50	1¼	63	0.15				
				33.0	1.6	5.28	
11:00							
11:10	1¾	64	0.147				
				80.0	3.7	2.96	
11:30							
11:45	2¼	65	0.12	120.0	2.5	3.0	
12:00 M.							
P. M.							
12:15	2¾	65	0.10	37.0	6.2	2.31	
12:45	3¼	66	0.106				
1:15	3¾	67	0.116				
				56.0	5.6	2.09	
1:30							
1:45	4¼	67	0.114				
				36.0	6.0	2.16	
2:00							
2:15	4¾	67	0.112				
				34.0	6.5	2.21	
2:30							
2:45	5¼	68	0.106				
				28.0	6.8	1.9	
3:30							
3:45	6¼	68	0.108				

Alimentary Glucose Test in a Case of Early Mild Diabetes

CASE 3.—J. S. B., male, aged 42. Sugar was accidentally discovered in his urine during a routine military examination. He was apparently in excellent health, but had noticed slight polydipsia, polyuria and polyphagia. Sugar was constantly present in the daily urine, but hourly specimens showed that it was excreted only after meals. His morning blood sugar on several examinations was about 0.1 per cent. and at these times his urine was sugar-free.

March 3, 1916, he was tested with 60 gm. of glucose. The results are shown in Chart 7 and Table 4. (One hour before the test the patient negligently drank a cup of sweetened coffee which accounts for the high preformed blood sugar value.) The blood sugar curve rises a little more rapidly than normal, but otherwise is of the latter type. The excretion of sugar is excessive and follows the increase of blood sugar. At the 5½ and 6¼-hour periods one can determine that the kidneys actively excrete glucose between blood sugar concentrations of 0.123 and 0.126 per cent., which is much lower than normal.

On Jan. 24, 1917, the test was repeated, using 33 gm. of glucose. The results are shown in Chart 8 and Table 5. The blood sugar is of normal value. The blood sugar curve again rises and falls rapidly. Glucose excretion is excessive and appears at a lower blood sugar concentration than normal.

TABLE 4 (CASE 3, J. S. B., 3/3/16).—ALIMENTARY GLUCOSE TEST IN A CASE OF EARLY MILD DIABETES

Time		Blood			Sugar		Urine		Sugar		Chlorids, Gm. per Hour	Fluid Intake. C.c.
A. M.	Hr.	Hemoglobin, Units	Cells, per Cent.	Plasma, per Cent.	In Whole Blood, per Cent.	In Plasma, per Cent.	C.c. per Hour	Sp. Gr.	Per Cent.	Gm. per Hour		
10:10	...	84.0	61	39	0.15	0.136	96.0	1.030	0.2	0.19	1.45	
10:15	60 gm. glucose			..	.....	.....	....	.....	...	....	....	300
10:30	¼	82.0	61	39	0.205	0.192						
							54.0	1.031	3.1	0.17	0.62	
10:45	½	80.5	58	42	0.228	0.216						
10:55												
11:00	¾	82.0	62	38	0.228	0.216	....	.....	...	....	....	300
11:15	1	83.0	63	37	0.216	0.204	84.0	1.033	5.3	4.45	0.7	
11:40												
11:45	1½	82.0	62	38	0.185	0.156	78.0	1.035	4.6	3.59	0.81	
P. M.												
12:15	2	83.0	63	37	0.114	0.088						
12:45	2½	83.0	65	35	0.09	0.068	31.8	1.029	1.0	0.318	0.48	
1:35	...	....	..	..	.....	.....	28.8	1.030	0.5	0.14	0.36	300
1:45	3½	83.0	65	35	0.12	0.10	....	.....	...	....	....	300
2:45	4½	83.0	60	40	0.12	0.11	78.0	1.017	0.0	0.0	0.2	
3:00												
3:45	5½	84.0	63	37	0.126	0.116	36.0	1.023	0.25	0.09	0.17	
4:00												
4:30	6¼	83.0	63	37	0.123	0.112	26.4	1.030	0.0	0.0	0.2	
4:45												

TABLE 5 (CASE 3, J. S. B., 1/24/17).—RESULTS OF SECOND TEST

Time		Blood Sugar per Cent.	Urine				Fluid Intake, C.c.
			C.c. per Hour	Sp. Gr.	Sugar		
A. M.	Hr.				Per Cent.	Gm. per Hour	
9:45	...	0.104	44.4	1.023	0.0	0.0	
10:00	33 gm. glucose		....	.....	....	.....	400
10:15	¼	0.141	34.2	1.022	0.71	0.24	
10:30	½	0.138					
10:40							
10:45	¾	0.129					
11:00	1	0.108					
11:15	1¼	0.114					
			24.0	1.030	1.66	0.398	
11:30	1½	0.104					
11:45	1¾	0.09					
12:00 M.	2	0.10					
P. M.							
12:30	2½	0.098					
			18.0	1.031	0.3	0.054	
1:00	3	0.10					
1:30	3½	0.10					
2:30	4½	0.10	17.4	1.028	0.0	0.0	
3:00							

In these two tests the extent of the hyperglycemia seems to vary directly with the amount of sugar ingested.

In the first test the blood volume (as indicated by the hemoglobin) increased 3.5 per cent. during the increase in blood sugar, later returning to normal. Urinary excretion decreased following the ingestion of glucose.

Alimentary Glucose Test in a Case of Diabetes of Long Standing Without Kidney Involvement

CASE 4.—S. O., female, aged 65, had symptoms of diabetes for fourteen years. Treated indifferently for that period. At time of examination she suffered from neuralgia, weakness, polyuria, polydipsia, polyphagia, and pruritis. The urine contained 6 per cent. glucose in the twenty-four-hour specimen; no protein or casts. Blood pressure: systolic, 150; diastolic, 90. Her morning blood sugar was 0.23 and 0.225 per cent. on two occasions, the

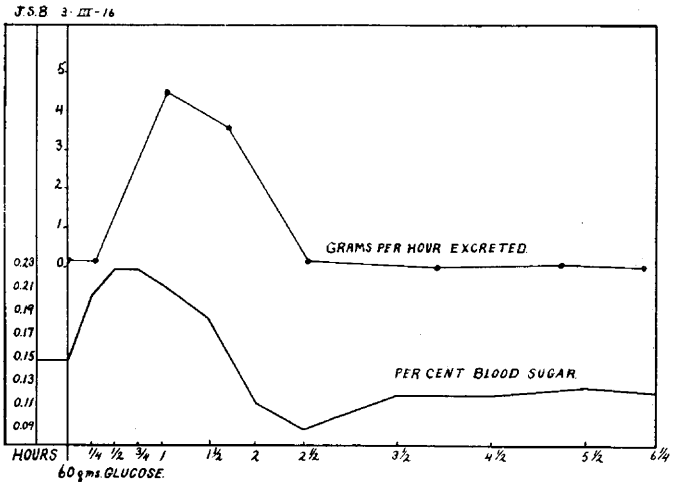

Chart 7

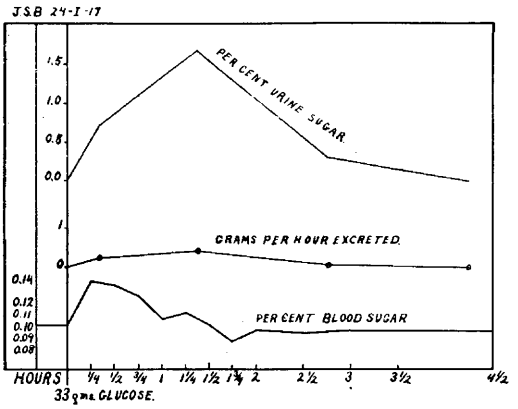

Chart 8

urine passed at the same period being free from sugar. Dec. 17, 1915, she was tested with 66 gm. of glucose. The results are shown in Chart 9 and Table 6. In this case the preformed sugar was high (0.22 per cent.), the blood sugar increased rapidly, reaching its highest point in three-quarters of an hour, and then quickly decreased. Unfortunately, specimens of blood could not be obtained after the 2¾-hour period. The urine at the beginning of the test was free from sugar.

TABLE 6 (CASE 4, S. O., 12/15/17).—ALIMENTARY GLUCOSE TEST ON A CASE OF DIABETES WITHOUT KIDNEY INVOLVEMENT

Time		Blood		Urine				Fluid Intake, C.c.
		Hemoglobin, Units	Sugar, per Cent.	C.c. per Hour	Sp. Gr.	Sugar		
A. M.	Hr.					Per Cent.	Gm. per Hour	
9:45	...	69	0.22	33.6	1.019	0.0	0.0	
10:00	66 gm. glucose		.....	.....	.....	...	...	600
				30.0	1.025	0.2	0.06	
10:15	¼	69	0.384					
10:30	½	68	0.432	147.6	1.026	3.1	4.57	
10:45	¾	68	0.492					
11:00	1	68	0.49					
11:15	1¼	68	0.472	210.0	1.025	4.9	10.29	
11:30	1½	68	0.448	150.0	1.030	6.5	9.75	
11:45	1¾	68						
12:00 M.								
P. M.								
12:15	2¼	69	0.36	129.6	1.032	6.2	8.03	
12:30								
12:45	2¾	69	0.32	60.0	1.031	5.3	3.18	
1:00	...	..	.....	33.6	1.020	4.6	1.54	250
1:30	...	..	.....	48.0	1.015	0.1	0.04	
2:10	...	..	.....	154.2	1.005	0.0	0.0	

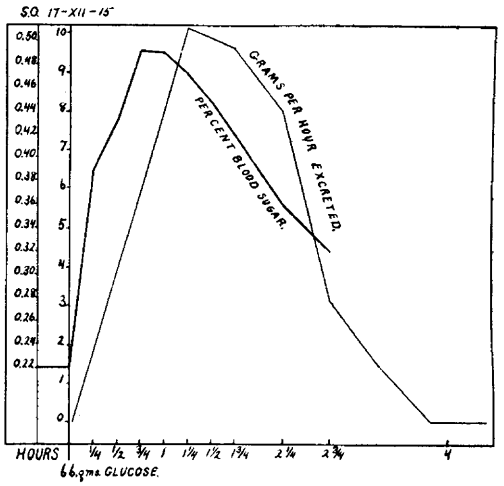

Chart 9

One cannot determine at what blood sugar concentration the kidneys actively excreted glucose, but it was between 0.22 and 0.384 per cent. The excretion of sugar was marked; it followed the blood sugar curve, and could no longer be detected with Benedict's solution at the end of four hours' time. Urine excretion decreased in the first quarter of an hour, later being uninfluenced by the increasing blood sugar. The blood volume (indicated by hemoglobin) was but slightly affected, increasing 1 per cent. This is due to the rapid response of the kidneys to fluid intake.

ALIMENTARY HYPERGLYCEMIA IN DIABETES

Alimentary hyperglycemia in diabetes, following the ingestion of glucose, has been frequently studied. Hopkins[11] examined nine cases and found a high preformed blood sugar value. Following the administration of 100 gm. of glucose there was a markedly prolonged hyperglycemia. Similar results have been found by Epstein,[21] Hamman and Hirschman,[13] and Cummings and Piness.[12] Chart 10 is a composite from tests made by Epstein on cases of diabetes without renal involvement; Chart 11 from tests made by the same author in cases

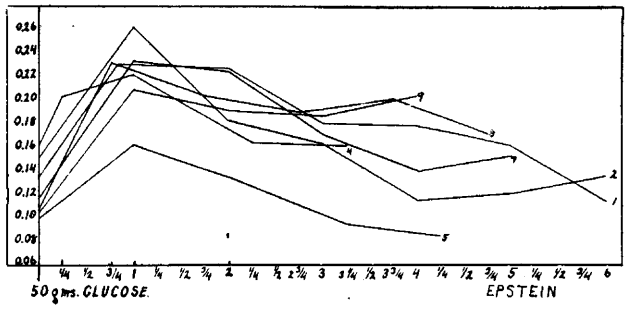

Chart 10

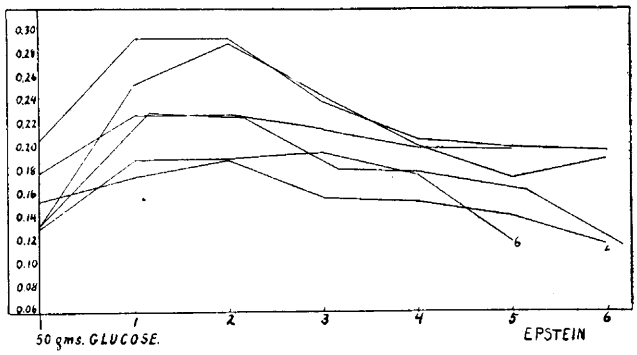

Chart 11

of diabetes with renal involvement. The effect of the nephritis was to increase the preformed blood sugar value and to prolong the hyperglycemia.

Alimentary Glucose Test in a Case of Chronic Interstitial Nephritis

CASE 5.—V. A., male, aged 27, had hemorrhagic nephritis following erysipelas seven years previous to admission. Frequent repeated attacks of great severity. At present, cardiac and vascular hypertrophy, retinitis; blood pressure: systolic, 235; diastolic, 160. Urine, 1,500 c.c.: specific gravity, 1.010; protein, moderate amount; an occasional granular cast; no sugar. Phenol-

sulphonephthalein excretion, 8 per cent. in two hours. Blood chemistry: sugar, 0.165 per cent.; uric acid, 10.5 mg. per 100 c.c.; creatinin, 8.3 mg. per 100 c.c.; urea nitrogen, 59 mg. per 100 c.c.; combines 50 c.c. carbon dioxid per 100 c.c. of plasma.

TABLE 7 (CASE 5, V. A., 11/18/16).—ALIMENTARY GLUCOSE TEST IN A CASE OF CHRONIC INTERSTITIAL NEPHRITIS

Time		Blood			Urine				Fluid Intake, C.c.
			Sugar				Sugar		
A. M.	Hr.	Hemoglobin, Units	In Whole Blood, per Cent.	In Plasma, per Cent.	C.c. per Hour	Sp. Gr.	Per Cent.	Gm. per Hour	
9:00	...	59	0.159	0.147	58.0	1.010	0.0	0.0	
9:15	75 gm. glucose	.....	.....		....	.....	...	....	330
					45.0	1.014	0.0	0.0	
9:30	¼	57	0.188	0.172					
9:40									
9:45	½	56	0.252	0.234					
10:00	¾	57	0.287	0.266					
					30.0	1.012	+	....	240
10:20	1+	58	0.296	0.272					
10:30									
10:45	1½	58	0.369	0.351					
					54.0	1.022	0.5	0.27	220
11:15	2	59	0.342	0.36					
11:30									
11:45	2½	58	0.296	0.296	....	.....	...	....	220
					66.0	1.006	0.1	0.06	
P. M.									
12:20	3	59	0.228	0.222					
12:30									
1:15	4	59	0.156	0.15	54.6	1.014	+		
1:30	...	..	.....	.....	....	.....	...	....	450
2:00	...	..	.....	.....	56.4	1.014	0.0	0.0	
2:15	5	59	0.126	0.117	60.0	1.010	0.0	0.0	
3:10									
3:15	6	59	0.144	0.132	60.0	1.014	0.0	0.0	
									220
3.45									

Feb. 18, 1916, he was tested with 75 gm. of glucose. The results are shown in Chart 12, Table 7. The preformed sugar is high, as is found in nephritis. The kidneys become permeable to sugar between 0.25 and 0.3 per cent. blood sugar. The blood sugar curve is delayed and prolonged, the highest point being reached in one and one-half hours, and the patient's normal not being regained before the four-hour period. The excretion of sugar is very slight, 0.27 gm. per hour being excreted with a blood sugar of 0.369 per cent.

Hemoglobin estimations show a 3 per cent. increase, which slowly returns to normal with the blood sugar. The excretion of urine decreases during the development of the hyperglycemia.

ALIMENTARY HYPERGLYCEMIA IN NEPHRITIS

Alimentary hyperglycemia in nephritis has been studied by Neubauer,[24] Tachau,[25] Hopkins,[11] Epstein,[21] Hamman and Hirschman[13] and others, following the administration of glucose by mouth (usually 100 gm.). Chart 13 is a composite of the results of the test in four patients examined by Hopkins; Chart 14 is a composite of the six cases of Hamman and Hirschman. In all of these cases

24. Neubauer: Biochem. Ztschr. **25**:284, 1910.
25. Tachau: Deutsch. Arch. f. klin. Med. **104**:448, 1911.

the curve is similar to that found in many cases of diabetes and shows the fallacy of alimentary hyperglycemic tests alone as a diagnostic method. Especially is this true of the practice of testing the blood at one-hour intervals, for in nephritis, as well as in diabetes (with renal involvement), the second hour specimen is apt to contain as much or more glucose than the first hour specimen.

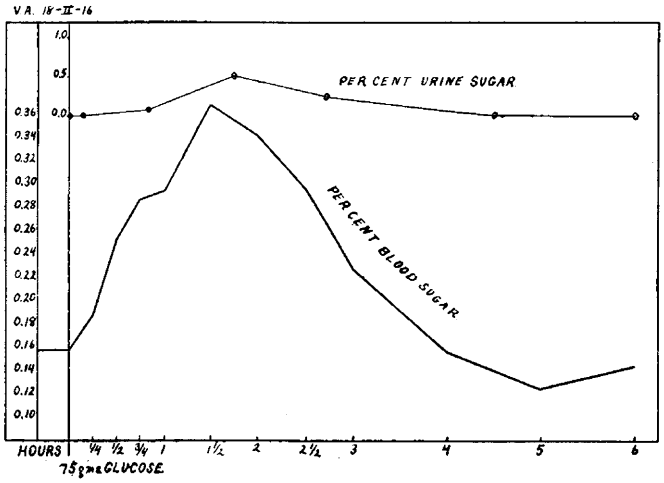

Chart 12

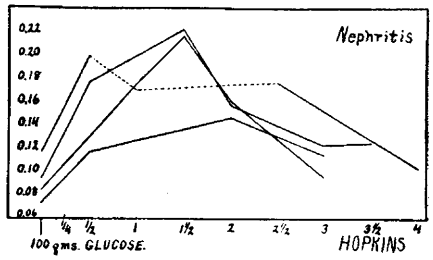

Chart 13

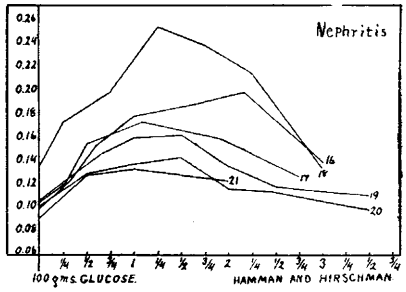

Chart 14

Alimentary Glucose Test in Diabetes with Renal Involvement

CASE 6.—C. M., male, aged 54. Glycosuria was discovered a few years prior to admission. The patient suffered from cardiac decompensation, dilatation, irregular pulse, edema, ascites, and dyspnea. The urine contained a moderate amount of protein and many hyaline and granular casts. Phenolsulphonephthalein excreted in two hours, 29 per cent. Blood pressure: systolic, 200; diastolic, 150. Blood chemistry: sugar, 0.21 per cent.; urea nitrogen, 16 mg. per 100 c.c. blood; uric acid, 3.6 mg. per 100 c.c. blood; creatinin, 2.9 mg. per 100 c.c. blood.

TABLE 8 (CASE 6, C. M., 12/9/15).—ALIMENTARY GLUCOSE TEST IN DIABETES WITH RENAL INVOLVEMENT

Time		Blood		Urine				Fluid Intake, C.c.
		Hemoglobin, Units	Sugar, per Cent.	C.c. per Hour	Sp. Gr.	Sugar		
A. M.	Hr.					Per Cent.	Gm. per Hour	
9:15	...	81.5	0.21	72	1.011	0.0	0.0	
9:30	33 gm. glucose		.....	..	.....	...	....	250
				?	?	0.0	0.0	
9:45	¼	81.5	0.24					
10:00	½	77.0	0.288					
10:15	¾	78.0	0.308	48	1.015	++	?	
10:30	1	80.0	0.301					250
10:45	1¼	80.0	0.301	96	1.013	0.61	0.58	
10:50								250
11:15	1¾	81.0	0.252	114	1.010	0.153	0.17	
11:45	2¼	81.0	0.25	90	1.011	++	?	250
P. M.								
12:15	2¾	81.5	0.235	120	1.011	+	?	
12:45	3¼	81.5	0.23	204	1.008	0.0	0.0	
1:15	3¾	83.0	0.215	120	1.012	0.0	0.0	
1:45	4¼	82.0	0.210	102	1.010	0.0	0.0	
2:45	5¼	81.5	0.205	72	1.010	0.0	0.0	

Dec. 9, 1915, he was tested with 33 gm. of glucose. The results are shown in Chart 15 and Table 8. The striking features are the high preformed blood sugar value, the rapid rise in blood sugar, reaching its highest point in three-quarters of an hour, the great delay in returning to normal (four and one-fourth hours), and the very slight excretion of sugar.

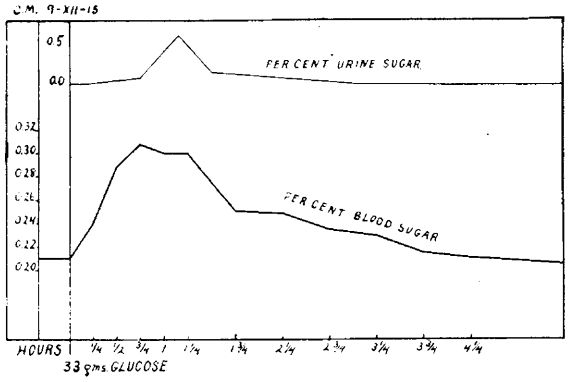

Chart 15

Blood volume increased 4.5 per cent. (as indicated by hemoglobin) during the hyperglycemia, later returning to normal. Urinary excretion fell off markedly, greatly increasing as the hyperglycemia subsided.

CASE 7.—I. A., female, aged 46. Diabetes eleven years. Chronic interstitial nephritis. Daily urine contained from 3 to 6 per cent. sugar on ordinary diet, a trace of albumin, and a few hyaline and granular casts. Blood chemistry: sugar, 0.26 per cent.; urea nitrogen, 30 mg. per 100 c.c. blood; uric acid, 6 mg. per 100 c.c. blood; creatinin, 3 mg. per 100 c.c. blood. Phenolsulphonephthalein, 52 per cent. excreted in two hours. Morning urine free from sugar.

TABLE 9 (CASE 7, I. A., 11/1/16).—DIABETES WITH RENAL INVOLVEMENT

Time		Blood		Urine						Fluid Intake, C.c.
					Sugar					
						Myers Method				
A. M.	Hr.	Hemoglobin, Units	Sugar, per Cent.	C.c. per Hour	Benedict's Method, per Cent.	Per Cent.	Gm. per Hour	Chlorids, Gm. per Hour	Sp. Gr.	
9:15	...	67	0.255	36.0	0.125	0.12	0.043	0.201	1.018	
9:30	30 gm. glucose	.....	.....	.....	....	....	....	.....	.....	400
				233.0	0.15	0.159	0.37	1.302	1.012	
9:45	¼	64	0.275							
10:00	½	64	0.352	258.0	0.72	0.54	1.39	0.516	1.010	
10:15	¾	61	0.424							
				468.0	1.4	1.08	5.05	0.748	1.008	
10:30	1	63	0.441							
10:45	1¼	64	0.459	420.0	1.58	1.41	5.92	0.714	1.010	
11:00	1½	64	0.459							
11:15	1¾	65	0.45	170.0	2.88	2.12	3.6	0.577	1.015	
11:30	2	66	0.441							
11:45	2¼	66	0.413							
12:00 M.	2½	67	0.392	117.0	2.76	2.35	2.75	0.444	1.019	
P. M.										
12:10										
12:30	3	66	0.364	94.0	2.58	2.0	1.87	0.374	1.020	
12:45										
1:00	3½	68	0.343	52.0	2.22	2.0	1.03	0.258	1.023	
1:15										
1:30	4	68	0.31	40.0	2.13	2.04	0.8	0.213	1.021	
2:00	4½	68	0.30							
2:30	5	68	0.29	38.0	1.68	1.47	0.55	0.226	1.025	
3:00	5½	69	0.275							
3:30	6	70	0.26	39.0	0.92	0.77	0.3	0.27	1.026	
4:00	6½	70	0.255							
4:30	7	70	0.24	39.0	0.92	0.78	0.3	0.226	1.025	
5:00	7½									

Nov. 1, 1916, she was tested with 30 gm. of glucose. The results are shown in Chart 16 and Table 9. The interesting points are the high preformed sugar value, the rapid and high hyperglycemia, the delay in returning to normal, and the permeability point to glucose being but slightly above the preformed sugar value, explaining the rapid appearance of glycosuria.

Alimentary Glucose Test in a Case of Hyperthyroidism

CASE 8.—J. K., male, aged 42, for the previous four months had weakness, loss of weight, irritability, tremors, palpitation, tachycardia, exophthalmos, enlarged pulsating thyroid, and glycosuria following meals. On the morning of May 20, 1915, he was given a hypodermic injection of 0.66 mg. of epinephrin. The results are shown in Chart 17 and Table 10. The preformed sugar was at the highest normal limit, probably due to his anxiety over the test. The kidneys actively excreted sugar when the blood sugar was between 0.165 and 0.171 per cent. Blood volume increased 3 per cent. during the development of the hyperglycemia (as shown by hemoglobin).

May 26, 1915, he was again tested with 1 mg. epinephrin hypodermically. The results are shown in Chart 18 and Table 11. Sugar appeared in the urine at a blood sugar concentration of 0.165 per cent. The hyperglycemia was more rapid, higher and more prolonged than when the smaller amount of epinephrin was given.

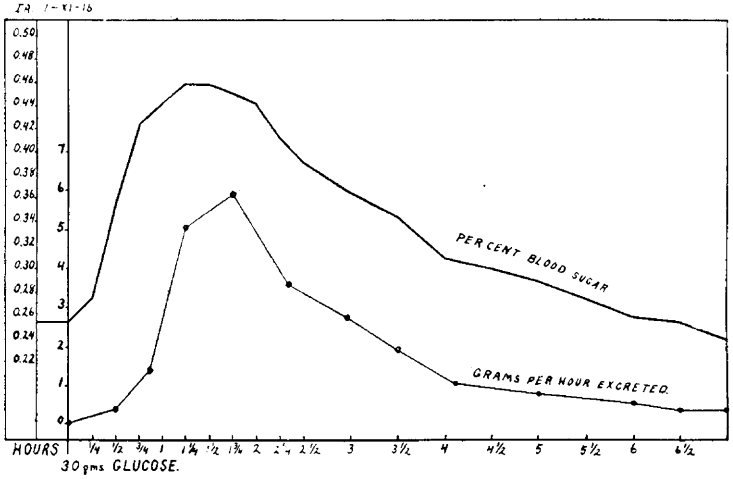

Chart 16

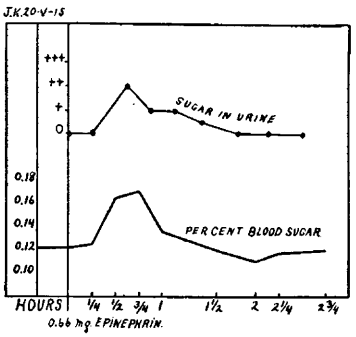

Chart 17

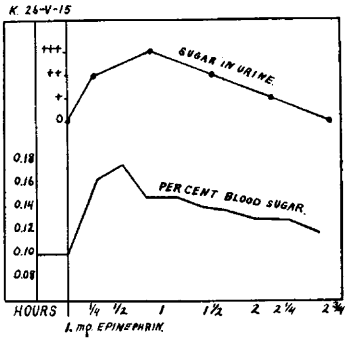

Chart 18

May 28, he was tested with 33 gm. of glucose. The results are shown in Chart 19 and Table 12. The blood sugar curve is of the normal type. Sugar was excreted at a blood sugar concentration between 0.15 and 0.174 per cent. Blood volume increased 5 per cent.

In these three tests the excretion of sugar closely followed the changes in blood sugar.

Alimentary Glucose Test in a Case of Myxedema

CASE 9.—M., male, aged 54, for the previous four years had obesity, falling hair, lassitude, mental hebetude, myxedema of face, limbs, and abdomen, atrophy of thyroid gland and myocarditis. Blood pressure: systolic, 125; diastolic, 85. Phenolsulphonephthalein excreted in two hours time, 53 per

TABLE 10 (CASE 8, J. K., 5/20/15).—ALIMENTARY GLUCOSE TEST IN A CASE OF HYPERTHYROIDISM

Time A. M.	Hr.	Blood Pressure	Blood: Hemoglobin Units	Blood: Sugar, per Cent.	Urine Sugar	Fluid Intake, C.c.
10:25	...	132-50	72	0.122	0.0	250
10:30	0.66 mg. epinephrin (hypo.)					
10:45	¼	160-70	69	0.124	0.0	
11:00	½	140-75	69	0.165	0.0	
11:15	¾	138-72	69	0.171	++	
11:30	1	133-60	69	0.136	+	
11:45	...	.....	..	.....	...	250
P. M.						
12:05	1½	125-63	69	0.12	0	
12:30	2	130-64	70	0.11	0.0	
12:45	2¼	132-65	70	0.118	0.0	
1:15	2¾	140-68	72	0.12	0.0	

TABLE 11 (CASE 8, J. K., 5/26/15).—SECOND TEST WITH EPINEPHRIN

Time P. M.	Hr.	Blood Pressure	Blood Sugar, per Cent.	Urine: C.c. per Hour	Urine: Sugar	Fluid Intake, C.c.
1:55	...	155-75	0.1	78.0	0.0	
2:05	1 mg. epinephrin (hypo.)					
2:25	¼+	193-70	0.165	18.0	++	250
2:40	½+	145-65	0.177			
2:55	1 —	132-60	0.147	36.0	+++	
3:05						
3:15	1¼—	130-55	0.147			
3:30	1½—	125-55	0.141	49.0	++	
3:45	1¾—	126-60	0.134			
4:05	2	130-65	0.132			
				120.0	+	
4:25	2¼+	130-78	0.130			
4:45	2¾—	123-62	0.118	56.0	0.0	
5:00						

TABLE 12 (CASE 8, J. K., 5/28/15).—GLUCOSE TEST

Time A. M.	Hr.	Blood: Hemoglobin, Units	Blood: Sugar, per Cent.	Urine: C.c. per Hour	Urine: Sugar, Per Cent.	Urine: Sugar, Gm. per Hour	Fluid Intake, C.c.
10:05	...	75.5	0.116	?	0.0	0.0	
10:30	38 gm. glucose	.....	.....	..	...	...	300
				48	0.0	0.0	
10:45	¼	71.0	0.15				
11:00	½	70.5	0.174	78	0.27	0.05	
11:15	¾	68.0	0.188	62	1.0	0.6	
11:25							
11:30	1	69.5	0.192	60	0.9	0.54	
11:45							
12:00 M.	1½	70.5	0.18	63	0.5	0.3	
P. M.							
12:15	...	....	.....	..	...	...	300
12:30	2	70.5	0.129	48	0.2	0.09	
12:45							
1:00	2½	71.5	0.104	78	0.0	0.0	
1:15							
1:30	3	72.0	0.118	62	0.0	0.0	
1:40							
2:00	3½	76.0	0.114	37	0.0	0.0	
2:15							
3:15	4¾	74.5	0.116	42	0.0	0.0	
3:45	5¼	75.0	0.112	36	0.0	0.0	

cent. Blood chemistry: urea nitrogen, 20 mg. per 100 c.c. blood; uric acid, 4.2 mg. per 100 c.c. blood; creatinin, 1.7 mg. per 100 c.c. blood.

July 9, 1915, he was tested with 1 mg. of epinephrin hypodermically. The results are shown in Chart 20 and Table 13. The preformed blood sugar was of normal value. The increase in blood sugar was very slow, the highest point being reached in from one to one and one-quarter hours, and had not returned to normal at the end of three and one-half hours. The highest blood sugar value was 0.141 per cent. and at no time was sugar excreted.

July 15, he was tested with 90 gm. of glucose. The results are shown in Chart 21 and Table 14. The preformed blood sugar was within normal limits. The blood sugar curve reached its highest point in one hour, but did not return to normal before the three and one-half to four-hour period. At no

TABLE 13 (CASE 9, M., 7/9/15).—ALIMENTARY GLUCOSE TEST IN A CASE OF MYXEDEMA

Time A. M.	Hr.	Hemoglobin Units	Blood Sugar, per Cent.	Urine Sugar
9:25	...	69	0.112	0.0
9:30	1 mg. epinephrin (hypo.)			
9:45	¼	65	0.12	0.0
10:00	½	70	0.132	0.0
10:15	¾	68	0.138	
10:30	1	67	0.141	0.0
10:45	1¼	70	0.141	
11:00	1½	68	0.138	
11:15	1¾	68	0.138	
11:30	2	68	0.135	0.0
11:45	2¼	64	0.132	
12:00 M.	2½	66	0.129	
P. M.				
12:15	2¾	63	0.126	
12:30	3	65	0.126	0.0
12:45	3¼	66	0.126	
1:00	3½	66	0.126	

TABLE 14 (CASE 9, M., 7/15/15).—GLUCOSE TEST

Time A. M.	Hr.	Hemoglobin Units	Blood Sugar, per Cent.	Urine Sugar, per Cent.	Fluid Intake, C.c.
9:00	...	68.0	0.12	0.0	
9:15	90 gm. glucose	....	.....	...	400
9:45	½	64.0	0.188	0.0	
10:00	¾	66.0	0.212		
10:15	1	67.0	0.216	0.0	
10:30	1¼	68.0	0.204		
10:45	1½	68.0	0.2		
11:00	1¾	68.0	0.196	0.0	
11:15	2	67.0	0.188		
11:45	2½	68.0	0.18		
P. M.					
12:15	3	68.0	0.156	0.0	
12:45	3½	68.0	0.135		
1:15	4	67.0	0.094		
1:45	4½	68.0	0.096	0.0	
2:15	5	67.5	0.104		
2:55	5¾	68.0	0.106		
3:30	6¼	68.0	0.112	0.0	

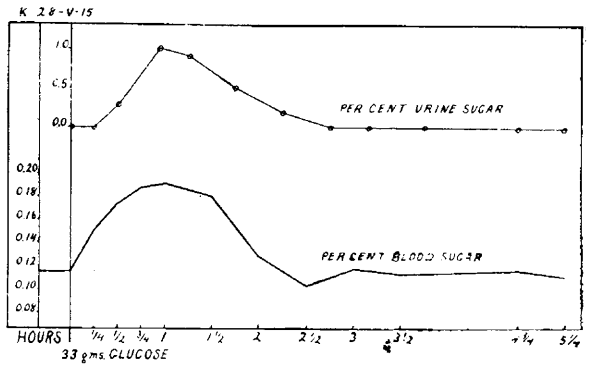

Chart 19

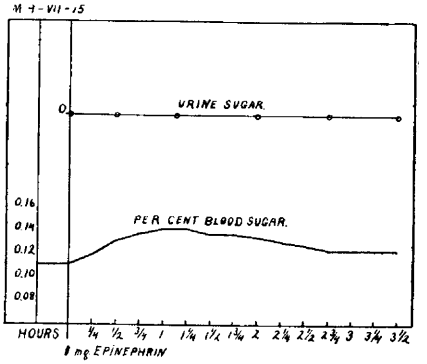

Chart 20

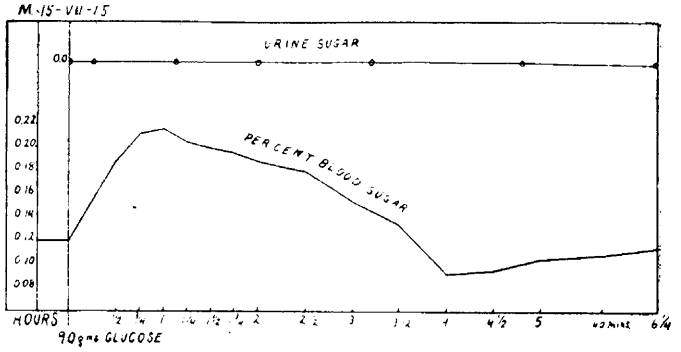

Chart 21

time was sugar excreted, although the blood sugar had reached a concentration of 0.216 per cent. Blood volume increased 4 per cent. on the development of the hyperglycemia, returning to normal as the blood sugar decreased.

The observations of Janney and Isaacson[26] on the blood sugar in thyroid and other endocrine diseases are of interest in connection with this and the following case.

Alimentary Glucose Test in Hypopituitarism

CASE 10.—E. L., female, aged 18, had the hypophysis removed by operation one year prior to admission. Marked obesity. Urine volume, 6,000 c.c. daily. No sugar, protein, or casts. Phenolsulphonephthalein, 62 per cent. excreted in two hours. Blood chemistry: urea nitrogen, 10 mg. per 100 c.c. blood; uric acid, 3.1 mg. per 100 c.c. blood; creatinin 1.8 mg. per 100 c.c. blood. The patient had been tested on two occasions with 250 gm. of glucose, and the twenty-four-hour specimen examined for sugar without any being found.

TABLE 15 (CASE 10, E. L., 1/31/16).—ALIMENTARY GLUCOSE TEST IN HYPOPITUITARISM

Time		Blood			Urine					Fluid Intake, C.c.
			Sugar				Sugar			
A. M.	Hr.	Hemoglobin, Units	In Whole Blood, per Cent.	In Plasma, per Cent.	C.c. per Hour	Sp. Gr.	Per Cent.	Gm. per Hour	Chlorids, Gm. per Hour	
9:35	...	71	0.12	0.105	270.0	1.010	0.0	0.0	0.216	
10:15	240 gm. glucose		.....	.....	.....	.....	...	....	....	400
10:30	¼	71	0.259	0.224						
					36.0	1.014	0.2	0.72	0.1	
10:45	½	68	0.315	0.297						
11:00	vomited 36.9 gm. glucose									
10:10										
11:15	1	67	0.369	0.351						
					288.0	1.024	0.9	2.59	0.4	
11:45	1½	66	0.378	0.333						
12:00 M.										
P. M.										
12:15	2	67	0.344	0.304						
					342.0	1.023	0.4	1.36	0.27	
1:00	2¾	67	0.287	0.252						
1:15	...	..	.....	.....	.....	.....	...	....	....	240
1:30	3¼	68	0.252	0.222						
					192.0	1.009	0.0	0.0	0.192	
2:30	4¼	68	0.184	0.16						
2:40	...	..	.....	.....	.....	.....	...	....	....	240
3:45	5½	68	0.105	0.066	306.0	1.022	0.0	0.0	0.24	
4:00										

Jan. 31, 1916, she was tested with 240 gm. of glucose. This was dissolved in 400 c.c. of weak tea and administered by means of a small stomach tube. The results are shown in Chart 22 and Table 15. The preformed blood sugar was within normal limits. Alimentary hyperglycemia reached its highest point in one and one-half hours, and returned to normal in five and one-half hours. Notwithstanding the high concentration of blood sugar, 0.378 per cent., the excretion of glucose was comparatively slight. Sugar was actively excreted at a blood sugar concentration of 0.26 per cent.

26. Janney and Isaacson: Arch. Int. Med. **22**:160, 1918.

The excretion of urine greatly decreased in the three-quarters hour following the ingestion of the glucose, later increasing. The excretion of chlorids decreased as the glucose solution was being absorbed.

Blood volume increased 5 per cent. (as indicated by hemoglobin decrease) during the hyperglycemia, later returning to normal.

Alimentary Glucose Test in a Case of Dyspituitarism

CASE 11.—S., male, aged 27, was obese, of feminine figure, with small wrists, tapering fingers, beardless face, and was mentally inferior. His morning blood sugar was 0.1 per cent.

TABLE 16 (CASE 11, S., 5/12/16).—ALIMENTARY GLUCOSE TEST IN A CASE OF DYSPITUITARISM

Time		Blood				Urine			Fluid Intake, C.c.
			Sugar						
A. M.	Hr.	Hemoglobin, Units	In Whole Blood, per Cent.	In Plasma, per Cent.	In Corpuscles, per Cent.	C.c. per Hour	Sp. Gr.	Sugar	
9:25	...	75	0.132	0.10	0.123	30	1.025	0	400
9:30	75 gm. glucose		.....	.....	.....	..	.....	...	
						25	1.030	0	
9:45	¼	72	0.178	0.2	0.2				
10:00	½	70	0.198	0.197	0.188				
10:15	¾	69	0.193	0.18	0.172	21	1.033	0	
10:40	1¼	70	0.183	0.156	0.172				
11:00	1½	69	0.148	0.14	0.155	43	1.036	0	
11:30	2	71	0.132	0.111	0.134				
12:00 M.	2½	73	0.118	0.094	0.128	20	1.041	0	
P. M.									
12:30	3	74	0.097	0.086	0.114				
						21	1.040	0	
1:15	3¾	74	0.111	0.099	0.123				
						21	1.043	0	
2:00	4½	73	0.111	0.114	0.128				
2:30	5	74	0.112	0.105	0.141	16	1.043	0	
3:00	5½	76	0.118	0.111	0.141				
						15	1.040	0	
4:00	6½	75	0.108	0.111	0.141				

May 12, 1916, he was tested with 75 gm. of glucose. The results are shown in Chart 23 and Table 16. The preformed blood sugar was slightly above normal. The blood sugar curve was of normal type. The urine remained free from sugar, although the blood sugar had reached a concentration of 0.198 per cent. The excretion of urine decreased during the development of the hyperglycemia, increasing as the blood sugar began to fall.

Hemoglobin estimations showed a blood volume increase of 6 per cent., which returned to normal with the blood sugar.

Alimentary Glucose Test in a Case of Parenchymatous Nephritis with Constant Glycosuria

CASE 12.—J. P., male, aged 62, had symptoms of nephritis for the previous two years. No symptoms of diabetes mellitus. For the previous six months he had generalized edema, retinitis, cardiac hypertrophy. Blood pressure: systolic, 190; diastolic, 130. Urine, 625 c.c., specific gravity, 1.025; dry protein per liter, 3.1 gm.; chlorids, 6.6 gm.; sugar, 0.6 per cent.; many hyaline and granular casts. Phenolsulphonephthalein excreted in two-hour test, 8 per cent. Blood chemistry: sugar, 0.18 per cent.; urea nitrogen, 23 mg.; uric acid, 4 mg.; creatinin, 1.9 mg. per 100 c.c. of blood. For ten months, up to the time of the patient's death, the urine constantly contained glucose, the concentration always being in the neighborhood of 0.5 per cent.

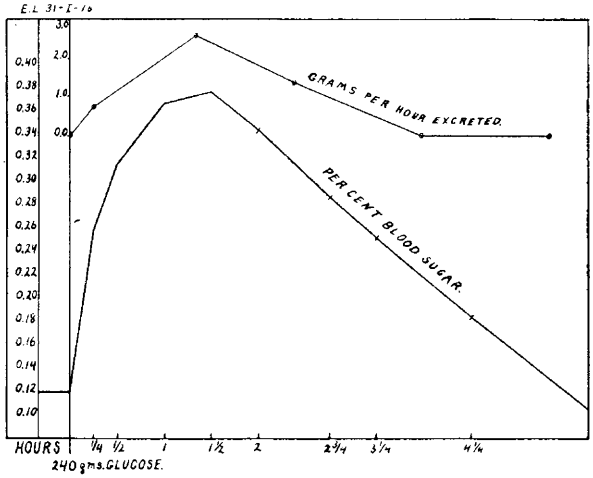

Chart 22

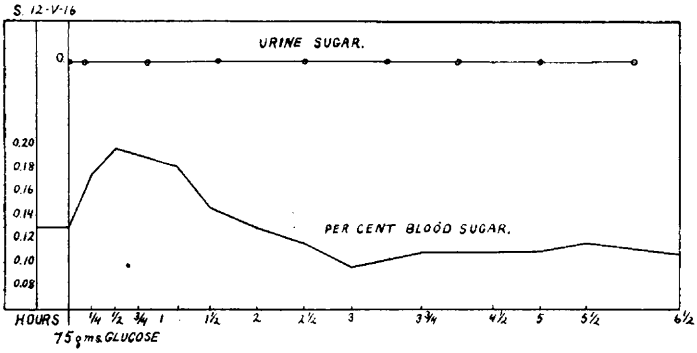

Chart 23

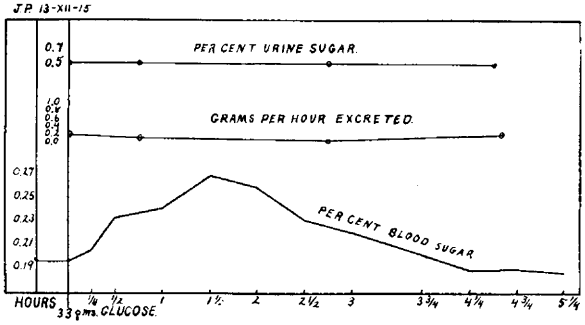

Chart 24

Dec. 13, 1915, the patient was tested with 33 gm. of glucose. The results are shown in Chart 24 and Table 17. The preformed blood sugar was high, as commonly found in nephritis. The blood sugar curve was greatly prolonged, the highest point being reached in one and one-half hours, not returning to normal before four and one-half hours had elapsed. The urine passed in this period contained about 0.5 per cent. glucose, and this independent of the blood sugar concentration. The actual excretion of glucose was less during the hyperglycemia than during the fasting state. In this case the sugar excretion varied directly with the excretion of urine.

March 11, 1916, the test was repeated, using 75 gm. of glucose. The results are shown in Chart 25 and Table 18. Again in this test the excretion of glucose was less during the hyperglycemia, although the urine sugar increased to 1.1 per cent. The time periods for the blood sugar curve are slightly longer than in the previous test; less than half the amount of glucose was ingested.

In each of these tests the excretion of urine decreased following the ingestion of glucose. Hemoglobin decreased during the development of the hyperglycemia, indicating an increase in blood volume at this time. The volume returned to normal on the subsidence of the hyperglycemia. Table 17 shows a decreased excretion of chlorids as the blood sugar increased. This retention is probably due to the increase in body fluid from the fluid intake and decreased excretion of urine.

TABLE 17 (CASE 12, J. P., 12/13/15).—GLUCOSE TEST IN PARENCHYMATOUS NEPHRITIS WITH CONSTANT GLYCOSURIA

Time		Blood		Urine					Fluid Intake, C.c.
		Hemoglobin, Units	Sugar, per Cent.	C.c. per Hour	Sugar		Sp. Gr.	Chlorids, Gm. per Hour	
A. M.	Hr.				Per Cent.	Gm. per Hour			
9:25	...	67.5	0.196	42	0.52	0.22	1.015	0.193	
9:30	33 gm. glucose		.....	..	....	....	.....	.....	250
9:45	¼	64.0	0.208						
10:00	½	65.0	0.234	..	....	....	.....	.....	250
				36	0.51	0.186	1.015	0.123	
10:30	1	65.5	0.24						
11:00	1½	67.5	0.27						
11:30	2	67.0	0.26						
12:00 M.	2½	68.0	0.232						
P. M.									
12:30	3	67.5	0.224	33	0.51	0.17	1.016	0.142	
1:15	3¾	67.5	0.204						
1:30									
1:45	4¼	67.5	0.196						
2:15	4¾	68.0	0.196	42	0.52	0.21	1.013	0.19	
2:45	5¼	67.5	0.192						

SUMMARY

In the series of cases reported one finds variations in the blood sugar value after fifteen hours' fasting. Normal values are found in cases of renal diabetes, early mild diabetes, hyperthyroidism, hypothyroidism, hypopituitarism, dyspituitarism, and in a normal case. High blood sugar values are found in cases of nephritis, and diabetes of long standing with or without renal involvement. In the synchronous urine specimens two only showed the presence of glucose by Benedict's test. One was from a patient with a blood sugar of 0.098 per cent. whose kidneys at that time were excreting glucose at the rate of 2 gm. per hour. The other case showed a constant glycosuria of 0.5 per cent. independent of the diet.

In the twenty-four-hour urine specimens, glucose was found in the cases of renal diabetes, early mild diabetes, diabetes with and without renal involvement, hyperthyroidism, and chronic parenchymatous nephritis with constant glycosuria.

TABLE 18 (CASE 12, J. P., 3/11/16).—SECOND TEST

Time		Blood		Urine				Fluid Intake, C.c.
		Hemoglobin, Units	Sugar, per Cent.	C.c. per Hour	Sp. Gr.	Sugar		
A. M.	Hr.					Per Cent.	Gm. per Hour	
9:20	...	65.0	0.2	144	1.015	0.5	0.72	450
9:30	75 gm. glucose	.....	.....	...	.....	...	....	
9.45	¼	65.0	0.258					
10:05	½	65.0	0.256					
10:20	¾	64.0	0.252	52	1.013	1.0	0.52	
10:35	1	64.0	0.329					250
11:00	1½	63.5	0.368					
11:20								
11:30	2	63.5	0.405					500
P. M.								
12:45	3¼	64.0	0.39	56	1.015	1.1	0.61	
1:30								
3:15	5¾	65.0	0.25					
4:15	6¾	65.0	0.22	?	1.014	0.5	?	
7:35								

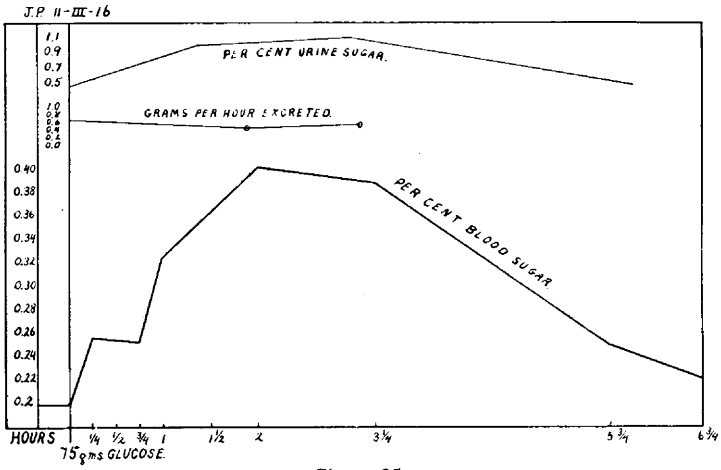

Chart 25

Following the ingestion of glucose the type of blood sugar curve varied in the different cases, showing a rapid increase and decrease in uncomplicated mild diabetes; in the cases of dyspituitarism, hyperthyroidism, renal diabetes, and normal, the curves are of the type found in normal individuals by various investigators.

In nephritis the curve was delayed and prolonged. In diabetes with renal involvement, the increase in blood sugar was at the normal rate, but there was a very slow return to the preformed value.

A higher blood sugar at the end of the first hour than at the end of the second was found in normal, renal diabetes, early mild diabetes, diabetes of long standing without renal involvement, diabetes with cardiac incompetence, hyperthyroidism, myxedema, hypopituitarism, and dyspituitarism.

Higher values at the end of the second hour were found in chronic interstitial nephritis, diabetes with interstitial nephritis, and chronic parenchymatous nephritis with constant glycosuria.

The concentration of blood sugar at which glycuresis occurred varied greatly in these cases, being less than 0.088 per cent. in the case of renal diabetes, 0.125 per cent. in early mild diabetes, 0.165 per cent. in hyperthyroidism, 0.167 per cent. in the normal case, 0.2+ per cent. in dyspituitarism, 0.216 per cent. in hypothyroidism, 0.26+ per cent. in hypopituitarism, 0.29 per cent. in nephritis, and 0.3+ per cent. in two cases of diabetes with renal involvement.

Cases showing an excretion of over 1 gm. of sugar in the six hours following the ingestion of from 60 to 75 gm. of glucose were: renal diabetes, early mild diabetes, diabetes of long standing without renal involvement, parenchymatous nephritis with constant glycosuria, those excreting less than 1 gm. were normal, interstitial nephritis, myxedema and dyspituitarism.

Cases showing an excretion of more than 1 gm. in the six hours following the ingestion of 30 to 33 gm. of glucose were renal diabetes, diabetes with renal involvement, parenchymatous nephritis with constant glycosuria; those excreting less than 1 gm. were: early mild diabetes, diabetes with cardiac incompetence, and hyperthyroidism.

The rate of sugar excretion was uninfluenced by changes in excretion of urine in all excepting Case 12. In this patient glycosuria varied directly with the amount of urine excreted and not according to changes in the blood sugar. A similar case has been reported by Epstein[21] (Chart 26).

Sixty estimations are given comparing the sugar content of whole blood and that of plasma. The results show 15 per cent. more in whole blood than in plasma. (A source of error in the technic employed lies in the fact that the plasma specimens were allowed to stand at room temperature for half an hour, during which time glycolysis may have occurred; the whole blood estimates were made at once.)

In twenty-six estimations the corpuscles contained 5 per cent. more reducing substance than the plasma (the technic being the same for both).

In thirteen tests, changes in blood volume were recorded following the ingestion of glucose. During the rise in blood sugar, blood volume increased from 1 to 7.5 per cent. (the average increase being 4.2 per cent.). The volume returned to normal on the subsidence of the hyperglycemia.

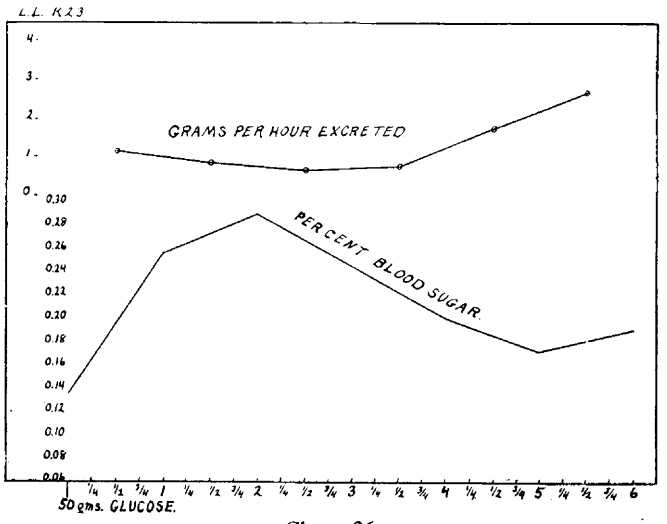

Chart 26

CONCLUSIONS

1. Sugar is a constant constituent of normal urine, and, during a fasting and thirsting state, the concentration in the urine approximates that in the blood.

2. Following the administration of small amounts of glucose (30 gm. or less) the blood sugar increases, and its demonstration depends entirely on the frequency of the estimations.

3. In a normal person the sugar in the urine parallels that in the blood up to the latter's concentration of 0.16 to 0.17 per cent. Above that the kidneys actively excrete sugar. In returning to the normal value the decrease in blood sugar precedes that in the urine.

4. Alimentary hyperglycemia in uncomplicated diabetes is characterized by a rapid rise and fall.

5. When diabetes is complicated by renal involvement, alimentary hyperglycemia is prolonged.

6. Alimentary hyperglycemia is prolonged in myxedema and hypopituitarism.

7. In nephritis alimentary hyperglycemia is delayed and prolonged.

8. The concentration of blood sugar at which glycuresis occurs varies in different individuals, and is influenced by disease, being abnormally low in early diabetes, high in diabetes of long standing, in nephritis, and in deficiency of the thyroid or hypophysis.

9. Glycuresis is a kidney function and is excessive in diabetes and hyperthyroidism. It is greatly decreased in nephritis and in deficiency of the thyroid or hypophysis.

10. Blood sugar estimations one hour after the ingestion of glucose may be the same in renal diabetes, early diabetes, or normal cases.

11. Blood sugar estimations two hours and three hours after the ingestion of glucose may be the same in diabetes of long standing, in nephritis, myxedema, or in hypopituitarism.

12. Blood volume increases with the development of a hyperglycemia, returning to normal with the blood sugar.

13. Blood sugar is about equally divided between plasma and corpuscles.

14. Sugar in the corpuscles increases in proportion to that in the plasma.

15. Excretion of sugar is uninfluenced by the rate of urinary excretion, excepting in some cases of parenchymatous nephritis.

16. Morning blood sugar estimations are of great diagnostic value. The urine excreted at the same time should be tested for sugar and the rate of excretion determined. As the morning blood sugar varies under treatment, diagnostic tests should be made after the patient has been on regular diet for several days.

17. Tests of alimentary hyperglycemia are of little clinical value; especially is this true of tests made at one hour intervals.

18. Examination of the twenty-four-hour urine for sugar (Benedict's new method[27]), or better, fractional examinations, detects cases of excessive glycuresis.

19. Test of alimentary glycuresis following the ingestion of glucose (100 gm. for a person of average weight, that is, 1.7 gm. per kilogram) is a valuable diagnostic and prognostic method, the urine sugar being estimated at frequent intervals for the succeeding six hours, and the total excretion determined. This, in conjunction with the morning blood and synchronous urine sugar estimation, probably tells us as much about the case as do the elaborate tests herein reported.

I wish to thank Prof. Edward Quintard, director of the Department of Medicine, and Prof. Victor C. Myers, director of the Laboratory of Pathological Chemistry, for their many courtesies, help and advice.

303 East Twentieth Street.

27. The conclusions regarding clinical tests are largely in accord with those of Rogers: Boston M. & S. J. **175**:152 (Aug. 3) 1916.