STUDY OF BLOOD SUGAR CURVES FOLLOWING A STANDARDIZED GLUCOSE MEAL*

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The following study is concerned with the effort to demonstrate the main factors which influence the duration of hyperglycemia after a glucose meal. More than 200 cases have been studied critically. There is extensive literature on the subject of blood sugar curves after various sorts of carbohydrate meals. In some studies standardized meals were given, in others not. Many clinicians have assigned diagnostic importance to an increased hyperglycemia following glucose ingestion.

The interpretation of the value of sugar curves depends on the following factors: (1) The technic of the administration of the glucose meal; (2) the collection of blood samples; (3) the method of doing the blood sugar determination, and (4) the wide application of the test so as to learn the many factors which influence these curves.

We believe it necessary, in order to support our conclusions, to discuss the first three of these points in detail.

Standardized Glucose Meal.—The standardized Janney[1] glucose meal was used. Glucose is the sugar of choice because it is most readily absorbed and because there are data as to the rate of its absorption from the gastro-intestinal tract. Fisher and Wishart[2] and Janney[3] have shown, by different methods, that from 66 to 80 per cent. of injected glucose is absorbed in the course of two hours.

The question of absorption is an important one. The curves here studied would indicate that absorption is fairly constant for the individual. This is brought out by the similarity of repeated curves (Table 1) on the same individual. The constancy of these curves is rather striking, especially where the symptoms and signs have not greatly changed. It is probable, therefore, that the absorption rate is fairly constant, at least for each individual. Again, in analyzing two hundred curves only six were found with a sudden increase in hyperglycemia at the end of the second hour, there having been no hyperglycemia the first hour. In other words, nearly all curves reach the maximum at the end of the first hour and the second hour levels are usually lower, or only slightly higher, than the first hour ones. This would show that absorption is quite rapid.

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1. Janney: Proc. Soc. Exper. Biol. & Med. **15:** 1917-1918. Janney and Isaacson: J. A. M. A. **70:**1131 (April 20) 1918.
2. Fisher & Wishart: J. Biol. Chem. **13:**49, 1912.
3. Janney: J. Biol. Chem. **22:**191, 1915.

Sansum and Woodyatt [4] have shown that the maximum intravenous tolerance rate of man and animals without glycosuria is 0.85 gm. per hour per kilo of weight. Intravenous tolerance methods, although scientifically desirable, are not practical. The known facts for determining a standard alimentary dose are: The above noted intravenous tolerance and the average absorption rate of 66 per cent. in two hours. The theoretical dose would be $(2 \times 0.85 \times \frac{100}{66})$ or about 2.5 gm. sugar per kilo. Janney has recommended 1.75 gm. per kilo as a

TABLE 1.—Repeated Curves

Diagnosis	Date	Blood Sugar Values, per Cent.				Curve Classification
		Fasting	1st Hr.	2d Hr.	3d Hr.	
Dyspituitarism	12/21/20	0.092	0.124	0.085	0.075	S
	2/ 4/21	0.092	0.120	0.085	0.063	S
Neuritis of sciatic nerve	2/ 8/21	0.085	0.190	0.150	0.130	III
	2/14/21	0.085	0.185	0.175	0.150	III
Hypothyroidism	10/14/20	0.090	0.110	0.065	0.065	S
	10/19/20	0.090	0.110	0.085	0.065	S
Manic-depressive psychosis	12/13/20	0.090	0.160	0.170	0.140	III
	1/10/21	0.100	0.188	0.195	0.175	III
	1/20/21	0.140	0.192	0.140	0.140	III
Lethargic encephalitis	12/ 8/20	0.100	0.110	0.090	0.080	S
	12/13/20	0.090	0.087	0.080	0.090	S
Exophthalmic goiter	6/ /20	0.168	0.280	0.220	0.113	II
	10/27/20	0.175	0.440	0.220	0.095	II

TABLE 2.—Showing Composition of Glucose Meal

Weight, Pounds	Glucose, Gm.	Lemon Juice, C.c.	Water, C.c.
90	72	54	126
100	80	60	140
110	88	66	154
120	96	72	168
130	104	78	172
140	112	84	196
150	120	90	210
160	128	96	224
170	136	102	238
180	144	108	252
190	152	114	266
200	160	120	280
210	168	126	294
220	176	132	308
230	184	138	322
240	192	144	336

standard dose. This amount of glucose for a man weighing 150 pounds, for instance, would amount to 120 gm. of glucose, or 480 calories. Such a man in basal state plus 10 per cent. increase for the specific dynamic action of glucose would be burning from 70 to 75 calories per hour. This dosage of glucose is, therefore, greatly in excess of caloric needs under ordinary circumstances and would show, with an absorption efficiency of 66 per cent., the glycogenic function of the individual or his ability to store the excess of an amount of sugar, commensurate

4. Sansum and Woodyatt: J. Biol. Chem. **30**:155, 1917.

with his weight, absorbed in a unit of time. Sansum and Woodyatt [4] have also shown that injecting animals in excess of the tolerance rate with varying concentrations of glucose made no difference in the amount of glucose in the urine, but that it did make a difference in the height of the blood sugar. It is, therefore, better technic to use a 40 per cent. solution of glucose using water and lemon juice as a solvent.

It seems obvious that one should not give 100 gm. glucose to an individual weighing 200 pounds and a like amount to one weighing 100 pounds and expect duplicate results in blood sugar concentration. It has been fairly well established that blood volume varies approximately with weight. Normally sugar is stored both in the liver and in the muscles. Palmer [5] found that in the diabetic animal the amount of glucose in the tissues varied with the hyperglycemia. It is possible, therefore, that sugar storage might take place in some abnormal conditions in other tissues besides the liver and muscles, and it would seem that the weight of the individual is our best index to his available space for storing glucose.

TABLE 3.—SHOWING THE ABSENCE OF RELATIONSHIP BETWEEN WEIGHT AND THE TYPE OF CURVE

Weight in Pounds *	Number of Individuals	
	Normal Curve	Subnormal Curve
90–100	4	3
100–110	8	5
110–120	2	6
120–130	6	5
130–140	6	2
140–150	6	5
150–160	3	2
160–180	1	2
180–200	5	2
200 plus	2	

* What the average weight of all hospital patients is, is not known, but the table shows the size of the patient does not influence the curve.

In some of the latest work in blood sugar determinations [6] after a glucose meal, a constant amount of glucose was used for all individuals. The results would have been more constant if the weight of the individuals had been taken into consideration (Table 3). The same can be said for the amount of water given with the meal.

Blood Sugar Determinations.—The blood was drawn with a 5 or 10 c.c. syringe and introduced into a test tube containing a few crystals of potassium oxalate and gently shaken. The first specimen was taken with the patient in a basal state, twelve hours after the last food. After the collection of the blood, the standardized meal was given. The blood was drawn again at the end of one, two and three hours. The third hour specimen was found to be of great importance. It is necessary that the blood should be precipitated immediately after taking the sample.

5. Palmer: J. Biol. Chem. **30**:79, 1917.

6. Allen, Wishart and Smith: Arch. Int. Med. **24**:523 (Oct.) 1919. Boothby: J. A. M. A. **77**:252 (July 23) 1921.

Meyers and Bailey's[7] modification of Benedict's first method was used: 3 c.c. blood was added to 12 c.c. saturated picric acid solution and a few crystals of picric acid. The blood was thoroughly shaken and filtered after five minutes. The standard glucose solution was made up of 1 mg. glucose to 5

TABLE 4.—Comparison of Blood Sugar Values by Benedict's and Shaffer's Methods

Case	Fasting 1st, 2d and 3d Hours		Classification	
	Benedict's Method, per Cent.	Shaffer's Method, per Cent.	By Benedict	By Shaffer
1	0.089 0.135 0.123 0.100	0.077 0.149 0.125 0.064	N*	N
2	0.087 0.159 0.136 0.117	0.096 0.171 0.143 0.125	II	II
3	0.103 0.169 0.135 0.095	0.088 0.138 0.119 0.074	N	N
4	0.104 0.089 0.113 0.064	0.096 0.090 0.099 0.095	S	S
5	0.086 0.163 0.156 0.117	0.099 0.143 0.138 0.127	II	III
6	0.095 0.148 0.167 0.137	0.090 0.157 0.166 0.109	III	II
7	0.143 0.195 0.138 0.142	0.115 0.195 0.142 0.114	III	III
8	0.098 0.190 0.206	0.096 0.176 0.181	III ?	III ?
9	0.102 0.096 0.088	0.095 0.082 0.088	S	S
10	0.089 0.118 0.091	0.079 0.106 0.093	S	S
11	0.126 0.236 0.154 0.139	0.113 0.191 0.156 0.135	III	III
12	0.082 0.224 0.226 0.143	0.072 0.230 0.189 0.101	III	II

* N, normal; S, subnormal; II, 2 hour sustained; III, 3 hour sustained.

c.c. saturated picric acid; this solution being part of the same sample of saturated picric acid that was used to precipitate the blood.

Cowie and Parsons[8] have shown how much more sensitive picric acid solutions are to such substances as acetone, diacetic acid and epinephrin than

7. Meyers and Bailey: J. Biol. Chem. **24**:147, 1916.
8. Cowie and Parsons: Arch. Int. Med. **26**:333 (Sept.) 1920.

to sugar itself. This work explains the very high blood sugars obtained in the cases of diabetes mellitus, but in the absence of acetone bodies the method is fairly accurate.

Since the publication by Shaffer and Hartmann[9] of their iodometric method, a considerable number of curves have been determined by both methods. In only minor respects has the classification of curves been changed by values obtained by the Shaffer method. In fifty blood sugar determinations done by both methods varying from 0.06 to 0.30 per cent., the averages at different levels by the two methods agree within a few per cent.

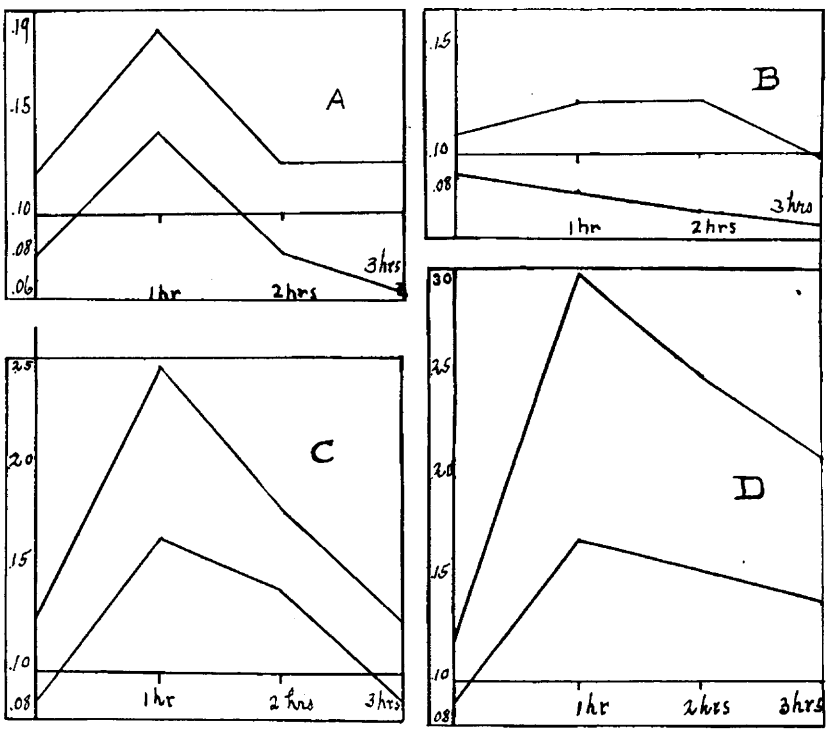

Fig. 1.—In each curve the two lines represent the limits between which the curves of that type falls. Ordinates show percentage of blood sugar. A, Normal curve; B, subnormal curve; C, Type II curve; D, Type III curve.

Classification of Curves.—In dealing with a considerable number of curves some sort of classification is necessary. This introduces the question of terminology. Sugar tolerance work began by feeding sugar by mouth and watching for its appearance in the urine. If an individual could take 100 gm. glucose and show no sugar in his urine, his "tolerance" would be considered normal; if he could take more than 100 gm. without glycosuria his "tolerance" was increased, and if he showed glycosuria on taking 100 gm. his "tolerance" was decreased.

9. Shaffer and Hartmann: J. Biol. Chem. **45**:365, 1921.

It is impossible to transpose this term "tolerance" into the terminology of blood sugar because a higher "tolerance" means a low blood sugar curve and a low "tolerance" means a high blood sugar curve. It has been our experience that the use of the word "tolerance" only leads to confusion and it would, therefore, seem to be better to use the term "blood sugar curve after glucose meal" or "blood glucose curve."

In consideration of the classification of curves it has not been considered important to include fasting hyperglycemia because it has been found that a fasting hyperglycemia is not a common condition, except where there is a loss of power to oxidize glucose, or in the presence of ashyxia or severe toxemia. As a rule, fasting hyperglycemia has not been found in endocrine or neurologic cases.

Normal curves were constructed on five normal individuals and also on about forty patients in the hospital who showed no demonstrable cause for a disturbed glycogenic function. These normal curves agree with those of other observers [10] in that after the normal fasting level there is a hyperglycemia at the end of the first hour of from 0.14 to 0.19 per cent. and at the end of the second hour the blood sugar level is within normal limits, or from 0.08 to 0.12 per cent. The third hour is still within normal limits from 0.06 to 0.12 per cent. We have assumed a higher normal hyperglycemia at the end of the first hour than other observers. However, this seemed justified when the procedure was so well controlled and the clinical data carefully studied. Many of the normal curves show a marked hypoglycemia at the end of the second and third hours. This hypoglycemia may be to the extent of from 0.06 to 0.08 values—so low that mere changes in blood volume would scarcely account for them. We cannot offer an explanation but have observations to show that by the end of the fourth hour the blood sugar values return to normal levels.

Abnormal curves have been divided into two main classes. The sustained curve, showing an abnormally sustained hyperglycemia, and the subnormal curve, which shows no normal hyperglycemia and even a hypoglycemia after a glucose meal. The curves showing sustained hyperglycemia we have divided into two groups: those showing hyperglycemia the second hour but with a return to normal levels the third hour; and those showing hyperglycemia at the end of three hours. The reason for this division of sustained curves into two groups will appear later.

Subnormal curves show a hypoglycemia or a normal fasting blood sugar. No hyperglycemia follows the administration of a glucose meal. The failure of the appearance of hyperglycemia may be due to one or both of two possibilities: Either a delayed absorption rate or an

10. Hammon and Hirschman: Arch. Int. Med. **20**:761 (Dec.) 1917.

increased glycogenic function. There are data [11] to show that in one condition, hypothyroidism, there is no delayed absorption in spite of the subnormal curves. Delayed absorption may occur in some conditions, such as hypopituitarism.

DISCUSSION OF MATERIAL

In the cases studied we noted age; weight; pulse rate and temperature; diagnosis (as obtained from the history sheet); gonads; children; menses; sexual power and desire; sympathetic symptoms; sweating; vasomotor instability; emotional tendencies, fear, anxiety; reflex excitability; gastro-intestinal symptoms; pituitary: sella (roentgen ray); bones; hair; eyegrounds; visual fields; secondary sexual characters; thyroid: vascular activity in gland itself; tremor; external ocular movements; size; exophthalmos; skin; special tests: basal metabolism; goetsch; hemoglobin.

In this study emphasis has been laid particularly in the selection of cases, on the so-called suspected endocrine disturbances of the thyroid and the pituitary; on the fatigued states, and on the hysterias and true dementias.

Many other conditions show abnormal curves, but the nature and constancy of their influence on the glycogenic function is even more uncertain than the above mentioned conditions. Such conditions are any mild toxemia, such as that in low grade bacterial infection; malignancy, etc., acidosis of any origin; drugs, such as opium and its derivatives, or salicylates. It is probable that these conditions can disturb blood sugar curves; certainly they affect general metabolism to some degree.

In this type of case the curves presented are not as numerous as one would wish. A few furunculosis cases (Fig. 2) show sustained curves. Some carcinomas of the gastro-intestinal tract, especially when metastases have taken place, show the same curve. Others with localized carcinoma show a normal curve. A normal curve is usually found in arthritis, but in the presence of fever or after foreign protein injections there is a high curve. If sugar curves are to be of value from an endocrine or a neurologic point of view, such conditions as may disturb glycogenic function should be avoided. Too little is known about them and there is no reason to believe their influence on the glycogenic function is a constant one. It seems more probable that a sustained curve in such conditions is a part of the general effect of incidental toxemia rather than a specific characteristic of a definite metabolic disturbance.

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11. Janney and Isaacson: Arch. Int. Med. **22**:160 (Aug.) 1918. Janney and Henderson, Arch. Int. Med. **26**:297 (Sept.) 1920.

Focal Infection.—Pemberton [12] has shown the effects of low grade inflammatory infection on delaying glycogenesis. Not only in cases of arthitis, but in other focal inflammatory processes, he found higher curves than in his normals. He did not use the standardized glucose meal. In a few cases he observed a return to normal curves after the removal of the foci of infection.

The manner in which toxins may influence the height of blood sugar curves is open to much speculation.

1. The toxin may directly stimulate the action of the diastase of the liver and muscles, or it may inhibit their glycogenic power.[13] Langfeldt [14] has recently shown in vitro the optimum p_H at which liver diastase works in the presence of thyroid extract and epinephrin. Toxins from foci may possibly disturb the hepatic acid-base equilibrium.

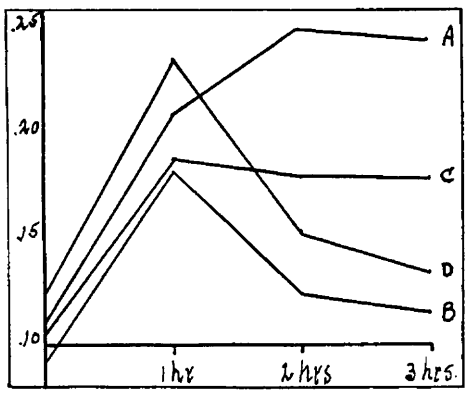

Fig. 2.—A and B curves are of arthritis cases. Curve A was taken two days following the intravenous injection of foreign protein. B, normal curve obtained in most cases of arthritis. C and D, curves of cases of furunculosis.

2. Focal toxins may act on glycogenolysis through their effect on suprarenal medulla directly or through autonomic reflex.

3. Focal toxins may also act on higher cerebral centers.

The association of fatigued state with focal infection is often noted. The curves of such conditions will be discussed later. Again, the focal toxins may disturb the mixture of food stuffs burned in the cell. The well known protein-sparing property of carbohydrate, especially in long sustained fevers, suggests that carbohydrate is burned most readily and possibly is mobilized to protect protein. The possibilities of the effects of toxins on glycogenesis and glycogenolysis have not

12. Pemberton and Foster: Arch. Int. Med. **25**:243 (Feb.) 1920.
13. Lusk: Science of Nutrition, p. 522, quoting Rosenthal, who showed that injection of diphtheria toxin prevented glycogen formation.
14. Langfeldt: J. Biol. Chem. **46**:381, 1921.

been exhausted, but enough has been mentioned to show the complexities of the possibilities. Certainly at present it is better to suppose that disturbance of glycogenic function in focal infection is a manifestation of the effects of infection just as hyperpyrexia or esthenia. The rationale of restricted diet in these cases can be questioned: Why deprive these patients of the protein sparing property of carbohydrate? Why feed typhoid fever patients carbohydrate and deny it to the arthitic? The great losses of weight seen in chronic arthitis would suggest that such patients are greatly in need of carbohydrate in abundance. The metabolism of arthitis does not differ from that of any other chronic focal infection. Certainly there is no loss of power to oxidize glucose, nor is there reason to believe that products of carbohydrate oxidation have a deleterious effect on periarticular inflammatory processes. Even if the toxins of the agent of infectious arthitis do cause sugar mobilization, that in itself should not suggest carbohydrate denial as a therapeutic indication. The experience of this clinic with low carbohydrate diet in arthitis has been quite disappointing.

Thyroid Diseases.—The influence of the thyroid gland on sugar curves has long been appreciated. The internal secretion of the thyroid excites two influences: (1) the delaying of glycogenesis, or an increased glycogenolysis; (2) an increased or stimulated metabolism.

When thyroid is fed carbohydrate is burned rapidly. One would therefore suppose that curves of exophthalmic goiter patients (Fig. 3) would be high but fall quickly, the rapid fall being associated with the increased metabolism. This is brought out by the fact that in spite of the height of the curves, normal blood sugar levels were reached by the end of three hours. Basal metabolism was performed on many cases. As found by Janney, there is no relationship between the height of metabolism and the height of the blood glucose curve. If the metabolism were extremely high one would suppose that the glycogen stores would be exhausted continually and the sugar, which with a lower metabolism would remain mobilized, is burned up; the result being a lower curve than is found in milder cases. We found this to be the case. One of the lowest curves in Figure 3 is from a patient having a basal rate of + 100 per cent. The reverse also is true; patients showing the highest curves had basal rates of about + 50 per cent.

The curves in exophthalmic goiter cases clearly indicate the nature of the dietetic treatment of hyperthyroidism: (1) To protect protein, a high carbohydrate intake; (2) to avoid hyperglycemia, the feeding in hyperthyroid cases should consist of many and small meals.

With clinical evidence of lack of thyroid secretion, curves were obtained which substantiate those already published [11] (Fig. 4). Janney did not find the constancy in hypoglycemia after the glucose meal that is shown in Figure 4. Cases under treatment are not included in this

chart. In some cases the curves very quickly become high under treatment, while others remain low. It has been shown experimentally in animals whose thyroids have been removed that there is no delay in intestinal absorption.[11] If this be true, the low curves in hypothyroidism must be due to increased sugar storage.

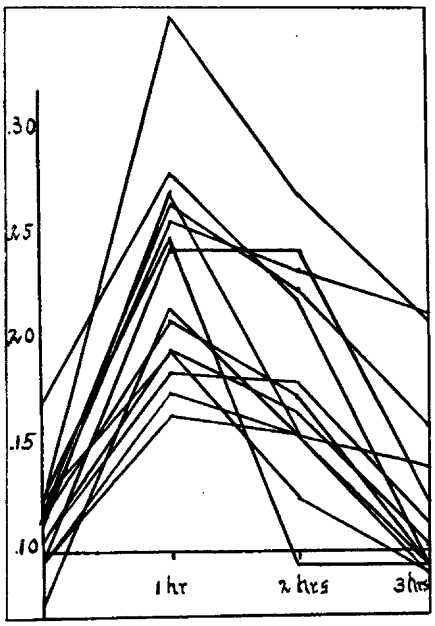

Fig. 3.—Curves of hyperthyroidism.

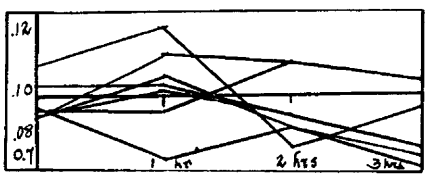

Fig. 4.—Curves of hypothyroidism.

Pituitary Cases.—The posterior lobe of the pituitary gland has been shown to affect the glycogenic function;[15] in acromegaly there is a low "tolerance" while in hypopituitary disease the "tolerance" is high.[16] Glycosuria following experimental stimulation of the pituitary has been shown to take place reflexly to the splanchnic area and also after all known nervous paths have been cut, indicating a true hormone glycogenolysis. No cases have been observed clinically or metabolically

15. Cushing: The Pituitary Body and Its Disorders, Lippincott, 1911.
16. Weed, Cushing and Jacobson: Bull. Johns Hopkins Hosp. **24**:40. 1913.

showing high curves, but a large number of cases diagnosed "hypopituitarism," "dyspituitarism" and "polyglandular syndrome" show low curves. It is in this type of case that the factor of delayed absorption may play a part. We have observed delayed water absorption in some of these cases.

Mild Diabetes.—The necessity of pancreatic hormone for glycogen formation was early demonstrated in perfusion experiments.[14] It is not known whether an increased secretion by the islands of Langerhans ever occurs, but a decrease in pancreatic hormone has two effects; loss of glycogenic power and loss of ability to oxidize glucose. It would, therefore, be reasonable to suppose that even if there is loss of oxidative power to a small degree, or, in other words, a very mild diabetes, the hyperglycemia would be sustained to a more marked degree than any other condition affecting glycogenesis.[10] That such is the case is shown by the curves in Figure 5. One of the greatest uses for blood sugar curves is in doubtful cases of mild diabetes. With a normal fasting blood sugar and a carbohydrate tolerance of from 150 to 200 gm. the curves following a glucose meal are quite distinctive, and differ from any other curve seen in cases of glycosuria. At the end of three hours the hyperglycemia is commonly above 0.3 per cent.

Renal Diabetes.—The so-called "renal" diabetic shows glycosuria with normal fasting blood sugar levels. Two cases have been studied carefully. Both gave subnormal curves. In one case the threshold glycemia seemed to be 0.075. Great care must be taken to distinguish between the emotional glycosuria and this type of glycosuria. The emotional patient's curve rises to above normal limits the first hour and may be sustained still longer. The curves of the "renal diabetic" here observed are quite flat (Fig. 5).

Mental States.—It is not proposed here to enter into discussion as to whether disturbances of the higher cerebral centers act on glycogenic function through reflex action on the chromafin-sympathetic system. It is simpler to accept Cannon's [17] hypothesis that there is a reflex stimulation of epinephrin formation in some mental conditions. The purpose here is to make clear the very considerable influence of various disturbances of the mental state on blood sugar curves. There is, however, one condition which would give distinct evidence of the effect of suprarenal medulla on sugar curves; namely, Addison's disease. With hypofunction of the suprarenal medulla and the absence of other factors influencing them, low curves should be obtained. Two cases have been followed for several months. The first patient had tuberculosis of the lungs and gave a normal curve; the second patient,

17. Cannon: Bodily Changes in Pain, Hunger, Fear and Rage, New York, D. Appleton, 1920.

the pathology of whose suprarenal was unknown, gave a subnormal curve (Fig. 6). The first case shows the effect of the bacterial intoxication as well as the deficiency of medullary-adrenal secretion.

Cannon found that pain, rage and fear in animals caused, in a considerable number of cases, the appearance of glycosuria. The same

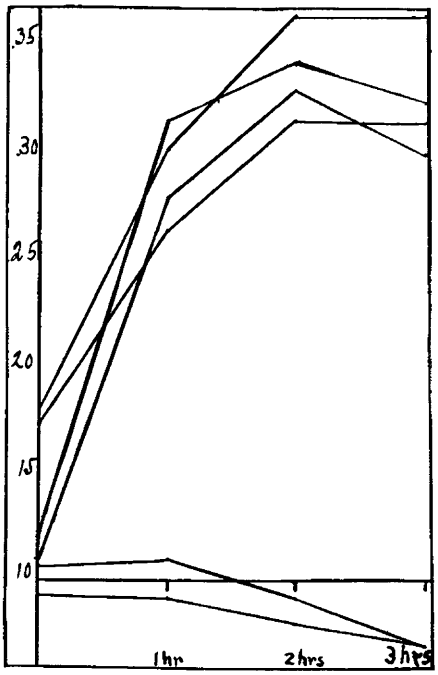

Fig. 5.—The upper curves are those of mild cases of diabetes mellitus. Compare with Figures 3 and 8. The lower curves are of "renal" diabetes. Compare with Figures 7 and 8.

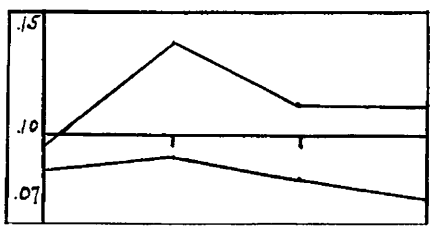

Fig. 6.—Curves of two cases of Addison's disease. The upper of the two is from a patient who had an active tuberculous lesion which would tend to raise the curve.

has been observed in man, especially in states of excitement and after severe mental effort. We have studied the blood sugar curves of a considerable number of cases diagnosed as neurasthenia after a search was made for organic lesions; cases of hypochondriasis; hysteria;

epilepsy, both of organic origin and ordinary type; dementia praecox and manic depressive insanity,[18] and the outstanding fact is that no prediction can be made as to the nature of the curve from diagnosis alone. It may be possible for the psychiatrist or neurologist to determine what the particular mental condition is that stimulates glycogenolysis. Some of the interesting facts are as follows:

Hysterical individuals usually give a normal curve (Fig. 7) in spite of their intense emotional state. Hypochondriacs and manic depressive patients (Fig. 8) show, in the majority of cases, high curves. Neurasthenics and dementia praecox patients may show any type of curve. The uncertainty of the response in these cases makes the interpretation of blood sugar curves difficult.

Summary of Factors Influencing Curves.—To summarize these factors influencing glycogenesis and glycogenolysis in muscle and liver the following outline may help.

Glycogenesis; necessary hormones:

1. Pancreas,
2. Parathyroid (?)

Glycogenolysis; increased by:

1. Increased p_H of muscle, liver or blood. Found in such pathologic conditions as starvation acidosis, nephritic acidosis, etc.
2. Increased secretion of thyroid hormone.
3. Increased secretion of pars nervosa of the pituitary.
4. Increased activity of sympathetic-chromafin system may occur with:
   (*a*) Reflex stimulation from cerebral, peripheral or splanchnic areas.
   (*b*) Blood born stimuli, such as infections, malignant, in pernicious anemia, leukemia, etc.
5. Substances in the blood acting directly on glycogen stores in the muscles and liver, such as any of 4b.

So far as known the pancreas has the most definite and profound influence on formation of the glycogen. The evidence for the parathyroids lies in the fact that their removal causes glycosuria.[19] There seem to be many more factors stimulating sugar mobilization. Anything increasing H ion concentration of blood or locally in the tissues seems to stimulate glycogenolysis. This has been shown by intravenous injections of acids and in perfusion experiments.

18. For permission to study these cases we are indebted to Prof. Sidney I. Schwab.

19. Underhill and Hilditch: Am. J. Physiol. **25**:66, 1909. Underhill and Blatherwick: Am. J. Chem. **18**:87, 1914.

The livers of experimental animals can be almost freed from glycogen by feeding thyroid.[20] Although respiratory quotients show no decrease in burning power for glucose during feeding,[21] it is undoubtedly the strongest stimulus known to sugar mobilization. The increased metabolism accompanying thyroid feeding tends to lessen

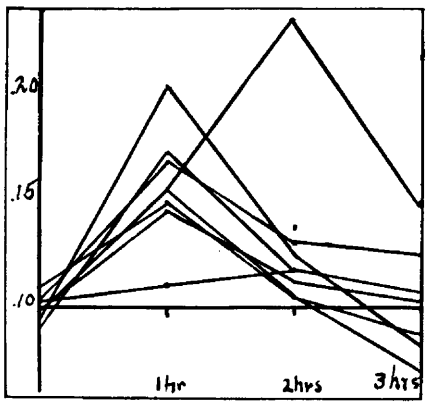

Fig. 7.—Cases of hysteria, many of which show intense emotional excitement. Seventy-five per cent. of uncomplicated cases of hysteria give normal curves.

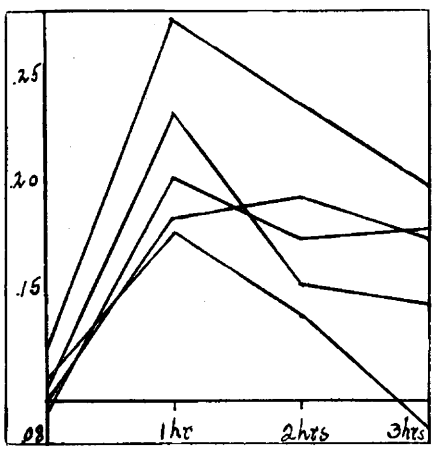

Fig. 8.—Cases of manic depressive insanity. Compare these curves with those of hyperthyroidism.

the glycemia by the rapid burning of sugar. Hyperthyroid blood sugar curves are high but steep, and show an interesting distinction from the high curves due to psychic disturbance which are not high but tend to be sustained. The explanation of increased glycogenesis when thyroid

20. Cramer and Krause: Quart. J. Exper. Physiol. **11**:59, 1917.
21. Cramer and McCall: Quart. J. Exper. Physiol. **12**:81, 1918.

hormone is decreased is only guesswork. If one considers the hormones of thyroid and suprarenal as opposed or balanced against the pancreatic hormone, disturbance of this balance increases or decreases glycogenesis. The increased glycogen storage coincident with thyroid deficiency might be taken as evidence that the pancreatic hormone overacts when not counterbalanced by thyroid.

TABLE 5.—SUMMARY OF CASES

Curves are classified thus: N, normal curve; S, subnormal curve; II, second hour sustained hyperglycemia; III, third hour sustained hyperglycemia. *

Diagnosis	Total No. of Cases	Curve Classification			
		N	II	III	S
Endocrine:					
Hyperthyroidism and exophthalmic goiter	19	1?	12	4	2?
Hypothyroidism and myxedema	10	1	0	0	9
Dyspituitarism; hypopituitarism; polyglandular syndrome	15	9	1	0	5
Addison's disease	2	1	0	0	1
Neurologic:					
Neurasthenia	15	4	4	2	5
Hysteria	16	8	1	3	4
Hypochondriasis	3	2	0	0	1
Organic Central Nervous System Lesions:					
Encephalitis	2	0	1	0	1
Tumor of brain (not pituitary)	4	2	1	0	1
Syphilis	9	4	2	2	1
Neuritis	2	0	1	1	0
Epilepsy	12	3	5	1	3
Constitutional inferiority	4	0	1	2	1
Psychoses:					
Dementia praecox	12	5	3	3	1
Manic depressive insanity	7	0	3	4	0
Senile dementia	2	0	0	2	0
Focal Infection:					
Arthritis, chronic	4	2	1	0	1
Arthritis, acute	1	0	0	1	0
Prostatitis, chronic	2	0	2	0	0
Appendicitis, chronic	2	2	0	0	0
Sinusitis	1	1	0	0	0
Keratitis	2	1	0	0	1
Furunculosis	2	0	0	2	0
Neoplasms:					
Carcinoma, stomach	1	0	1	0	0
Carcinoma, intestinal	2	1	1	0	0
Hodgkin's Disease	1	0	1	0	0
Miscellaneous:					
Goiter	3	3	0	0	0
Lead poisoning	1	0	1	0	0
Arteriosclerosis	..	0	2	1	0
Myocarditis	..	0	1	0	1
Nephritis	..	1	0	0	0

* Diagnoses with only one curve are not included.

In the above outline nervous effects on glycogenolysis are indicated as reflex through the agency of adrenalin. It must be borne in mind that this question is still a disputed one. It is also to be remembered that blood borne stimuli to glycogenolysis may act through adrenalin. These possibilities are quite hypothetical and are mentioned only as such. Again it is not known whether the many toxic substances disturbing the glycogenic balance toward the side of increased sugar mobilization act directly on the liver and muscles; on the nervous system or on the suprarenal medulla. All are possibilities.

CONCLUSIONS

1. The basis for the standardization of the technic of the administration of the glucose meal is pointed out. The necessity for such standardization is made clear.

2. The discussion of the many known factors which influence blood glucose curves shows the importance of the consideration of all of them when such curves form part of any study.

3. The pathologic conditions in which the form of blood glucose curve is usually (within certain limits) constant, are: (1) hyperthyroidism and hypothyroidism; (2) hypopituitarism, and (3) diabetes mellitus.

4. There are certain conditions which, in general, show increased curves after the glucose meal. The curves obtained in such conditions do not even approximate the fair degree of constancy found in the above mentioned conditions. Our present knowledge of glycogenic function in these conditions is rather meager. In this class belong the effects of infectious toxins; those of cancerous origin; those supposedly found in pernicious anemia and leukemia; Hodgkin's disease, etc. Here also belong conditions of the mental state. "Functional" disturbances, usually spoken of as neurasthenia, very definitely disturb the height of blood sugar after glucose meal.