CLINICAL CALORIMETRY

SEVENTEENTH PAPER

METABOLISM AND TREATMENT IN DIABETES*

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The experiments here to be described concern two patients with moderate diabetes treated by the oatmeal method in the metabolism ward of the Russell Sage Institute of Pathology and four Rockefeller Hospital patients with more severe diabetes transferred to Bellevue Hospital for study in the respiration calorimeter during various stages of the fasting treatment. Only very brief mention is possible of the literature¹ concerning the subjects touched upon in the experiments, namely, (1) the oatmeal and fasting treatment, (2) the dextrose-nitrogen ratio, (3) the respiratory quotient under certain conditions, and (4) the total metabolism in diabetes.

1. According to literature previously reviewed,² the von Noorden school no longer holds that oatmeal stands entirely alone in respect to the capability of utilization by diabetic patients, but nevertheless maintains that for some unknown reason it is superior to other forms of carbohydrate. On the other hand, Blum³ and a series of later authors have been able to observe no difference in the clinical effects of oatmeal and other carbohydrates. Also von Noorden has claimed that cases of the worst type are the ones that do best on oatmeal, whereas in mild cases the method often fails. The opposing authors found that oatmeal, like other carbohydrates, was tolerated better in mild cases and worse in severe cases. Furthermore, even in the seemingly favorable cases where the carbohydrate balance is strongly positive, respiration experiments have usually shown little or no combus-

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1. A fuller review by one of the authors (F. M. A.) is to be published elsewhere.

2. Allen, Frederick M.: *Studies Concerning Glycosuria and Diabetes*, Harvard University Press, Cambridge, Mass., 1913.

3. Blum, L.: *Les Hydrates de Carbone dans le Traitement du Diabète Sucré*, *Semaine Médicale*, 1911, xxxi, 313; *Ueber Weizenmehlkuren bei Diabetes mellitus*, *Beitrag zur Theorie der Verwendung der Kohlehydrate in der Therapie der Zuckerkrankheit*, München. med. Wchnschr., 1911, lviii, 1433; *Die Diät bei Diabetes gravis*, *Med. Klin.*, 1913, p. 702.

tion of carbohydrate. Thus Benedict and Joslin⁴ concluded that the carbohydrate ingested produced no material effect upon the metabolism; and Joslin⁵ shows the failure of either oatmeal or potato to raise the respiratory quotient, notwithstanding positive carbohydrate balances as high as 100 gm. Falta⁶ states, without giving details, that a diabetic patient taking 400 gm. oatmeal daily without glycosuria showed no rise in the respiratory quotient on the first or second days, but on the third day a marked rise in the quotient occurred. Normal persons showed the usual prompt rise in the quotient; but when subjected to the customary program of the "oat cure," namely, first a period of carbohydrate-free diet, then the customary fasting or vegetable-day, then a period of 400 gm. oatmeal daily, a normal person showed the same behavior as the diabetic, in that the quotient rose only on the third day. The reason was believed to be that the organism, impoverished in carbohydrate, first stored the ingested starch as glycogen without burning any considerable quantity. The records of Rolly⁷ and Roth⁸ concerning the administration of different carbohydrates to diabetics show no appreciable changes in the quotients during the series of successive days in their experiments. Joslin⁵ pointed out that the respiratory quotient of Benedict's fasting man rose promptly on taking mixed diet at the end of a thirty-one-day fast. Confirmation is necessary before it can be accepted that either a diabetic or a normal subject will store the carbohydrate of 400 gm. oatmeal for two days, and then suddenly show active combustion on the third day. Any such change in the respiratory quotient of a diabetic patient would more probably indicate an improvement in the power of carbohydrate combustion.

Von Noorden and all other writers admit that many cases of diabetes are so severe that neither the glycosuria nor the acidosis is cleared up by the oatmeal treatment. The method recently introduced,⁹

4. Benedict, F. G., and Joslin, E. P.: *Metabolism in Diabetes Mellitus*, Carnegie Institution of Washington, 1910, Pub. No. 136, pp. 203, 215; *A Study of Metabolism in Severe Diabetes*, Carnegie Institution of Washington, 1912, Pub. No. 176; *Ueber den Stoff- und Energieumsatz bei Diabetes*, *Deutsch. Arch. f. klin. Med.*, 1913, cxi, 333.

5. Joslin, E. P.: *Carbohydrate Utilization in Diabetes*, *THE ARCHIVES INT. MED.*, 1915, xvi, 693.

6. Falta, W.: *Zur Theorie und Behandlung des Diabetes mellitus*, *Med. Klin.*, 1914, x, 9.

7. Rolly, F.: *Zur Theorie und Therapie des Diabetes mellitus*, *Deutsch. Arch. f. klin. Med.*, 1912, cv, 494.

8. Roth, N.: *Ueber Mehltage bei Diabetes*, *Wien. klin. Wchnschr.*, 1912, xxv, p. 1864.

9. Allen, Frederick M.: *Studies Concerning Diabetes*, *Jour. Am. Med. Assn.*, 1914, lxiii, 939; *Boston Med. and Surg. Jour.*, 1915, clxxii, 242; *New York State Jour. Med.*, 1915, xv, 330; *Am. Jour. Med. Sc.*, 1915, cl, 480; *Exercise*, *Boston Med. and Surg. Jour.*, 1915, clxxiii, 743; *Investigative and Scientific Phases of the Diabetic Question, with Their Probable Relations to Practical Problems of Clinical Medicine*, *Jour. Am. Med. Assn.*, 1916, lxvi, No. 20, p. 1525.

consisting of a prolonged initial fast with subsequent strict regulation of all elements of the diet, has proved successful in clearing up both the urinary and the clinical symptoms in a considerable number of cases, even of very severe diabetes. The underlying principles will be discussed more fully elsewhere, but one feature considered theoretically important for the beneficial results has consisted in a diminution in the metabolism, not merely of the sugar-forming materials (carbohydrate and protein) but also of fat. The question of diminution of metabolism could be settled only by experiments in the respiration calorimeter.

2. The first dextrose-nitrogen ratio was established by Minkowski, who discovered that totally depancreatized dogs, fasting or on carbohydrate-free diet, excreted in the urine approximately 2.8 gm. of glucose for each gram of nitrogen. A constant ratio at this level indicates that 45 per cent. of the protein catabolized is being formed into glucose and excreted, and that no sugar is being formed from fat. The original interpretation was furthermore that 45 per cent. represents the maximum proportion of protein convertible into sugar. Lusk¹⁰ and collaborators demonstrated that phlorhizinized dogs eliminate approximately 3.65 gm. of glucose for each gram of nitrogen, thus proving that at least some species of animals are capable of converting nearly 60 per cent. of the protein molecule into glucose. Also, there is no formation of sugar from fat under these conditions. Mandel and Lusk¹¹ demonstrated the 3.65 ratio in a human patient with severe diabetes. They urged the prognostic value of determinations of the relations of sugar and nitrogen on carbohydrate-free diet; and because the total loss of power to use carbohydrate indicated by the 3.65 ratio supposedly precluded improvement, they referred to this as the "fatal ratio." Foster and Greenwald¹² also described cases showing this ratio. For other literature, reference may be made to Lusk.¹³ Inasmuch as the case described by Allard showed a fall in the ratio on fast-days, Lusk considered it no longer certain that the 3.65 ratio is necessarily permanent or fatal.

10. Lusk, G.: Phlorhizinglukosurie, *Ergebnisse der Physiologie*, 1912, xii, 315.

11. Mandel, A. R., and Lusk, G.: Stoffwechselbeobachtungen an einem Falle von Diabetes mellitus, mit besonderer Berücksichtigung der Prognose, *Deutsch. Arch. f. klin. Med.*, 1904, lxxxii, 472; *Diabetes Mellitus. Report on a Case, Including a New Method of Prognosis*, *Jour. Am. Med. Assn.*, July 23, 1904, p. 241.

12. Foster, N. B.: Wie hoch ist der Dextrose: Stickstoff-Quotient bei schwerstem Diabetes? *Deutsch. Arch. f. klin. Med.*, 1913, cx, 501; Greenwald, I.: *Jour. Biol. Chem.*, 1913-14, xvi, 375; and 1914, xviii, 115.

13. Lusk, G.: Metabolism in Diabetes, *THE ARCHIVES INT. MED.*, 1909, iii, v; Note on "A Case of Pancreatic Diabetes Mellitus," by Herman O. Mosenthal, *THE ARCHIVES INT. MED.*, 1912, x, 122. Allard: *Arch. f. exper. Path. u. Phar.*, 1907, lvii, 1.

3. The level of the respiratory quotient theoretically to be expected in diabetes has been discussed by Magnus-Levy¹⁴ and by Lusk.^{15, 16} On the basis of the newer information concerning the amino-acid content of proteins, the latter calculates that when the dextrose-nitrogen ratio is 3.65, the quotient of protein is 0.632. The formation and excretion of acetone bodies also tends to lower the quotient in a manner which can be calculated; but at the same time such acid substances may react with sodium bicarbonate to set free carbon dioxide, so that the precise theoretical value of the quotient in diabetes cannot be determined. The actual observations in phlorhizinized dogs and human patients with the 3.65 ratio are found to meet the theoretical expectations with quotients approximating 0.69. Two features of the recent literature concerning the respiratory quotient require mention in the present connection. One is the absence, in exact modern work, of the very low quotients previously found in diabetes and other conditions. Leimdörfer¹⁷ is the only recent author who reports such low quotients; and as they are so numerous in his experiments, while his cases of diabetes were obviously of no extraordinary severity, it is apparent that something in his methods tended to give low values. Grafe and Wolf,¹⁸ though reporting dextrose-nitrogen ratios indicating formation of sugar from fat, found no support for this hypothesis in the respiratory quotient, which was about 0.74. Technical errors, especially in connection with the oxygen measurements (Benedict¹⁸), may be assumed to explain the low values in the early literature. The average quotient of Benedict and Joslin's severe cases of diabetes was 0.73; and Joslin⁵ presents a table of the other cases in the literature, showing the general average to be 0.73. Respiration experiments therefore stand opposed to the doctrine of sugar-formation from fat in human

14. Magnus-Levy, A.: Respirationsversuche an diabetischen Menschen, *Ztschr. f. klin. Med.*, 1905, lvi, 83.

15. Lusk, G.: Clinical Calorimetry, Paper Eight. On the Diabetic Respiratory Quotient, *THE ARCHIVES INT. MED.*, 1915, xv, 939.

16. Williams, H. B., Riche, J. A., and Lusk, G.: Animal Calorimetry II. The Metabolism of the Dog Following the Ingestion of Meat in Large Quantities, *Jour. Biol. Chem.*, 1912, xii, 349, 356.

17. Leimdörfer, A.: Ueber den respiratorischen Stoffwechsel des Diabetikers bei verschiedener Kostform, *Biochem. Ztschr.*, 1912, xl, 326.

18. Benedict, F. G.: A Comparison of the Direct and Indirect Determination of Oxygen Consumed by Man, *Am. Jour. Physiol.*, 1910, xxvi, 15; Factors Affecting Basal Metabolism, *Jour. Biol. Chem.*, 1915, xx, 263; Metabolism During Inanition, Harvey Lectures, 1906-07.

Benedict, F. G., and Emmes, L. E.: The Basal Gaseous Metabolism in Men and Women, *Jour. Biol. Chem.*, 1914, xviii, 139; A Comparison of the Basal Metabolism of Normal Men and Women, *Proc. Nat. Acad. Sc.*, 1915, i, 104; A Comparison of the Basal Metabolism of Normal Men and Women, *Jour. Biol. Chem.*, 1915, xx, 253; Benedict, F. G., and Smith, H. M.: The Metabolism of Athletes as Compared with Normal Individuals of Similar Height and Weight, *Jour. Biol. Chem.*, 1915, xx, 243.

diabetes. The second feature to be mentioned consists in the unexpectedly high quotients shown by some cases of severe diabetes, as observed independently by Benedict and Joslin and by observers in the Russell Sage laboratory. Table 5 in the paper by Joslin¹⁹ contains the record of a patient with severe diabetes, fasting except for from 2 to 5 gm. protein and from 15 to 24 gm. alcohol daily, yet with respiratory quotient of from 0.74 to 0.76. Joslin¹⁹ mentions other observations of a rise in the respiratory quotient of severely diabetic patients during fasting, even up to the neighborhood of 0.8. The cause of such high quotients is not known. Nothing analogous has been described in the study by Benedict²⁰ and earlier workers of cases of prolonged fasting; they found that in normal persons the quotient falls and remains low during fasting. Aside from the presumably scanty supply of stored carbohydrate, Joslin has suggested the acetone bodies as the only known material capable of raising the quotients of diabetic patients by combustion under these conditions.

4. The total metabolism in diabetes has been an actively discussed subject. The earlier literature is critically reviewed by Benedict and Joslin.⁴ It has been universally agreed that the basal metabolism of mild cases of diabetes is normal, and that of most severe cases is found increased when reckoned per kilogram of body weight. But in addition to accuracy in measuring the gas exchange and heat production, there is the further requirement of an accurate basis of comparison between diabetics and other persons. Magnus-Levy¹⁴ called attention to the fact that the emaciation of most patients with severe diabetes alters the relation of their body weight and surface, and suggested that it might be more nearly correct to compare on the basis of the original normal weight of the diabetics. Benedict and Joslin rejected this proposal, because the surface of the diabetic apparently diminishes with the body mass and the skin shows no tendency to fall in folds or wrinkles. They chose, as the most accurate means available, to compare groups of patients with severe diabetes with groups of normal and mildly diabetic persons, as nearly like them as possible in size and figure. On this basis they estimated that their severely diabetic patients showed an increase of from 6 to 7 per cent. in carbon dioxid excretion, of from 16 to 21 per cent. in oxygen consumption, and of about 15 per cent. in heat production. Lusk²¹ criticized the findings in various particulars, and by recalculation concluded that the metabolism

19. Joslin, E. P.: *Present-Day Treatment and Prognosis in Diabetes*, Am. Jour. Med. Sc., 1915, cl, 485.

20. Benedict, F. G.: *The Influence of Inanition on Metabolism*, Carnegie Institution of Washington, 1907. *A Study of Prolonged Fasting*, Carnegie Institution of Washington, Pub. No. 203, 1915.

21. Lusk, G.: *Science*, 1911, N. S., xxxiii, 433-434.

represented was not 15 per cent. but only 5 per cent. above normal. Benedict and Joslin⁴ in their second publication added to the number of diabetics and especially of control subjects studied, and reckoned that the basal metabolism in this group of diabetics was approximately 20 per cent. above normal. Lusk²² calculated that an increase of from 5 to 10 per cent., and in exceptional instances 15 per cent., above normal was shown. Leimdörfer¹⁷ found an increase of metabolism in severe cases of diabetes on the basis both of the weight and of the body surface as figured by Meeh's²³ formula. Diminution of metabolism observed after oat or vegetable days was held to confirm this interpretation. Rolly⁷ found in severe diabetes an increased oxygen consumption per kilogram of body weight, especially soon after admission to hospital; after a period of treatment the findings were lower. Seib²⁴ also reported the respiratory metabolism increased in proportion to the severity of the case. In Paper 10 of the present series is described the height-weight formula for calculating the body surface, which has been found more accurate and reliable for this purpose than the Meeh formula, especially when the body form varies in any way from the average normal. It is possible by this formula to recalculate any results recorded in the literature, wherever the height and weight of the subject have been given. It is believed that the second of the requirements mentioned is thus fulfilled, and that, granting accurate experimental observations, a correct basis of comparison is afforded between diabetic and other subjects in a manner not possible heretofore.

The causes of the departure of the diabetic basal metabolism from the normal are partly known, perhaps partly unknown. It may be taken as an axiom that the diabetic, excreting sugar formed from protein, must catabolize more protein during fasting than the nondiabetic person under identical conditions, and that the specific dynamic action of protein will therefore give rise to a higher metabolism in the diabetic, unless some other factor prevents or neutralizes the effect of the protein. The suggestion was offered by Benedict and Joslin that acidosis may be a cause of increased metabolism. They observed the discrepant fact that a sudden slight acidosis is accompanied by an increase of metabolism out of proportion to that noted with prolonged high acidosis. At the present time the subject of acidosis is a confused one;

22. Lusk, G.: *Animal Calorimetry XI. An Investigation into the Cause of the Specific Dynamic Action of the Foodstuffs*, Jour. Biol. Chem., 1915, xx, 555.

23. Meeh, K.: *Oberflächenmessungen des menschlichen Körpers*, Ztschr. f. Biol., 1879, xv, 425.

24. Seib, K.: *Experimentelle Untersuchungen über den respiratorischen Gaswechsel bei Diabetes mellitus nach Eiweisszufuhr und bei Hyperthermie*, Zentralbl. f. Physiol., 1913-14, xxvii, 930.

it can no longer be regarded as a simple condition resulting from lack of carbohydrate.⁹ Greater clearness concerning the effect upon metabolism may now result from separate consideration of individual factors present. First, some or all cases of sudden acidosis are accompanied by increased protein breakdown, which may be a cause of increased metabolism. Second, if acidosis in the strict sense increases metabolism, not only should subjects with high acidosis show higher metabolism than those with low acidosis, but also alkali given in sufficient quantity should in suitable cases cause a fall in metabolism. Third, it is possible that acetone bodies, even in the form of neutral salts, may stimulate metabolism if present in excess in the blood and tissues. Here the suggestion is analogous to that of Lusk²⁵ that diabetic lipemia may be a cause of increased metabolism. Increased concentration of combustible materials may be expected to result in a stimulation of metabolism, unless the power of combustion is diminished, or the specific dynamic action otherwise prevented. At the same time, the narcotic and depressant action of the acetone bodies might conceivably tend to depress metabolism, especially in the long-standing cases with high ketonemia. Other influences unquestionably tend to depress metabolism in such cases, as for example undernutrition and muscular relaxation. The effect of muscular mass and tone is evident in the higher metabolism of men as compared with women, and of athletes as compared with other men (Benedict¹⁸ and collaborators); and Lusk²² has shown that mere prolonged cage life may reduce a dog's basal metabolism by 16 per cent., though the diet and weight remain the same. The subject will be further considered below.

An account of the metabolism in a case of diabetes of remarkable intensity was recently published by Geyelin and DuBois.²⁶ To facilitate reference, some of the findings in this case are briefly reproduced in Table 1.

METHODS AND CALCULATIONS

The procedures used for the chemical determinations were as follows: for the blood-sugar, the method of Lewis and Benedict;²⁷ for the urinary sugar, titration with Benedict's solution; for nitrogen, the usual Kjeldahl method; for ammonia, the Folin method; for acetone bodies, the Shaffer method. Foods were weighed raw and the composition estimated from the Atwater-Benedict tables, unless special mention is made of analyses. For separating the twenty-four-hour urines,

25. Lusk, G.: The Influence of Food on Metabolism, *Proc. Am. Soc. Biol. Chem.*, December, 1914; *Jour. Biol. Chem.*, 1915, xx, 8.

26. Geyelin, H. R., and Du Bois, E. F.: *Jour. Am. Med. Assn.*, 1916, lxvi, No. 20, 1532.

27. Lewis, R. C., and Benedict, S. R.: A Method for the Estimation of Sugar in Small Quantities of Blood, *Jour. Biol. Chem.*, 1915, xx, 61.

TABLE 1.—THE CASE OF CYRIL K. (SUMMARY FROM GEYELIN AND DUBOIS)

Date	Food				Urine			Respira- tory Quotient	Calories per Sq. M. per Hour Linear Formula	Blood	
	Total Calories	Fat, Gm.	Nitrogen, Gm.	Carbo- hydrate, Gm.	Nitrogen, Gm.	Glucose, Gm.	Dextrose- Nitrogen Ratio	Beta- oxy- butyric, Gm.		Glucose, Mg. per 100 c.c.	CO ₂ Combining Capacity, mm.
Dec. 8-9	438*	0	0	0	27.9	74.9	2.68	43.8		313	30.4
Dec. 9-10	336*	0	0	0	20.8	78.3	2.61	34.6		...	
Dec. 10-11	0	0	0	0	24.8	74.2	2.95			340	26.6
Dec. 11-12	405	17.7	2.8	41.5	30.6	108.0	2.17	60.0		312	21.1
Dec. 12-13	1,058	69.6	8.0	50.0	34.5	112.0	1.80	53.0		...	22.7
Dec. 13-14	938	58.5	8.8	50.0	35.4	118.7	1.93	57.9		...	22.5
Dec. 14-15	936	51.2	9.8	53.3	37.7	118.5	1.73	55.2		...	
Dec. 15-16	934	41.0	19.0	23.5	36.4	167.9	3.97	70.9	0.687	45.7†	20.0
Dec. 16-17	458	5.6	15.9	0.4	38.3	153.4	4.01	75.1	0.714	42.6†	19.6
Dec. 17-18	191	2.9	6.3	0.4	36.3	140.3	3.87	87.4		...	
Dec. 18-19	0	0	0	0	20.0	55.1	2.76	58.5	0.707	150	35.4
Dec. 19-20	0	0	0	0	16.7	44.3	2.65	56.8		...	53.4
Dec. 20-21	36	0	1.6	1.0	14.1	35.3	2.44	41.2	0.721	177	49.7
Dec. 21-22	60	0	3.2	1.6	14.4	39.7	2.65	26.2		170	52.5
Dec. 22-23	80	0.1	3.4	5.6	18.3	26.0	1.12	11.0	0.734	181	
Feb. 16						0	0	0	0.915	...	52.9
										25.4	

* Alcohol.

† After breakfast, not basal.

patients emptied the bladder at precisely 5 a. m. daily, and care was taken that no urine was lost under any conditions. The entire planning and organization of the ward was for the purpose of exact metabolic studies, and accuracy in matters of dietary control, collection of excreta and other details is fully assured.

At the time of the diabetes experiments the calorimeter was in perfect working order and the staff was well trained. Alcohol checks lasting two or three hours gave respiratory quotients in which even the third decimal place was not far from the theoretical. In experiments on man it has never before been felt advisable in this laboratory to print more than two significant figures in the respiratory quotients, but it has seemed justifiable to use three in the present work, both on account of the extreme care in the experiments and of the importance of the third decimal point in some of the calculations. In no case are deductions made from single hours but only from the averages of periods as long as possible.

The calculations concerning the metabolism where there was sugar formation from protein followed the method described by Lusk.¹⁶ In the normal metabolism each gram of nitrogen in the urine indicates the combustion of 6.25 gm. protein with the liberation from this protein of 26.51 calories, 9.35 gm. carbon dioxid and the absorption of 8.45 gm. oxygen. It is obvious that if part of this protein molecule is unoxidized in the diabetic organism and is excreted in the urine, all of these figures will be lowered by exactly the number of calories and grams of carbon dioxid and oxygen lost in the glucose. With a dextrose-nitrogen ratio of 3.65 to 1, 1 gram of nitrogen in the urine indicates the combustion of 6.25 gm. protein with the liberation of 26.51 minus 13.47 calories, 9.35 minus 5.35 gm. carbon dioxid, and the absorption of 8.45 minus 3.89 gm. oxygen. When the dextrose-nitrogen ratio is lower, the calculation is easily made as follows: The calories, carbon dioxid and oxygen ascribed to the metabolism of protein are calculated from the number of grams of nitrogen excreted per hour by using the normal factors given by Lusk.¹⁶ Knowing the number of grams of glucose excreted per hour, one can make the proper subtractions, since each gram of glucose represents a loss of 3.692 calories, 1.467 gm. carbon dioxid and 1.067 gm. oxygen. In this way it is possible to determine the nonprotein respiratory quotient and the heat production by the method of indirect calorimetry. If there is no glycosuria, or if the sugar of the urine is all derived from ingested carbohydrate, the calculations are exactly the same as for normal persons. No attempt has been made to calculate the combustion of the acetone bodies or the ingested alcohol, the conditions of experimentation rendering this impossible.

For reasons fully stated in previous papers, the method of indirect calorimetry is used as the standard, and the divergence of the direct calorimetry from this is expressed in terms of percentage. In typhoid fever, exophthalmic goiter, anemia and cardiorenal disease there is a tendency for the direct calorimetry to average from 2 to 3 per cent. lower, probably on account of heat lost through the warming of the bed and clothing, possibly also because of errors in measuring the average temperature of the body. This same tendency to a small minus error is seen in most of the diabetes experiments. The total divergence of the two methods in the present work is 2.3 per cent., and the average

Fig. 1 (Gerald S.).—Clinical findings shown graphically. The columns at the base represent the calories of the food; vertical lines, carbohydrate; crossed lines, protein; diagonal lines, alcohol; blank space, fat calories.

divergence in individual experiments is plus or minus 5.5 per cent. The agreement of the two methods is therefore satisfactory, and would be still closer but for the peculiar divergence of the findings in the case of Gerald S. on the last day of the prolonged fast and during the following two weeks. This point is discussed in the history of his case, which follows.

CASE REPORTS

CASE 1.—Gerald S. (severe diabetes), plumber, aged 17, unmarried. Healthy family and past life, habits good, normal weight 60 kg. Polyuria and polydipsia were noticed January, 1914. Entered Bellevue Hospital June, 1914, weighing

TABLE 2.—GERALD S.:—

Date, 1914	Food						Urine N, Gm.	Urine Glucose, Gm.
	Total Calories	Protein, Gm.	Fat, Gm.	Carbo., Gm.	Alcohol, Gm.	Food N, Gm.		
Nov. 8-9.....	1,056*	31.2	91.7	18.3		4.99		
Nov. 9-10.....	2,550	96.2	204.4	62.2		15.40		
Nov. 10-11.....	2,078	67.0	166.4	62.1		10.72	14.71	106.43
Nov. 11-12.....	540	1.3	9.5	2.3	62.6	0.20	10.76	41.95
Nov. 12-13.....	526	0	0	0	75.2	0	10.40	24.49
Nov. 13-14.....	614	0	0	0	87.7	0	10.87	15.68
Nov. 14-15.....	380	0	0	0	54.3	0	9.30	8.91
Nov. 15-16.....	555	0	0	0	79.3	0	11.10	6.53
Nov. 16-17.....	438	0	0	0	62.6	0	8.52	7.10
Nov. 17-18.....	497	0	0	0	71.0	0	8.24	2.80
Nov. 18-19.....	468	0	0	0	66.8	0	6.11	0.76
Nov. 19-20.....	622	12.2	1.8	2	79.3	1.95	7.12	0
Nov. 20-21.....	578	14.5	2.4	2	71.0	2.82	5.72	0
Nov. 21-22.....	892	24.1	25.8	2	79.3	3.85	8.41	0
Nov. 22-23.....	787	21.0	25.1	2	66.8	3.36	6.45	0
Nov. 23-24.....	878	34.6	47.7	2	41.8	5.53	9.13	0
Nov. 24-25.....	887	37.6	50.5	2	37.6	6.01	7.23	0
Nov. 25-26.....	1,464	57.9	95.9	3	50.1	9.26	6.56	0
Nov. 26-27.....	1,635	65.7	95.6	2	71.0	10.51	8.20	0
Nov. 27-28.....	1,752	61.1	110.8	2	71.0	9.77	7.17	0
Nov. 28-29.....	1,929	61.1	130.0	2	71.0	9.77	7.18	Trace
Nos. 29-30.....	2,175	68.4	151.5	2	75.0	10.75	8.58	Trace
Nov. 30-Dec. 1.....	1,795	56.0	140.6	2	41.8	8.96	6.89	Trace
Dec. 1-2.....	2,077	55.1	146.7	2	75.2	8.81	6.73	1.71
Dec. 2-3.....	1,845	57.3	138.9	2	50.1	9.16	5.72	0
Dec. 3-4.....	2,034	55.7	148.1	2	66.8	8.91	5.94	Trace
Dec. 4-5.....	1,606	53.9	126.6	2	33.4	8.62	5.49	0
Dec. 5-6.....	1,893	53.4	126.2	2	75.2	8.54	7.23	0
Dec. 6-7.....	1,942	56.9	130.0	2	75.2	9.10	6.30	0
Dec. 7-8.....	1,614	54.4	127.2	2	33.4	8.70	6.61	0
Dec. 8-9.....	1,872	56.4	128.9	2	66.8	9.02	6.95	0
Dec. 9-10.....	2,022	56.2	146.6	2	66.8	8.99	6.56	0
Dec. 10-11.....	2,111	54.8	145.9	2	66.8	8.76	7.28	0
Dec. 11-12.....	2,191	52.9	166.0	2	66.8	8.46	7.06	0
Dec. 12-13.....	2,308	60.0	175.6	2	66.8	9.60	7.73	0
Dec. 13-14.....	2,208	61.1	164.3	2	66.8	9.77	7.17	0
Dec. 14-15.....	2,221	59.2	166.6	2	66.8	9.74	6.22	0
Dec. 15-16.....	2,368	68.4	172.1	2	75.2	10.94	7.45	0
Dec. 16-17.....	2,532*	46.4	211.9	2	58.5	7.49		

* Not complete.

—CLINICAL DATA

Urine NH ₃ , Gm.	Beta-oxy- butyric, Gm.	Total Acetone Bodies as Beta- oxybutyric Gm.	Feces N, [†] Gm.	Excreta N, Gm.	Nitrogen Balance, Gm.	Water Intake, Gm.	Urine Volume, c.c.	Body Weight, c.c.	Blood Sugar, Per Cent.
....						1,450	1,300		
?						2,220	?	42.19	
3.40	7.128	13.218		15.78	— 1.07	2,960	3,526		
4.75	2.071	3.811	0	10.76	—10.75	3,705	3,460	41.27	0.305
4.46	1.815	2.517	0	10.40		2,398	1,909	40.15	
3.68	0.594	0.990	0			2,065	2,700	39.86	
2.18	0.616	1.048	0			2,197	1,836	38.97	
1.50	0.475	1.155	0			2,450	2,563	38.92	0.286
0.90	0.416	0.656	0			1,570	1,428	38.80	
0.71	0.308	0.588	0			2,385	2,128	39.05	0.284
0.60	0.064	0.164	0			1,725	1,153	38.74	
0.57	0.436	0.592	0.234	7.35		2,685	3,115	39.55	0.198
0.42	0.186	0.322	0.29	6.01		2,185	1,980	38.74	
0.51	0.208	0.373	0.46	8.87		2,883	2,360	40.22	
0.48	0.341	0.613	0.40	6.85		2,375	1,940	41.87	0.156
0.49	Lost		0.66	9.79		2,235	1,643	42.66	
0.56	0.258	0.423	0.72	7.95		1,500	1,835	44.02	0.182
0.44	0.250	0.358	1.11	7.49	+ 1.77	1,550	1,200	44.14	
0.68			1.11	9.31	+ 1.20	2,500	3,540		
0.46			1.11	8.28	+ 1.49	2,450	3,220	45.15	
0.50			1.11	8.29	+ 1.48	2,175	2,955	45.64	0.161
0.58			1.11	9.69	+ 1.06	2,780	4,005	45.27	
0.46			1.11	8.00	+ 0.96	1,870	2,225	44.27	
0.82			1.11	7.84	+ 0.97	1,795	3,085	45.35	0.208
0.38			0.945	6.67	+ 2.49	2,100	2,473	44.76	
0.55			0.945	6.885	+ 2.025	2,500	3,815	45.42	
0.30			0.945	6.435	+ 2.185	2,050	3,178	43.94	
0.57			0.95	8.18	+ 0.36	2,980	4,525	44.77	
0.44			0.95	7.28	+ 1.82	2,875	3,980	43.82	0.177
0.38			0.95	7.56	+ 1.14	1,455	2,327	42.58	
0.52			0.95	7.90	+ 1.12	2,010	3,610	43.32	
0.35			1.34	7.90	+ 1.09	3,070	3,750	42.61	
0.55			1.34	8.62	+ 0.14	3,000	3,880	41.74	
0.49			1.34	8.40	+ 0.06	3,250	3,865	42.43	
0.68			1.34	9.07	+ 0.53	2,510	3,110	42.30	
0.75			1.34	8.51	+ 1.26	2,730	3,010	42.36	0.113
0.60			1.34	7.56	+ 2.18	2,850	3,650	42.55	
0.71			1.34	8.79	+ 2.15	2,800	3,030	41.79(?)	
....						2,605	1,565	42.67	

[†] Feces N calculated as 12% of Food N, up to November 26.

47 kg. After twenty-five days he was discharged weighing 57 kg. Glycosuria was said to have been 10 per cent. on admission, 5 per cent. on discharge. A dose of salts taken October 24 left him very weak, and thereafter he lost weight and strength rapidly. He was admitted to Rockefeller Hospital Nov. 7, 1914. Height 172 cm., weight 41.6 kg., extremely weak. Heart, lungs and abdomen negative; blood-pressure 85 systolic, 75 diastolic; clinical picture of acidosis, with drowsiness and increased respiration threatening coma. His diet containing

Fig. 2 (Gerald S.).—Laboratory findings shown graphically.

carbohydrate was continued, and he was transferred next day to the Russell Sage metabolism ward at Bellevue Hospital, where he remained until the close of the metabolism experiments, then returned to the Rockefeller Hospital.

The diet shown in Table 2 was all he could eat on November 8 to 10 inclusive. At 6 a. m. on November 11 he received 50 c.c. cream, then developed nausea without vomiting. Fasting was begun at this time because of the complete repugnance to food and the dangerously threatening coma symptoms. No bicarbonate was given except 10 gm. on November 11. The fast lasted eight days,

and the condition cleared up, as shown in the table. Alcohol was given in the form of whisky during the fast, in quantities just short of producing any discomfort or intoxication symptoms. Notwithstanding the extreme initial weakness, the clinical condition perceptibly improved during the fast. The first food added to the alcohol after the fast was protein—eggs at first, later meat. More protein and fat were gradually added, until the unduly high diet of over fifty calories per kilogram of weight was reached. Bulk was contributed to the diet by the use of from 750 to 1,000 gm. of thrice-boiled vegetables daily, some samples of which were analyzed for carbohydrate. The rapid gain in weight shortly after the fast was due to the water retention common in such patients. Improvement continued in subsequent treatment. The carbohydrate tolerance remained low, but the patient became able to exercise freely, and he and his parents considered him fit for work. For this reason he refused to be further controlled, and was dismissed from the hospital and from all further supervision, with due warning of the consequences. The discharge was on Feb. 8, 1915, the diet at that time being about 1,400 calories, with no glycosuria or ketonuria, and the body weight 44 kg. He progressed rapidly downward and died March 9, 1915.

CASE 2.—William G. (severe diabetes), printer, age 29, married. Family, personal history and habits negative. Figure thin; normal weight from 66 to 69 kg. Thirst and dry mouth noticed in June, 1913. Progress was steadily downward in spite of treatment. Entered Presbyterian Hospital July 25, 1914. His condition there was dangerous on carbohydrate-free diet and worse when it was attempted to add carbohydrate. The dextrose-nitrogen ratio was found to be about 3. He was transferred to Rockefeller Hospital on July 28. Height 179 cm., weight 50 kg. Physical examination negative. Table 3 contains part of the laboratory data for this period. Carbohydrate of food was determined only by calculation. Other food values for the first two days are calculated. After that, nitrogen and fat were analyzed in food and feces.

Thus the emaciated patient, spending most of the twenty-four hours in bed and the rest of each day sitting limply in a chair, was unable to maintain his body weight even on utilizable calories in excess of the needs of a normal person of equal weight. The excess of fat failed to prevent nitrogen loss. Yet high protein feeding is known to aggravate diabetes, even though temporary nitrogen equilibrium is attained. This is the old dilemma. As soon as the appetite partly failed, on August 1, the nitrogen deficit became large. Fasting had to be inaugurated on August 2 because of symptoms of beginning coma. Along with the fall in glycosuria, within two days the level of nitrogen excretion characteristic of advanced inanition was attained. Feeding with green vegetables was commenced August 7. Gradual increase of vegetables up to August 12 showed a carbohydrate tolerance of 38.5 gm. Other food was then given, and there seemed to be satisfactory improvement, with glycosuria and ketonuria absent as usual. The case then differed from others in that a gradual loss of tolerance manifested itself; diagnosis was impossible for several months, but the apparent explanation of the trouble was at length found in pulmonary tuberculosis. Vain attempts were made several times to increase strength by high feeding with disregard of glycosuria. In January, 1915, with no sign of tuberculosis, the patient spent some time in the Russell Sage metabolism ward for investigation before and after such a period of high diet

TABLE 3.—WILLIAM G.: CLINICAL DATA DURING FIRST PART OF STAY IN THE ROCKEFELLER HOSPITAL

Date	Body Weight, Kg.	Water Intake, c.c.	Urine					Nitro-gen Balance*	Food					So-dium Bicarbonate, Gm.	Cal-cium Carbo-nate, Gm.
			Vol-ume, c.c.	Acetone Bodies as Beta-oxyl butyric Acid, Gm.	Am-moniac Nitro-gen, Gm.	Dex-trose Gm.	Dex-trose Nitro-gen Ratio	Total Nitro-gen, Gm.	Nitro-gen	Nitro-gen, Gm.	Carbo-hydrate, Gm.	Alco-hol, Gm.	Calories in Food		
July 29-30.....	40.4	1,800	3,424	26.05	2.88	61.63	2.6	23.27	- 6.86	17.29	6.9	...	2860.7	2448.1	20
July 30-31.....	47.4	2,540	2,570	20.51	2.16	64.99	3.3	17.48	- 0.66	17.70	11.5	...	2693.9	2297.6	20
July 31-Aug. 1	47.0	2,200	2,970	19.69	2.73	58.24	2.7	20.49	+ 0.39	21.78	7.7	30	3135.5	2762.6	20
August 1-2.....	47.4	2,810	3,165	38.62	3.48	60.46	2.4	24.36	-12.63	12.61	5.8	30	2730.9	2261.2	20
August 2-3.....	47.4	2,642	1,285	15.56	4.25	17.85	1.2	14.83	-15.71			102	714.0	593.9	30
August 3-4.....	48.0	1,950	2,185	8.80	2.08	1.93	0.26	7.22				97	682.5	592.9	20
August 4-5.....	48.4	1,870	1,840	2.47	0.44	2.04	0.34	5.99				80	560.0	469.3	5
August 5-6.....	48.2	2,092	2,815	2.09	0.88	0		7.04				102	714.0	656.0	..
August 6-7.....	47.6	2,722	2,100	2.97	1.07	0		10.20				92	644.0	582.2	..
August 7-8.....	47.0	2,785	2,365	4.95	1.16	0		6.72	- 7.26	0.34	5.8	82	610.3	535.0	..
August 8-9.....	47.2	2,545	1,625	3.10	1.06	0		7.66	- 7.69	0.85	15.7	85	688.6	626.2	..

* Average daily N in feces 0.875 gm.

† Calories lost in urine and feces subtracted from calories of diet.

(Table 4). He was subjectively and objectively so much better when kept free from glycosuria and ketonuria, that this was done nearly constantly until March 11, 1915. Then the course of the tuberculosis was becoming very rapid. Death occurred from diabetes and bronchopneumonic tuberculosis on March 22, 1915.

CASE 3.—Joseph U. (severe diabetes), manufacturer, aged 44, married. His family, personal history and habits were negative. Normal weight 75 kg. In 1907, loss of weight, and medical diagnosis of diabetes. At first kept free from glycosuria occasionally by treatment, but it has been continuous for the past three or four years. Emaciation and weakness have been the principal symptoms. Patient was bedridden for the six weeks preceding admission to hospital. He was brought on a cot from his home in Indiana and entered Rockefeller Hospital Nov. 28, 1914. Height 179 cm., weight 44.2 kg. Physical examination was negative, except for emaciation and a yellow tinge like pernicious anemia, which diagnosis was excluded by blood examination. Blood pressure not certain. On January 18, when he appeared much stronger and was beginning to sit up a little, systolic blood pressure was 76, diastolic 60. Glycosuria and ketonuria heavy. Ammonia nitrogen 2.5 gm on November 28-29, 2.78 gm. on November 29-30. No symptoms of acidosis.

Treatment was conducted by Dr. Stillman. The patient fasted November 30 to December 7, inclusive, receiving 70 c.c. whisky daily, and on December 7 receiving also 500 gm. thrice-boiled vegetables. Eggs and butter were added gradually until on December 10 the diet contained 52 gm. protein, 95 gm. fat, 100 c.c. whisky, and 500 gm. thrice-boiled vegetables. On this day a glycosuria of 9.5 gm. appeared. The strength and well-being had improved from the outset; but though ketonuria had diminished, it had never cleared up satisfactorily. The carbohydrate tolerance was literally nothing. Details will be published elsewhere. Briefly, it was necessary to keep him on a diet of about 700 calories daily, about half of which was alcohol, until February 3. He was warm and quiet in bed except for short daily periods. The weight on February 3 was 40.3 kg., and strength continued to improve. It was toward the close of this prolonged undernutrition that the calorimeter tests were made, on January 31 and February 1. It then became possible to increase the diet somewhat, but fast-days were still used frequently. The ferric chlorid reaction slowly diminished to traces, but did not become regularly negative until the latter part of May. The patient was discharged June 28, 1915, at precisely his initial weight, namely, 44.2 kg., with urine normal on a diet of 80 gm. protein, 15 gm. carbohydrate and 1,950 calories. He has since conducted his business. Carelessness with his diet brought back glycosuria and required his return to the hospital on Oct. 17, 1915; but the condition was much more favorable than before and the tolerance higher on discharge from the hospital this time (Jan. 18, 1916) than on the previous occasion.

CASE 4.—Edward M. (moderately severe diabetes), customs inspector, aged 34, married. His family, personal history and habits were negative, except for chronic indigestion and constipation since the age of 22. Normal weight 80 kg. In July, 1913, occurred sudden attack of dizziness, colic, vomiting and diarrhea, with fever for one day. From that time on he was constantly thirsty and lost weight and strength. Diabetes diagnosed in September. Under inefficient treatment he was sugar-free for only two periods of one week each. Entered Rockefeller Hospital July 15, 1914. Weight 60.4 kg. Highly neurasthenic, but no serious emaciation or acidosis. Physical examination negative except for sallow color and enlarged liver. On restricted diet there was marked ketonuria and a negative carbohydrate balance of about 12 gm. Four days of fasting from July 18 to 21, inclusive, were required to stop glycosuria. Feeding was begun on July 23, with vegetables containing 12.2 gm. carbohydrate.

TABLE 4.—WILLIAM G.: CLINICAL DATA DURING STAY AT BELLEVUE HOSPITAL JANUARY 10 TO 15

Date	Body Weight, Kg.	Water Intake, c.c.	Urine					Nitrogen Balance	Food				
			Volume, c.c.	Diabetic Acid	Ammonia Nitrogen, Gm.	Dextrose, Gm.	Dextrose-Nitrogen Ratio		Total Nitrogen, Gm.	Nitrogen, Gm.	Carbo-hydrate, Gm.	Alcohol, Gm.	Calories
Jan. 10-11	43.3	2,130	1,465		1.48	0		5.27†	—0.17	5.8	...	57.4	1,775
Jan. 11-12	43.2	1,910	1,177	++	1.60	0		6.47	+1.14	9.78	0.6	30.6	2,016
Jan. 12-13	43.3	2,650	1,995	++	2.81	11.4	1.27	8.49	+1.13	10.93	0.6	57.4	2,441
Jan. 13-14		2,350	2,520	++	2.76	15.3	2.02	7.18	+1.99	10.42	0.6	57.4	2,250
Jan. 14-15	44.9	3,100	3,665	++	4.05	23.0	2.28	9.63	+1.73	12.91	1.0	57.4	2,738
Jan. 15-16*	44.0	1,150	876		1.18	9.9	3.93	2.42		4.41	0.4	11.5	902
Jan. 16-17	42.8	1,150	2,500	++		43.8	3.14	13.91	—3.96	11.3	...	20.0	1,811
Jan. 17-18	42.0	1,335	2,770	++	3.40	42.8	3.10	13.82	—3.19	12.08	...	20.0	2,305
Jan. 18-19	40.8	750	2,775	++		46.7	3.44	13.59	—2.96	12.08	...	22.5	2,183
Jan. 19-20	40.6	1,850	2,925	++		69.6				14.3	2.2	20.0	2,369
Jan. 20-21		2,700	4,385	++		76.7	3.82	20.1	—6.51	14.29	...	20.0	2,335
Jan. 21-22	42.4	4,080	4,700	++		45.				15.15	2.2	22.5	2,508
Jan. 22*	43	2,000	1,390	++		8.8	3.15	2.81	—2.81		...	40.0	280

* Incomplete.

† Only for the calorimeter periods.

TABLE 5.—FELIX K.: CLINICAL DATA

Date	Total Calories	Fat, Gm.	Carbo., Gm. in Food	Glucose, Gm. in Urine	N in Food, Gm.	N in Urine, Gm.	Body Weight, Kg.	Urine Volume, c.c.	Remarks
1/14/14	2,046	155.4	57.7	12.05	14.2	12.13		820	
1/15/14	2,016	145.4	62.5	21.50	15.8	18.61		1,000	
1/16/14	2,092	163.0	62.4	12.50	12.5	12.61		920	
1/17/14	1,989	141.6	64.3	13.80	15.6	14.79	56.51	1,180	
1/18/14	2,304	177.7	58.2	10.00	16.0	15.19		1,300	
1/19/14	2,065	149.0	64.3	6.45	16.9	11.99	56.33	940	
1/20/14	1,964	140.1	62.9	0	15.6	15.52		1,580	
1/21/14	2,369	181.8	59.8	9.65	16.5	16.08	57.52	1,380	
1/22/14	2,667	216.4	60.4	9.11	15.8	12.16	56.52	1,170	
1/23/14	2,852	236.5	59.8	5.88	15.9	13.90		1,360	
1/24/14	2,684	218.5	59.8	8.08	15.9	12.39	57.07	1,300	
1/25/14	3,138	247.4	59.8	5.68	16.0	10.31		1,040	
1/26/14	2,733	173.7	59.8	7.14	16.1	11.77	56.76	1,360	
1/27/14	2,773	178.3	60.0	8.70	15.9	10.54		1,200	
1/28/14	3,059	183.3	59.8	5.88	16.0	12.33	57.01	1,120	
1/29/14	921	76.7	20.8	0	4.7	9.36		1,330	
1/30/14	2,986	179.9	60.5	0	16.2	13.84	56.98	1,460	
1/31/14	3,458	180.0	59.7	0	16.1	13.28		1,520	
2/ 1/14	3,492	182.1	61.9	Trace	16.5	13.84		1,600	
2/ 2/14	3,488	182.8	60.5	0	16.2	14.01	57.97	1,910	
2/ 3/14	3,492	203.8	60.5	6.88	16.2	12.95		2,220	
2/ 4/14	3,579	192.2	60.5	8.08	16.5	11.77	58.76	1,860	
2/ 5/14	3,580	192.2	60.7	5.68	16.3	11.54		1,640	
2/ 6/14	3,615	197.3	60.5	0	15.9	10.65		1,400	
2/ 7/14	3,663	201.5	59.7	6.90	16.4	13.34	58.25	1,330	
2/ 8/14	3,620	186.3	60.5	10.00	16.3	11.21		1,140	
2/ 9/14	3,310	181.6	62.3	8.34	16.2	13.17		1,180	
2/10/14	982	81.7	20.8	0	5.3	9.92	58.17	1,300	Green day
2/11/14	929	77.1	20.8	0	5.1	9.33	57.56	1,155	Green day
2/12/14	2,138	124.1	178.1	13.80	9.9	11.59	57.84	1,515	Oatmeal day
2/13/14	2,177	127.1	178.1	19.22	10.3	10.87	57.93	1,580	Oatmeal day
2/14/14	2,171	126.7	178.1	31.08	10.2	10.54	57.80	1,930	Oatmeal day
2/15/14	917	76.1	20.8	0	4.8	9.92		970	Green day
2/16/14	3,487	181.9	61.6	0	16.2	14.96	57.35	1,130	Green day
2/17/14	3,464	180.1	60.7	Trace	16.3	12.89	57.75	1,000	
2/18/14	3,421	175.9	60.1	13.20	16.1	14.74	58.88	1,650	
2/19/14	3,361	170.2	59.7	9.10	15.9	14.01	58.45	1,320	
2/20/14	3,469	181.1	59.7	13.70	16.1	16.08	58.24	1,600	

TABLE 5.—FELIX K.: CLINICAL DATA—(Continued)

Date	Total Calories	Fat, Gm.	Carbo., Gm. in Food	Glucose, Gm. in Urine	N in Food, Gm.	N in Urine, Gm.	Body Weight, Kg.	Urine Volume, c.c.	Remarks
2/21/14	3,347	171.2	59.5	5.88	15.0	11.10	58.89	1,310	
2/22/14	3,396	173.9	61.2	Traces	15.7	10.70		1,460	
2/23/14	3,329	176.7	60.4	Traces	16.0	11.54	59.02	1,760	
2/24/14	3,318	174.8	38.6	Traces	14.7	11.45	59.17	1,405	Bread every two hours
2/25/14	3,460	181.3	58.3	Traces	16.0	12.10		1,080	
2/26/14	920	76.6	20.6	0	4.8	9.09	58.60	1,110	
2/27/14	3,622	174.8	12.1	0	14.6	15.08		1,480	
2/28/14	3,254	181.8	13.4	0	15.9	12.78	59.00	1,300	
3/ 1/14	3,494	218.4	38.2	0	14.4	15.08		1,900	
3/ 2/14	3,341	177.6	39.6	0	15.6	15.60	59.16	2,120	
3/ 3/14	3,336	177.7	38.4	0	15.6	13.79	58.87	1,540	
3/ 4/14	3,375	177.6	47.2	0	15.8	12.72	59.51	1,400	
3/ 5/14	3,400	178.4	50.3	0	16.0	12.89	60.08	1,540	
3/ 6/14	3,486	179.6	65.0	0	16.5	12.69	60.07	1,440	
3/13/14	3,360	178.5	58.5	5.75	15.2	15.20	59.52	1,650	Oatmeal every two hours
3/14/14	943	78.4	20.8	0	5.0	10.87	59.37	1,400	Green day
3/15/14	927	77.1	20.8	0	4.8	5.77	59.22	870	Green day
3/16/14	2,007	112.0	178.0	24.39	9.1	10.31		1,580	Bread day
3/17/14	2,013	112.6	178.0	27.03	9.2	8.85	58.81	1,390	Bread day
3/18/14	2,057	116.0	178.0	37.38	9.6	8.34		1,786	Bread day
3/19/14	942	78.1	20.8	0	5.0	6.48	58.42	930	Green day
3/20/14	946	78.7	21.2	0	4.8	7.88		1,877	Green day
3/21/14	3,388	173.1	61.4	0	15.6	11.98		2,130	
3/22/14	3,359	173.4	58.3	15.86	14.9	10.31		1,250	
3/23/14	3,164	199.5	66.7	Trace	15.0	11.04		1,820	

The vegetables were increased until on July 30 he was taking 70.5 gm. carbohydrate, without glycosuria. Protein and fat were then slowly added, and an adequate diet attained without difficulty. Patient is a gourmand, and in September he was allowed to bring back his old symptoms by excess of fat in the diet, as an object-lesson. Two days' fasting stopped this glycosuria and suitable diet was resumed. In the latter part of October the average daily diet was approximately 114 gm. protein, 120 gm. carbohydrate, and from 2,600 to 2,900 calories. Calorimeter experiments were performed on October 30 and 31 and November 5. Patient was discharged on Nov. 9, 1915, weighing 61.2 kg. He has done his usual work since, with only an occasional temporary glycosuria after eating too much.

CASE 5.—Felix K. (mild diabetes), clerk, 47 years old, born in Ireland. As a young man the patient had pneumonia, urethritis, and about four years ago an attack of malaria. He was a heavy drinker of beer and whisky up to five months ago. Lately he has taken but little alcohol. About one year ago he first noticed a loss of weight, with polyuria and weakness. Since then he has lost from 40 to 50 pounds. On admission to Bellevue, Oct. 28, 1913, he

was so weak that he could hardly walk upstairs. He is an emaciated man of medium stature. The lungs are emphysematous. There is slight exophthalmos, but no enlargement of the thyroid gland. Wassermann reaction ++; hemoglobin 98 per cent.; leukocytes 9,500; blood pressure: systolic 110, diastolic 75. His urine contained 61 gm. of glucose, 2.14 gm. ammonia, and small amounts of betaoxybutyric acid. The patient was in the general ward and it was difficult to control his diet. He was discharged on November 25, and on January 13 was readmitted, this time to the metabolism ward. Weight January 16, 56.5 kg. On a restricted diet his carbohydrate tolerance improved and his weight and strength increased rapidly (see Table 5). He was discharged March 24, 1914, in excellent condition. Since then he has reported from time to time, feeling perfectly well and strong, but showing sugar in the urine when he departs from his diet.

CASE 6.—John O'C. (mild diabetes, morphinism), clerk, aged 32. His father was an alcoholic. At the age of 15 the patient had typhoid, and he has suffered from "pleurisy" eight times in the past few years. At the age of 16 he began to smoke opium, later taking to hypodermic injections of the drug, and one year ago he added cocain in increasing doses. Before admission he was taking 80 grains of cocain and 22 of morphin a day. This is his first attempt at breaking the habit. About two years ago he noticed polyuria and polydipsia and his doctor found sugar in the urine. He did not follow treatment and lost weight rapidly. He was very constipated, and so weak that he could hardly walk. Admitted to Bellevue Hospital March 13, weight March 24, 31.3 kg., height 163 cm. He was found to be nothing but skin and bones, toothless, with bent figure and ratlike, pathetic face. His whole body was covered with abscesses and scars of infections from hypodermic injections. There was a small ulcer on the sole of each foot. His pulse was very small, the beat normal, his tongue fissured, glassy and moderately red.

On a restricted diet the patient improved slowly and the glycosuria and acidosis cleared up (Table 6). He grew stronger but it was almost impossible to increase his weight without causing glycosuria. It was necessary to give him a grain of morphin every four hours. His systolic blood pressure varied between 104 and 125. On May 1, 1915, he was discharged and sent to a sanitarium, where he stayed a short time, then went back to his old habits and died a few months later.

SUMMARY AND COMMENT

1. *The Oatmeal Treatment.*—The mildly diabetic patient, Felix K., on a regulated diet containing about 60 gm. carbohydrate daily, showed a constantly positive carbohydrate balance and maintained his weight and well-being. February 10 and 11 were "green" days. Then from February 12 to 14, inclusive, 200 gm. oatmeal were given daily in the usual manner; then followed, February 15 to 16, two more "green" days. For comparison, beginning March 14, the same program was instituted, using bread instead of oatmeal, namely, first two "green" days, then March 16 to 18, inclusive, 265 gm. bread daily, equivalent in carbohydrate to the previous oatmeal, with fat, protein and calories also corresponding to the oatmeal period; then March 19 and 20 two more "green" days. Comparison was also made in a different manner, as follows: On February 24 he was given 18 gm. bread and 9 gm. butter every two hours, and on March 13 was given the equivalent carbohydrate in the form of 13.6 gm. oatmeal with 9 gm. butter every two hours.

TABLE 6.—JOHN O'C.:

Date	Food					
	Total Calories	Protein, Gm.	Fat, Gm.	Carbo., Gm.	Alcohol, Gm.	Food, N, Gm.
March 24-25	2,333	66.1	184.2	85.7		10.57
March 25-26	1,842	81.1	131.2	70.4		12.97
March 26-27	2,095	69.0	160.9	77.0		11.04
March 27-28	2,021	79.4	147.3	84.2		12.70
March 28-29	2,410	82.1	185.9	83.9		13.13
March 29-30	2,508	82.1	195.9	85.2		13.13
March 30-31	2,610	106.6	186.6	87.3	11.47	17.06
March 31-April 1	2,279	87.5	164.3	56.6	22.94	14.00
April 1- 2	2,488	88.7	183.7	62.4	22.94	14.19
April 2- 3	1,999	69.6	137.8	43.2	22.94	11.13
April 3- 4	294	0	0	0	42.00	0
April 4- 5	1,378	35.7	90.6	16.6	45.90	5.71
April 5- 6	1,941	44.1	126.5	142.5		7.05
April 6- 7	1,594	47.0	87.8	142.5		7.52
April 7- 8	1,753	47.0	104.8	142.5		7.52
April 8- 9	2,148	57.2	194.3	25.9		9.15
April 9-10	1,489	39.8	132.0	23.9		6.36
April 10-11	1,783	48.1	154.4	36.6		7.70
April 11-12	2,282	71.3	193.2	47.1		11.41
April 12-13	2,435	76.0	200.7	61.6		12.16
April 13-14	2,321	77.9	199.2	36.5		12.46
April 14-15	2,178	70.6	187.6	35.0		11.29
April 15-16	1,723	28.9	145.6	28.5	89.10	4.62
April 16-17	1,784	43.7	144.8	23.8	22.94	4.62
April 17-18	1,600	34.4	114.4	25.3	42.00	5.50
April 18-19	1,748	31.0	128.5	25.5	45.90	4.96
April 19-20	1,579	41.4	110.2	41.5	30.59	8.62
April 20-21	1,919	49.6	152.8	32.8	22.94	7.93
April 21-22	1,854	49.2	148.0	28.2	22.94	7.87
April 22-23	1,952	77.3	140.3	41.4	22.94	12.37
April 23-24	2,063	100.9	142.2	40.8	22.94	16.14
April 24-25	1,679	67.6	115.2	41.8	22.94	10.82
April 25-26	385	16.8	34.0			2.69
April 26-27	1,761	99.0	133.0	28.9		15.84
April 27-28	737	25.3	60.6	16.7		4.05
April 28-29	1,652	47.5	93.4	143.6		7.60
April 29-30	1,674	47.0	96.3	142.5		7.52
April 30-May 1	1,652	47.5	93.4	143.6		7.60

CLINICAL DATA

Urine							Body Weight Kg.
Urine N, Gm.	Excreta N, Gm. §	N Balance, Gm.	Urine Glucose, Gm.	Urine NH ₃ , Gm.	Diacetic Acid	Urine Volume, c.c.	
13.34	14.40	-3.92	78.1			1,395	31.25
12.72	14.02	-1.05	55.7	1.70	Small amount	1,130	31.94
.....							32.16
{ 9.53*	11.20	+1.50	39.4			900	32.61
{ 9.93†	11.40	+1.73	43.7			1,480	33.80
10.09	11.23	+1.90	70.9	2.04	++	2,310	33.88
9.92	10.95	+6.11	53.3	1.80	+	2,000	33.63
10.54	11.94	+2.06	40.6	2.18	+++	1,550	33.14
9.53	10.95	+3.24	33.4	1.96	++	1,125	32.89
9.25	10.36	+0.97	23.6	1.96	+	920	32.89
6.02			+++	0.67	0	500	32.11
6.81	7.38	-1.67	0	0.26	0	735	32.69
8.41	9.12	-2.09	20.7	0.41	0	1,280	
6.44	7.19	+0.33	40.6	0.41		3,875	34.81
4.51	5.35	+2.17	29.7	0.75	0	2,900	32.71
5.76	6.68	+2.47	Heavy trace	0.57	0	1,490	32.26
6.72	7.36	-1.00	0	0.61	0	2,670	32.52
7.31	8.09	-0.39	0	0.39		1,620	31.79
6.22	7.36	+4.05	0	0.49	0	1,400	
8.28	9.50	+2.66	11.8	0.96	0	2,570	32.38
6.73	7.98	+4.48	7.2	0.82	Slight trace	1,440	31.79
8.99	10.12	+1.17	11.4	1.12	+	2,240	32.46
5.55	6.01	-1.39	2.6	0.79	Trace	1,200	32.52
5.04	5.74	+1.25	Slight trace	0.76	Heavy trace	1,880	32.12
5.04	5.59	-0.09				2,500	
5.37	5.87	-0.91				1,925	32.05
6.22	7.08	+1.54	0		0	1,820	31.61
5.80	6.59	+1.34				1,840	32.35
5.39	6.18	+1.69	0	0.51	0	1,940	32.52
6.35	7.59	+4.78	0	0.47	0	2,000	32.25
9.83	11.44	+4.70	0	0.59	0	1,725	32.45
9.18	10.26	+0.56	4.8		0	825	32.44
6.37	6.64	-3.95	0		Very heavy trace	600	
11.43	13.01	+2.79	0	0.98	Heavy trace	960	31.04
9.30	9.71	-5.66	0	0.93	Slight trace	660	31.88
8.58	9.34	-1.74	15.9	1.04	Trace	1,105	31.43
6.48	7.23	+0.29	21.2	1.14	0	1,960	32.46
6.39	7.15	+0.45	23.1	1.17	0	1,825	32.45

* 23 hours.

† 24 hours.

§ Urine N + 10 per cent. of Food N.

TABLE 7.—DATA OF—

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calo- rimetry, Cal.	Heat Elimi- nated, Cal.
Gerald S. 11/9/14 42.15 Kg. 1.44 Sq. M.	Prelim.	11:15							
	1	12:15	15.94	16.17	0.717	20.22	0.561	52.19	43.97
	2	1:15	16.32	16.39	0.724	20.85	0.561	52.94	47.51
	3	2:15	16.34	16.58	0.717	20.96	0.561	53.55	51.11
Gerald S. §..... 11/12/14 40.15 Kg. 1.41 Sq. M.	Prelim.	11:15							
	1	12:15	16.27	15.87	0.746§	22.44	0.307	52.15	49.24
	2	1:15	16.95	17.45	0.706	23.81	0.307	56.71	54.44
	3	2:15	15.50	17.61	0.640	24.32	0.307	57.19	56.77
Gerald S. 11/14/14 38.97 Kg. 1.40 Sq. M.	Prelim.	10:24							
	1	11:24	15.41	16.00	0.700	17.66	0.441	51.87	45.12
	2	12:24	15.35	15.84	0.705	18.65	0.441	51.35	49.85
	3	1:24	15.30	15.87	0.701	18.71	0.441	51.45	51.61
Gerald S. 11/16/14 38.77 Kg. 1.40 Sq. M.	Prelim.	11:22							
	1	12:22	13.85	14.29	0.705	29.82	0.347	46.34	43.67
	2	1:22	14.59	14.84	0.715	26.65	0.347	48.18	49.69
	3	2:22	15.27	14.73	0.754	24.96	0.347	48.23	50.03
	4	3:22	14.53	15.57	0.680	23.60	0.347	50.55	49.39
Gerald S. 11/18/14 38.74 Kg. 1.40 Sq. M.	Prelim.	11:06							
	1	12:06	12.17	12.41	0.713	13.42	0.247	40.40	34.51
	2	1:06	13.00	13.45	0.718	13.97	0.247	42.82	38.89
	3	2:06	14.19	13.43	0.769	14.61	0.247	44.27	41.69
	4	3:06	13.76	14.44	0.693	14.75	0.247	47.06	44.15
	5	4:06	13.45	13.06	0.685	14.47	0.247	42.85	40.50
Gerald S. 11/20/14 38.74 Kg. 1.40 Sq. M.	Prelim.	11:06							
	1	12:06	13.37	12.50	0.778	17.60	0.22	41.60	39.42
	2	1:06	12.20	12.82	0.692	16.68	0.22	42.06	41.23
	3	2:06	12.28	12.13	0.736	16.19	0.22	39.92	41.02
	4	3:06	15.43	14.29	0.785	16.43	0.22	47.67	43.08
Gerald S. 11/23/14 42.84 Kg. 1.45 Sq. M.	Prelim.	11:15							
	1	12:15	13.02	13.54	0.699	12.99	0.232	44.14	38.70
	2	1:15	13.64	12.61	0.786	13.10	0.232	41.76	38.23
	3	2:15	12.56	13.11	0.697	14.15	0.232	42.72	42.79
Gerald S. 11/24/14 44.00 Kg. 1.46 Sq. M.	Prelim.	11:06							
	1	12:06	12.80	11.70	0.796	13.09	0.237	38.79	36.04
	2	1:06	13.56	13.94	0.707	13.95	0.237	45.44	39.79
	3	2:06	13.22	12.51	0.768	13.69	0.237	41.23	38.55
	4	3:06	12.10	11.85	0.742	14.13	0.237	38.78	38.96

§ Calculations in summary based on total O₂ and CO₂ for 3 hours.

—CALORIMETER EXPERIMENTS

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. Mech	
.....	36.28	..								Basal; D:N assumed to be 1.53 on basis of R.Q. Very quiet
55.18	36.61	71	4	0.704	22.4	77.6	0	1.24	35.01	
55.57	36.85	76	8	0.714	22.1	77.9	0	1.26	35.51	
51.13	36.86	77	4	0.705	21.8	78.2	0	1.27	35.92	
.....	37.14	..								Second day of fast; basal Asleep 50 min.
52.23	37.24	99	7.2	0.755	8.0	75.1	16.9	1.30	36.11	
54.77	37.26	102	10.5	0.711	7.4	91.3	1.3	1.41	39.27	Asleep 40 min.
55.45	37.23	99	2.0	0.639*	7.3	92.7	0	1.42	39.61	Asleep 30 min.
.....	36.54	..								Fourth day of fast; basal Asleep
49.33	36.68	81	7.8	0.68*	19.4	80.6	0	1.33	36.66	
41.13	36.42	..	7.6	0.69*	19.6	80.4	0	1.32	36.29	Asleep
51.95	36.44	79	12.0	0.68*	19.5	80.5	0	1.32	36.36	Asleep 45 min.
.....	36.16	..								Basal
40.14	36.08	..	9.0—	0.695	15.5	84.5	0	1.20	32.86	Asleep
53.54	36.16	..	13.0—	0.708	14.8	84.0	1.2	1.24	34.17	Asleep
48.88	36.08	70	15.8—	0.754	14.8	72.4	12.8	1.25	34.22	Drank 20 c.c. whisky at 1:27 p. m.
49.10	36.08	..	17.0—	0.665	14.2	85.8	0	1.30	35.85	Asleep
.....	35.76	..								Basal
26.05	35.51	..	4	0.697	15.5	84.5	0	1.04	28.65	Asleep
39.33	35.52	..	4	0.705	14.6	85.4	0	1.11	30.37	Basal, asleep Drank 20 c.c. whisky at 1:08 p. m.
53.62	35.84	..	12	0.764	14.1	70.1	15.8	1.14	31.40	
53.62	36.14	..	13	0.676	13.2	86.8	0	1.22	33.38	Asleep 40 min.
34.91	35.97	..	7	0.740	14.6	75.5	9.9	1.11	30.39	Asleep 55 min.
.....	35.88	..								Whisky, 20 c.c. at 11:08 a. m. Dozed
37.70	35.78	..	6	0.773	14.7	66.7	18.6	1.07	29.50	
40.06	35.75	..	4	0.673	14.5	85.5	0	1.09	29.83	Dozed
42.74	35.81	..	3	0.724	15.3	79.2	5.5	1.03	28.31	Dozed
46.44	35.92	..	19	0.782	12.8	65.2	22.0	1.23	33.04	Restless
.....	35.99	..								Basal
37.09	35.95	47	8	0.681	13.9	86.1	0	1.03	29.29	Asleep 30 min.
43.05	36.04	..	11	0.783	14.7	63.8	21.5	1.00	27.71	Awake
34.37	35.81	52	14	0.678	14.4	85.6	0	1.00	28.35	Awake
.....	35.85	..								Basal
36.30	35.85	52	4.0	0.794	16.2	59.9	23.9	0.90	25.29	Quiet
41.16	35.90	51	5.5	0.691	13.8	86.2	0	1.03	29.62	Quiet
40.63	35.96	..	5.0	0.762	15.2	69.2	15.6	0.94	26.88	Drank 1 drop of water Quiet
31.21	35.75	50	2.2	0.730	16.2	76.9	6.9	0.90	25.28	

* R. Q. assumed as 0.707 for calculations.

TABLE 7.—DATA OF CALORIMETER—

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calo- rimetry, Cal.	Heat Elimi- nated, Cal.
Gerald S. 11/25/14 44.04 Kg. 1.46 Sq. M.	Prelim.	11:15							
	1	12:15	12.72	12.29	0.753	14.98	0.235	40.32	36.55
	2	1:15	13.21	12.40	0.775	15.14	0.235	40.96	37.95
	3	2:15	13.03	12.29	0.771	15.61	0.235	40.59	38.83
	4	3:15	11.87	12.68	0.680	15.97	0.235	41.31	40.58
Gerald S. 11/30/14 44.27 Kg. 1.47 Sq. M.	Prelim.	11:27							
	1	12:27	14.38	14.09	0.742	21.28	0.228	46.18	39.28
	2	1:27	14.07	13.45	0.760	20.78	0.228	44.27	42.66
	3	2:27	14.80	14.13	0.762	20.24	0.228	46.63	41.57
	4	3:27	14.36	14.27	0.732	20.30	0.228	46.67	45.91
Gerald S. 12/2/14 44.76 Kg. 1.47 Sq. M.	Prelim.	11:12							
	1	12:12	15.59	15.21	0.745	24.90	0.208	50.03	42.79
	2	1:12	13.27	12.57	0.768	22.51	0.208	41.48	42.54
	3	2:12	16.92	16.38	0.751	24.10	0.208	54.02	50.44
	4	3:12	14.97	13.99	0.779	23.39	0.208	46.31	44.84
Gerald S. 12/4/14 43.94 Kg. 1.46 Sq. M.	Prelim.	11:09							
	1	12:09	15.81	14.79	0.778	19.79	0.204	48.99	41.38
	2	1:09	16.43			19.61	0.204	50.91*	44.13
	3	2:09	13.93	13.34	0.759	18.19	0.204	43.95	42.59
	4	3:09	14.85	14.53	0.743	18.78	0.204	47.68	45.98
Gerald S. 12/7/14 42.58 Kg. 1.45 Sq. M.	Prelim.	11:10							
	1	12:10	14.77	13.78	0.780	18.90	0.216	45.69	40.83
	2	1:10	15.08	15.19	0.722	19.31	0.216	49.59	45.09
	3	2:10	13.93	13.15	0.770	18.21	0.216	43.48	44.85
	4	3:10	14.40	13.69	0.765	18.41	0.216	45.18	45.10
William G. 1/11/15 43.28 Kg. 1.53 Sq. M.	Prelim.	11:20							
	1	12:20	13.39	12.62	0.772	16.14	0.170	41.83	40.94
	2	1:20	14.30	13.84	0.750	16.38	0.170	45.67	43.05
	3	2:20	13.74	14.26	0.701	16.45	0.170	46.60	47.13
William G. 1/15/15 43.84 Kg. 1.54 Sq. M.	Prelim.	11:07							
	1	12:07	15.11	14.72	0.747	24.83	0.291	48.34	42.16
	2	1:07	14.49	15.73	0.670	24.11	0.291	51.03	47.43
	3	2:07	14.21	14.66	0.705	24.30	0.291	47.56	49.04
William G. 1/22/15 37.87 Kg. 1.46 Sq. M.	Prelim.	11:12							
	1	12:12	15.29	16.38	0.679	17.02	0.382	53.05	49.18
	2	1:12	14.80	15.66	0.688	17.32	0.382	50.69	48.96
	3	2:12	15.46	15.87	0.708	18.36	0.382	51.42	51.88

* Calc., from CO₂, R. Q. assumed 0.778.

—EXPERIMENTS—(Continued)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbo-hyd.	Per Kg.	Per Sq. M. Meeh	
.....	36.12	..								Basal
33.16	36.03	48	3.5	0.743	15.4	74.8	9.8	0.97	26.27	Dozed
37.01	36.01	..	2.7	0.769	15.2	66.3	18.5	0.93	26.68	Dozed
37.25	35.95	..	0.5	0.765	15.4	66.2	18.4	0.92	26.44	At 1:17 drank 20 c.c. whisky from tube
33.07	35.75	51	2.8	0.659	15.1	84.9	0	0.94	26.91	Dozed
.....	36.31	..								Basal
37.96	36.28	58	4.7	0.732	13.1	79.8	7.1	0.86	24.61	Quiet
46.86	36.40	53	8.5	0.753	13.7	73.4	12.9	1.00	28.73	Quiet
40.21	36.32	56	16.5	0.755	13.0	71.0	16.0	1.05	30.26	Drank 170 c.c. water at 1:28 p. m.
44.22	36.28	52	9.4	0.720	13.0	82.8	4.2	1.05	30.29	Quiet
.....	36.66	..								Basal
39.51	36.58	56	5.1	0.738	11.1	78.6	10.3	1.12	32.24	Quiet
37.03	36.44	55	1.1	0.762	13.3	70.8	15.9	0.93	26.73	Quiet
52.36	36.50	58	15.4	0.745	10.2	76.3	13.5	1.21	34.81	Exercised 10 min.
49.81	36.64	53	5.8	0.774	11.9	68.9	19.2	1.04	29.84	Quiet
.....	36.08									
48.84	36.29	58	2.6	0.773	11.0	69.6	19.4	1.12	31.96	Exercised 10 min.
51.94	36.51	..	5.7							Exercised 10 min.
43.85	36.55	59	2.9	0.752	12.3	74.6	13.2	1.00	28.67	Quiet
43.22	36.48	..	2.8	0.734	11.3	81.4	7.3	1.09	31.11	Quiet
.....	36.46	..								Basal
43.09	36.53	55	21.2	0.776	12.5	65.4	22.0	1.07	30.42	Quiet
48.78	36.64	56	19.4	0.711	11.6	87.2	1.2	1.17	33.02	Quiet
43.58	36.61	54	25.4	0.765	13.2	67.9	18.9	1.02	28.95	Quiet
44.95	36.61	56	23.6	0.759	12.7	71.3	16.1	1.06	30.08	Quiet
.....	36.76	..								Basal
42.16	36.80	65?	2.9	0.767	10.8	69.7	19.5	0.97	27.57	Asleep
38.53	36.68	65?	10.7	0.743	9.8	79.7	10.5	1.10	30.10	Awake, quiet
48.46	36.72	53	7.4	0.689§	9.7	90.3	0	1.10	30.72	Awake, quiet
.....	36.75	..								Basal, D:N 3.81 †
37.58	36.63	64	7.0	0.757	7.9	75.2	16.9	1.10	31.57	Asleep
47.22	36.63	64	9.6	0.673	7.4	92.6	0	1.16	33.33	Asleep
52.84	36.74	62	9.6	0.712	8.0	90.7	1.3	1.10	31.06	Asleep
.....	36.98	..								Basal, D:N 3.12
46.13	36.89	64	8.5	0.679	10.8	89.2	0	1.40	38.19	Dozed
46.55	36.82	64	2.2	0.689	11.3	88.7	0	1.34	36.50	Quiet
52.30	36.84	63	6.5	0.713	11.1	88.9	0	1.40	37.02	Quiet

† D:N assumed as 3.65 for calculations.

§ R. Q. assumed as 0.707 for calculations.

TABLE 7.—DATA OF CALORIMETER—

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calo- rimetry, Cal.	Heat Elimi- nated, Cal.
Joseph U. 2/1/15 40.14 Kg. 1.45 Sq. M.	Prelim.	11:15							
	1	12:15	11.56	11.45	0.734	18.41	0.188	37.45	42.09
	2	1:15	11.57	11.26	0.747	17.79	0.188	36.99	42.18
	3	2:15	11.39	11.07	0.748	16.90	0.188	36.36	40.80
Edward M. 10/30/14 60.59 Kg.	Prelim.	11:15							
	1	12:15	20.58	18.19	0.823	25.35	0.391	60.77	62.97
	2	1:15	20.88	19.29	0.787	26.61	0.391	63.80	66.38
Edward M. 10/31/14 60.92 Kg.	Prelim.	11:33							
	1	12:33	21.62	19.88	0.791	23.02		66.23	54.37
	2	1:33	21.04	20.01	0.765	23.56		66.29	61.79
	3	2:33	22.64	20.27	0.812	24.87		67.89	66.77
Edward M. 11/5/14 62.16 Kg.	Prelim.	11:17							
	1	12:17	24.93	23.98	0.756	28.04	0.594	78.49	67.80
	2	1:17	25.27	24.55	0.748	28.96	0.594	80.21	76.64
	3	2:17	24.33	23.40	0.756	28.88	0.594	76.57	79.61
Felix K. 2/11/14 57.56 Kg.	Prelim.	11:15							
	1	12:15	20.18	19.36	0.758	22.51	0.325	63.74	66.09
	2*	2:15	44.10	43.06	0.745	44.78	0.650	141.40	140.20
Felix K. 2/12/14 57.84 Kg.	Prelim.	12:05							
	1	1:05	25.25	24.14	0.761	25.89	0.607	79.14	71.51
	2	2:05	26.63	24.85	0.779	31.64	0.607	81.91	89.43
	3	3:05	24.91	23.94	0.757	41.94	0.607	78.40	96.59
Felix K. 2/14/14 57.80 Kg.	Prelim.	11:08							
	1	12:08	25.79	23.83	0.787	23.97	0.481	78.91	75.60
	2	1:08	24.78	21.55	0.836	26.91	0.481	72.18	78.93
	3	2:08	24.53	21.55	0.828	27.60	0.481	72.03	80.44
Felix K. 2/24/14 58.70 Kg.	Prelim.	12:20							
	1	1:20	22.67	21.44	0.769	18.70	0.362	70.96	78.23
	2	2:20	22.61	20.06	0.819	19.99	0.362	67.13	77.64
	3	3:20	22.89	21.19	0.786	20.82	0.362	70.27	76.74
Felix K. 2/26/14 58.57 Kg.	Prelim.	11:02							
	1	12:02	21.00			18.95	0.326		75.40
	2	1:02	21.76	20.52	0.771	20.88	0.326	67.66	76.05
	3	2:02	21.64	19.60	0.803	20.55	0.326	65.30	74.30
Felix K. 3/13/14 59.29 Kg.	Prelim.	11:50							
	1	12:50	21.60	20.44	0.768	21.60	0.789	66.62	74.07
	2	1:50	21.63	20.31	0.774	20.94	0.789	66.29	72.80
	3	2:50	22.03	20.03	0.800	21.42	0.789	65.80	73.09

—EXPERIMENTS—(Continued)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbo-hyd.	Per Kg.	Per Sq. M. Meeh	
.....	36.56	..								Basal
36.33	36.39	72	3.0	0.723	13.3	82.6	4.1	0.93	25.95	Very quiet
40.52	36.35	72	2.5	0.738	13.5	76.5	10.0	0.92	25.63	Very quiet
30.62	36.05	73	12.0	0.739	13.7	76.3	10.0	0.91	25.20	Quiet
.....	37.31	..								Basal
55.09	37.16	52	34	0.827	17.1	48.0	35.0	1.00	32.74	Restless
55.99	36.96	53	21	0.784	16.3	70.2	21.1	1.05	34.37	Quiet
.....	36.76	..								97 gm. olive oil at 10:03 a. m.
58.10	36.84	64	27					1.09	34.74	Quiet
65.49	36.92	60	20					1.09	34.78	Quiet
66.45	36.92	55	46					1.11	35.62	Restless
.....		..						1.10	35.00	Urine lost
.....	36.94	..								Breakfast at 7
69.54	36.98	71		0.743	20.0	70.7	9.3	1.26	40.63	96 gm. olive oil at 9:17 a. m.
78.39	37.02	60		0.734	19.6	73.8	6.6	1.29	41.52	Quiet
78.80	37.01	67		0.743	20.6	70.2	9.2	1.23	39.63	Quiet
.....	37.18	..								Basal
49.49	36.84	..	5.6	0.751	14	73	13	1.11	34.74	Asleep
148.21	37.06	69	38.5	0.736	12	79	9	1.23	38.53	Fairly quiet
.....	37.53	..								At 10:45 to 10:52:
64.43	37.39	80	6.8	0.749	20	68	12	1.37	42.99	oatmeal, 125;
89.21	37.42	79	24.4	0.773	20	62	18	1.42	44.49	butter, 15; pro-
88.69	37.28	71	26.0	0.744	21	69	10	1.35	42.59	tein, 18.8; fat,
.....	37.21	..								19.8; carb., 89.1
70.91	37.12	76	12.5	0.783	16	62	22	1.37	42.89	At 9:45 to 9:53:
78.10	37.11	..	21.9	0.843	18	44	38	1.25	39.23	oatmeal, 125;
80.50	37.17	85	13.0	0.833	18	47	35	1.25	39.15	butter, 15
.....	37.19	..								
71.53	37.06	..	7.5	0.774	14	66	20	1.21	38.15	Bread, 18; butter,
74.35	37.00	69	8.3	0.822	14	52	34	1.14	36.09	9, every 2 hrs.,
77.84	37.03	75	7.4	0.783	14	63	23	1.19	37.78	last taken at
.....	37.08	..								11:37 a. m.
72.11	37.02	72	6.8							Basal
73.10	37.06	..	7.9	0.769	13	68	19	1.15	36.44	Very quiet
74.45	37.07	75	10.0	0.802	13	59	28	1.12	35.16	Very quiet
.....	36.87	..								Very quiet
65.35	36.70	76	9.0	0.751	31	58	11	1.12	35.59	Oatmeal 13.6,
72.95	36.71	76	7.2	0.760	32	55	13	1.12	35.41	butter 9, every
74.71	36.75	75	13.2	0.798	32	47	21	1.11	35.15	2 hrs., last
										taken at 11:07
										a. m.; asleep 1st
										period and half
										of second

TABLE 7.—DATA OF CALORIMETER—

Subject, Date, Weight, Surface Area Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calo- rimetry, Cal.	Heat Elimi- nated, Cal.
Felix K. 3/18/14 58.38 Kg.	Prelim.	11:25							
	1	12:25	23.83	22.18	0.781	22.75	0.373	73.47	71.91
	2	1:25	24.44	21.90	0.812	25.72	0.373	73.12	79.87
	3	2:25	22.15	19.18	0.840	24.78	0.373	64.42	73.67
	4	3:25	22.07	19.81	0.810	24.28	0.373	66.04	74.31
Felix K. 3/20/14 57.84 Kg.	Prelim.	12:00							
	1	1:00	18.79	17.54	0.779	18.15	0.338	57.97	60.50
	2	2:00	20.17	19.60	0.748	19.90	0.338	64.34	65.02
	3	3:00	20.25	18.92	0.778	20.94	0.338	62.58	64.95
John O'C. 4/28/15 31.43 Kg. 1.20 Sq. M.	Prelim.	11:34							
	1	12:34	14.26	9.92	0.732	24.34	0.381	46.05	47.99
	2	1:34	15.07	9.45	0.812	24.86	0.381	44.74	48.82
John O'C. 4/30/15 32.45 Kg. 1.22 Sq. M.	Prelim.	11:46							
	1	12:46	14.25	12.85	0.804	22.96	0.262	42.80	43.58
	2	1:46	14.87	14.14	0.765	26.25	0.262	46.63	50.53

Glycosuria: The urine always became promptly and completely sugar-free on "green" days. The total amount of glucose excreted during the oat period was 64.1 gm., during the bread period 88.8 gm. This difference is fully comparable to those in the literature upon which the claims of superiority of oatmeal have been based. But, as Blum pointed out, spontaneous fluctuations in diabetic glycosuria must be allowed for, even when all conditions are kept as uniform as possible, and a repetition of the same test sometimes gives a variation in the opposite direction. The more favorable carbohydrate balance in this instance speaks no more for oatmeal than the less favorable nitrogen balance during this same time speaks against oatmeal. This interpretation is supported by the results of the other test; for on the days when the carbohydrates were given in small divided doses it so happened that the glycosuria from bread was only a trace, while that from oatmeal amounted to 5.75 gm. A consistent difference in favor of oatmeal is therefore not present.

Respiration Experiments: This patient on February 12, while fasting in the morning after a "green" day of eggs, butter and green vegetables of the 5 per cent. class, derived from 10 to 13 per cent. of the calories from carbohydrate. On the first oatmeal day he derived 13

—EXPERIMENTS—(Continued)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. Meeh	
.....	37.16	..								At 9:45 to 10:06 a.m., bread 168, butter 15
63.34	36.99	67	11.3	0.777	13	66	21	1.12	39.67	
81.41	37.07	73	28.3	0.813	14	55	31	1.25	39.48	
69.51	37.01	71	22.2	0.847	15	44	41	1.10	34.78	
68.62	36.94	70	27.0	0.811	15	55	30	1.13	35.66	
.....	36.88	..								Basal
51.32	36.65	59	10.6	0.774	15	65	20	1.00	31.51	Asleep 30 min.
66.74	36.80	60	15.1	0.739	14	76	10	1.11	34.97	Quiet
67.66	36.88	62	13.3	0.774	14	66	20	1.08	34.01	Quiet
.....	36.43	..								1st oatmeal day.
45.42	36.34	58?	16.1	0.711	21.9	77.0	1.1	1.47	37.56	Oatmeal 50, butter 10, at 6:30 a. m. and again at 9:34 a. m., restless
48.22	36.33	76?	22.8	0.814	22.6	50.0	27.4	1.42	36.49	2d period
.....	36.32	..								3d oatmeal day. Same food as above
42.28	36.27	67	9.0	0.807	16.2	54.1	29.7	1.32	34.19	Quiet
46.71	36.15	72	18.0	0.757	14.9	69.4	15.7	1.44	37.25	Restless

per cent., and on the third oatmeal day 32 per cent. from carbohydrate. If the metabolism of carbohydrate continued at this rate of 32 per cent. throughout the day, he could have utilized about 145 gm. The positive carbohydrate balance on that day was 149 gm. On March 18, the third day on which he received the same amount of starch in the form of bread, he derived 31 per cent. of his calories from this source; he utilized about 130 gm., and the positive balance was 147 gm. He was able to derive 26 per cent. of his calories from carbohydrate after small divided meals of bread and butter, and as much as 24 per cent. while fasting on the morning after his usual diet, which just kept him sugar-free. After similar doses of oatmeal he derived only 15 per cent. from carbohydrate. The respiration experiments therefore show no significant difference between the starch of bread and that of oatmeal in this case.

The morphin addict, John O'C., with mild diabetes, gave exactly the same results, namely, on the first oatmeal day, April 28, 14 per cent. from carbohydrate, on the third day, April 30, 23 per cent. He was not tested with bread.

It is quite possible that the slightly lower combustion of carbohydrate indicated by the quotients on the first as compared with the

TABLE 8.—INDIRECT

Subject and Date	Character of Experiment	Calories per Kg.	Average Calories per Hour		Per Sq. M., Linear
			Per Sq. M., Mehn	Per Cent. from Average Normal, 34.7	
Gerald S.					
11/ 9/14	Basal.....	1.26	35.6	+ 2	36.7
11/12/14	Basal, second day of fast.....	1.38	38.3	+11	39.1§
11/14/14	Basal, fourth day of fast.....	1.32	36.4	+ 5	36.4
11/16/14	Basal, sixth day of fast.....	1.22	33.5	— 3	33.9
	Two hours after whisky.....	1.28	35.0	— 2	35.4
11/18/14	Basal, eighth day of fast.....	1.08	29.5	—15	29.8
	Three hours after whisky.....	1.15	31.7		32.0
11/20/14	Four hours after whisky.....	1.11	30.2		30.7
11/23/14	Basal, fifth day of feeding....	1.00	28.5	—18	29.6
11/24/14	Basal, sixth day of feeding....	0.93	26.8	—23	28.0
11/25/14	Basal, seventh day of feeding	0.92	26.5	—24	27.7
	Two hours after whisky.....	0.93	26.7		28.0
11/30/14	Basal (with water drinking)...	0.99	28.5	—18	31.4
12/ 2/14	Basal.....	1.02	29.5	—15	31.0
	Basal with exercise.....	1.12	32.3		34.8
12/ 4/14	Exercise with basal.....	1.07	30.6		32.7
12/ 7/14	Basal.....	1.08	30.6	—12	31.8
William G.					
1/11/15	Basal.....	1.03	29.5	—15	29.3
1/15/15	Basal.....	1.12	32.0	— 8	31.9
1/22/15	Basal.....	1.37	37.2	+ 7	35.5
Joseph U.					
2/1/15	Basal.....	0.92	25.6	—26	25.4
Edward M.					
10/30/14	Basal.....	1.03	33.6	— 3	
10/31/14	Two to five hours after 97 gm. olive oil	1.10	35.0		
11/ 5/14	Two to five hours after 96 gm. olive oil following breakfast	1.29	40.9	+17	
Felix K.					
2/11/14	Basal after 1 green day.....	1.19	37.3	+ 7	
2/12/14	1¼ to 4¼ hours after 125 gm. oatmeal, 15 butter	1.38	43.4		
2/14/14	1¼ to 4¼ hours after 125 gm. oatmeal, 15 butter; third oatmeal day	1.29	40.4		
2/24/14	After 18 gm. bread and 9 butter every two hours	1.18	37.3		
2/26/14	Basal.....	1.13	35.8	+ 3	
3/13/14	After 13.6 oatmeal and 9 butter every two hours	1.12	35.4		
3/18/14	1½ to 5½ hrs. after 168 bread and 15 butter, 3d bread day	1.18	37.4		
3/20/14	Basal after one green day....	1.06	33.5	— 4	
John O'C.					
4/28/15	After 100 gm. oatmeal and 20 butter, first oatmeal day	1.45	37.0	(+ 7)	37.7
4/30/15	After same food, third oatmeal day	1.38	36.7	(+ 3)	36.7

* On account of respiratory quotient, dextrose-nitrogen ratio assumed to be 1.53 for purpose of calculation.

† Nonprotein respiratory quotient assumed 0.707 for calculations.

CALORIMETRY SUMMARY

Per Cent. from Average Normal 39.7	Aver- age R. Q.	Aver- age Non- protein R. Q.	Per Cent. Cal. from Carb.	Per Cent. Diver- gence of Direct from Indirect Cal.	Aver- age Pulse	Remarks
— 8	0.719	0.707*	0	+ 2	75	Very quiet; D.-N. 1.53?*
— 1	0.697	0.700§	0§	— 2§	100	Asleep; D.-N. 3.5
— 8	0.702	0.68 †	0	— 8	80	Asleep; D.-N. 1.0
—15	0.710	0.701	1	— 1	..	Asleep; D.-N. 1.55
....	0.717	0.710	6	— 1	70	Asleep; D.-N. 1.55
—25	0.716	0.701	0	—21	..	Asleep; D.-N. 0.33
....	0.737	0.727	6	+ 6	71	Awake; D.-N. 0.33
....	0.748	0.739	10	+ 1	61	Dozed
—26	0.727	0.712	2	—11	49	Awake
—29	0.753	0.744	10	— 9	51	Quiet
—30	0.764	0.756	14	—14	48	Dozed
....	0.726	0.712	1	—14	51	Dozed
—21	0.749	0.740	10	— 7	55	Quiet
—22	0.757	0.750	13	—16	56	Quiet
....	0.765	0.760	16	+ 2	56	Flexed arms 10 min.
....	0.760	0.753	13	— 2	59	Flexed arms 10 min. in first two periods
—20	0.759	0.753	15	— 2	55	Quiet
—26	0.741	0.732	7	— 4	61	Quiet
—20	0.707	0.714	0	— 6	63	Very quiet, dozed; D.-N. 3.8†
—11	0.692†	0.693	0	— 7	64	Quiet; D.-N. 3.12
—36	0.743	0.733	8	— 3	72	Very quiet
....	0.805	0.806	28	—11	53	Fairly quiet
....	0.789			— 5	59	Fairly quiet; urine lost
....	0.753	0.740	8	— 4	69	Quiet; breakfast at 7 a. m., Prot. 44, fat 204, Carb. 38
....	0.749	0.741	10	— 4	69	Fairly quiet
....	0.766	0.755	13	+ 1	77	Fairly quiet
....	0.817	0.820	32	+ 3	81	Fairly quiet
....	0.791	0.793	26	+ 7	72	Quiet
....	0.787	0.786	24	+11	74	Very quiet
....	0.781	0.770	15	+ 7	76	Asleep one half exper.
....	0.811	0.812	31	+ 2	70	Fairly quiet
....	0.768	0.762	13	+ 0	60	Quiet
(— 5)	0.772	0.763	14	+ 3	64	Fairly quiet
(— 8)	0.784	0.782	23	— 1	69	Fairly quiet
				Av. ± 5.5		

† D:N ratio assumed to be 3.65 for calculations. .
§ Calculated from total O₂ and CO₂ for three hours.

third day of carbohydrate diet may indicate storage of glycogen after impoverishment on the preceding vegetable day, in harmony with the observations of Johansson and others on this point. The experiments fail to confirm Falta's conception of a striking difference in the manner of utilization of carbohydrate by diabetics on the first and third days of such a "cure." It would be desirable also to have information concerning the behavior of a normal subject under the same conditions, but such an experiment was not included in the present series.

Carbohydrate and water retention: The quantities of carbohydrate not accounted for by combustion are in all these experiments such as may easily be assumed to be stored as glycogen. The experiments are not of a character such as to throw light on the fate of carbohydrate under circumstances when, as Joslin⁵ reckons, as much as 520 gm. may be retained and not accounted for by differences in the respiratory exchange. The fate of carbohydrate under these conditions must be regarded as not definitely settled. Glycogen storage is known to be commonly associated with water retention. Aside from the edema which authors have shown to be attributable to sodium chlorid and bicarbonate, the gain in weight of some diabetics during the oatmeal treatment may be related to the carbohydrate retention. It will be noted that the patient John O'C. actually gained about a kilogram in weight during the oatmeal period. On the other hand, Felix K., with a larger carbohydrate intake and apparent storage, gained no weight during his oatmeal period and lost a trifle during the bread period. This result therefore stands in marked contrast to the well-marked increase in weight which ordinarily occurs when a normal person changes from carbohydrate-poor to carbohydrate-rich diet.

2. The Dextrose-Nitrogen Ratio.—The cases of interest in this connection are those of William G., Gerald S., and that of Cyril K., which was described by Geyelin and DuBois; also another case more recently observed, a description of which will be published shortly by Gephart, Aub and DuBois.

William G., as previously stated, at first upon admission to the Presbyterian and Rockefeller Hospitals was found to show a dextrose-nitrogen ratio of approximately 3, with a strongly negative nitrogen balance. Table 4 contains his record six months later, during a period of feeding in the attempt to improve his strength. Starting with sugar-free urine on January 11, increase of protein and fat in the diet produced prompt glycosuria, with dextrose-nitrogen ratios higher than before. At least on January 15 and 20 the ratio was that of "total" diabetes. The actual quantities of both sugar and nitrogen excreted were less than in the former period when the ratios were smaller; and the nitrogen deficit was less although the diet was lower than before in both protein and calories. The clinical condition changed so rapidly

for the worse and the patient on January 22 was so ill and drowsy that it was necessary to resort to fasting to avert coma.

In Gerald S. the dextrose-nitrogen ratio was confused by the presence of carbohydrate in the diet until November 11. On this day no food was taken except 50 c.c. cream at 6 a. m. The ratio for the twenty-four hours November 11-12 was 3.68. The excessive nitrogen excretion which was a prominent feature with William G. was absent here. The fall in both glycosuria and ratio during fasting is evident from Table 2.

Cyril K., the patient of Geyelin and DuBois, fasted five days without abatement of any of the diabetic symptoms, and with acidosis steadily increasing either because of the fast or in spite of it. Then, on account of dyspnea and drowsiness threatening coma, he was given low diet for a few days, consisting chiefly of protein, though containing also 53.3 gm. carbohydrate December 14 and 23.5 gm. December 15. The dextrose-nitrogen ratios for the next three days (December 15 and 17 inclusive) were 3.97, 4.01, and 3.87. The nitrogen loss at this period was greater than ever before described in uncomplicated diabetes. Beginning December 17, the condition gradually yielded to the second fast-treatment, as indicated by the fall of sugar, nitrogen, the ratio and the acidosis.

The case of Gephart, Aub and DuBois appeared at first to be of no extreme severity, and the urine was readily cleared up by fasting. Thereafter, in consequence of excessive protein-fat diet and the simultaneous development of an alveolar abscess, glycosuria suddenly appeared, and by the second day the 3.65 ratio was attained. The condition then yielded promptly to a repetition of fasting.

It is desirable here to discuss the dextrose-nitrogen ratio as respects (a) its occurrence in human diabetes, (b) its practical and (c) its theoretical significance.

(a) Lusk has insisted that trustworthy ratios are obtainable only when the diet contains no appreciable quantity of carbohydrate. The examples in the entire literature are very few, largely because the type of patients most likely to show the maximum ratio has so seldom been subjected to the conditions necessary to establish the ratio. Foster²⁸ says: "The diabetic patient is for several reasons an extremely difficult subject for these experiments. It is usually impossible to restrict him for a period of a week to a fat-protein diet." Benedict and Joslin⁴ mention the danger of placing a patient with severe diabetes upon a strict protein-fat diet for several days. Joslin⁵ also calls attention to possible errors due to excretion of retained carbohydrate unless ade-

28. Foster, N. B.: *Diabetes Mellitus*, Lippincott Co., Philadelphia and London, 1915, p. 30.

quate precautions are taken. The conditions involved in fasting differ in some respects from those of protein-fat diet. Though sometimes an existing ratio of 3.6 rapidly diminishes on fasting, and the glycosuria clears up, in other cases this ratio is clearly developed and persists for at least several days. Since the introduction of the fasting treatment, examples, mostly unpublished as yet, of such a ratio have been observed by several clinicians. It is probable that such observations will henceforth be made more frequently, not because the incidence of such "total" diabetes is increased by the fasting treatment, but because this method involves placing severely diabetic patients as a routine measure upon a program of complete carbohydrate abstinence for considerable periods, thus facilitating demonstration of the ratio with freedom from previous difficulties and errors. This is one of the features in which the new treatment has proved of service not merely for the practice, but also for the theory, of diabetes.

(b) Recent experience confirms the suggestion of Lusk¹⁸ that the presence of the above-mentioned ratio need not be permanent or carry a rapidly fatal prognosis. In the patient as in the phlorhizinized animal, the relation between sugar and nitrogen in the urine under suitable conditions is an index of the deficiency of carbohydrate combustion, and the maximal ratio shows total absence of utilization of the sugar formed from protein. This ratio does not necessarily indicate the highest possible quantity of protein catabolism or sugar excretion. The nitrogen excretion of Gerald S. was never high. William G. showed markedly excessive protein destruction at first; later (January 15) the ratio was maximal, but the protein breakdown moderate. Cyril K., as above remarked, showed the most rapid nitrogen loss ever recorded in a case of diabetes, and this loss was still excessive on December 22-23, when the ratio had fallen to 1.12. Phlorhizin given to Gerald S. could not have increased the ratio but would perhaps have increased the quantities of sugar and nitrogen excreted.²⁹ The reason for the remarkable intensity of protein catabolism in some cases is not known. There is no justification for the term "toxic" applied by Magnus-Levy and others. So far as existing data permit judgment, the difference does not lie in acidosis, for the patients mentioned seemed about equally close to coma. The bodily strength and nutritive state may play a considerable part. For example, Cyril K. (Geyelin and DuBois), with recent acute diabetes, had the necessary strength and reserves for intense waste of sugar and nitrogen, like the typical experimental animal. Gerald S. was weak and emaciated. William G.

29. This remark applies to fasting. On liberal protein-fat diet Benedict and Lewis (*The Influence of Induced Diabetes on Malignant Tumors*, *Proc. Soc. Exper. Biol. and Med.*, 1914, xi, 134), found the nitrogen excretion of human subjects not increased by "total" phlorhization (personal communication).

was weaker in the second of the periods described than in the first, and weighed some 5 kg. less. But this may not be the whole explanation. A specific disorder affecting protein metabolism in some patients, as in totally depancreatized dogs, is not excluded. The possibility of very rapid changes in the ratio, as exhibited most strikingly by the patient of Gephart, Aub and DuBois, is one of the strongest evidences in favor of the functional element in human diabetes. Such sudden changes for the worse or for the better are scarcely to be expected in the case of purely organic lesions, and are contrary to the results in animals when the islands of Langerhans have been lost. Because of the generally more favorable outlook for functional as opposed to organic disturbances, the dextrose-nitrogen ratio therefore contributes something to the prognosis in human diabetes. For the very reason that the process is at least partly functional and under appropriate treatment may be temporary, the dextrose-nitrogen ratio fails to define the later prognosis in any individual case. Aside from the duration of the trouble and other fallible clinical indications, there is now no basis for predicting which patients are likely to recover tolerance quickly and in considerable degree, and which are likely to improve slowly and in slight measure. Experience to date indicates that cases of brief acute course, when checked by radical treatment, may show a correspondingly more rapid improvement as compared with the more protracted cases in patients of corresponding age and type. The occurrence of the dextrose-nitrogen ratio of the phlorhizinized dog in any human patient may be taken as a sign of the gravest immediate significance. The few known to have exhibited this ratio during fasting have died, except the patient of Geyelin and DuBois. The exception is believed to be due to the skilful alternation of fasting and protein feeding in this case, but further experience will be necessary for decision. It is at least established that careful treatment offers some hope even in cases of this type, and that with the worst of ratios and other symptoms an appreciable carbohydrate tolerance may subsequently be regained.

(c) The principal debate concerning the dextrose-nitrogen ratio has been not whether values as high as those mentioned occur in human patients, but whether any higher values ever occur. Animal experiments aiming to prove the formation of sugar from fat have all miscarried; but a few authors still hold that occasional cases of exceptionally severe human diabetes show dextrose-nitrogen ratios so high as to be explainable only by the formation of sugar from fat. Some of the cases above described are not lacking in severity, but rather give the impression of being more severe than those in the literature in which sugar was supposed to have been formed from fat; and neither on protein-fat diet nor on fasting were any ratios observed which could justify the assumption of sugar-formation from fat. It may be argued

that the negative evidence in the present cases cannot overthrow positive evidence in other cases, which though not more severe may have been of peculiar character. Alone, it could not do so. But the carbohydrate hunger of patients on old-fashioned protein-fat regimen caused numerous writers to compare them to drug addicts with respect to their ingenuity, pertinacity and also mendacity in obtaining forbidden food, even when supposedly isolated and watched; and experienced observers are aware that only special environment and special qualifications of the nurse in charge can guarantee against this source of error. As accuracy of investigation has increased, the number of reports of ratios indicating sugar formation from fat has diminished. Apparently no such ratio has ever been described in America; and the experience of the majority of clinics and laboratories elsewhere is similar. The justification for questioning the alleged findings in occasional cases at a few European clinics is found in the large number of accurate observers who see numerous diabetics of various grades of severity, but are still waiting to see any case showing the excessive ratios mentioned. The general agreement of negative evidence is believed now sufficient to set aside the principal support of the doctrine of sugar formation from fat, namely, the supposed occurrence of this process in diabetic patients.

3. *The Respiratory Quotient*.—In the cases mentioned, except that of Cyril K., the Lusk dextrose-nitrogen ratio was present only for brief periods. The objection might therefore be raised that these ratios were purely accidental, and partly accounted for by sweeping out of more or less carbohydrate previously retained as glycogen or sugar. Here the necessary proof is afforded by the respiratory quotients. In the case of Gerald S. it was impossible to determine accurately the dextrose-nitrogen ratio November 9, the day after a considerable amount of carbohydrate in the food, so it was assumed for purposes of calculation to be 1.5, a figure which gave theoretical results. On the second day of the fast, the dextrose-nitrogen ratio being 3.5 during the calorimeter period, the total quotient was 0.697 and the nonprotein quotient 0.7. On the sixth and eighth days of the fast the nonprotein quotients were 0.701 and 0.701 respectively. For William G. in the last two experiments (January 15 and 22), with dextrose-nitrogen ratios of 3.81 and 3.12 during the calorimeter periods, nonprotein quotients of 0.714 and 0.693 were found. The average nonprotein quotient on all these days was 0.703, as compared with the theoretical figure of 0.707 for fat. These and the similar quotients observed in Cyril K. serve to show that the dextrose-nitrogen ratios obtained under the above conditions were not accidental, but at the times when the Lusk ratio was present the diabetes was actually "total." These quotients also agree with the results of Benedict and Joslin and other exact work in fur-

nishing additional testimony against the formation of sugar from fat, thus fully confirming the evidence afforded by the dextrose-nitrogen ratio.

The tables also show that during the fasting treatment the power to oxidize carbohydrate gradually improved, as would be expected from the urinary findings. On fasting and on low diet thereafter the patients were able to derive an appreciable percentage of the energy requirement from this source. Joseph U. was able thus to derive 8 per cent. of his requirement. Gerald S., from a condition of total inability to oxidize sugar, apparently became able to derive 15 per cent. of his energy from it. William G. illustrated the opposite change produced by protein-fat overfeeding. January 11, on low diet, he was deriving 7 per cent. of his requirement from carbohydrate. The protein and fat were then increased, and by January 15 "total" diabetes was present.

Brief mention may also be made of the two exercise experiments with Gerald S. on December 2 and 4. The exercise performed in the calorimeter consisted in flexing and extending the forearms for ten minutes at the beginning of a period. The labor performed was sufficient to raise the heat production by 18 per cent. for the hour period, or by about 100 per cent. for the ten minutes of actual exercise. The respiratory quotient showed no change during this hour, remaining at 0.75; but in the next hour the total quotient was 0.779 and the nonprotein quotient 0.77, which figures are higher than the averages obtained in any of the experiments with this patient at rest. On December 4 a similar ten minutes of exercise was inserted at the beginning of the preliminary period, immediately after the calorimeter was sealed, and also at the beginning of the first and second hours thereafter. The quotient in the first hour was 0.778, corresponding to that on December 2; the quotient in the second hour was lost through accident. The experiments at least give no indication of a lowering of the quotient due to any hypothetical exhaustion of glycogen in a patient supposedly glycogen poor. This aspect is to be emphasized more than the slight rise of the quotient, which might have been accidental in the two experiments, though it may perhaps suggest a slight increase in carbohydrate utilization, possibly bearing some relation to the therapeutic benefits of exercise.⁹

The most surprising feature pertaining to the respiratory quotients consisted in some unexpectedly high values obtained, similar to those described by Joslin. For example, Gerald S. fasted eight days, November 11 to 19, then received a gradually increasing protein-fat diet, with from 750 to 1,000 gm. of thrice-boiled green vegetables daily. On the fifth day of this diet, November 23, the quotient indicated that he was deriving 2 per cent. of his calories from the combustion of carbohydrate. The subsequent experiments, up to December 7, gave quo-

tients indicating combustion of between 10 and 15 per cent. carbohydrate, with an average of 12 per cent. During this period the basal metabolism averaged 1,042 calories per twenty-four hours. If he were deriving 12 per cent. of his calories from carbohydrate, he must have metabolized an average of 31.3 gm. a day or a total of 438 gm. in the two weeks. According to the analyses of the thrice-boiled green vegetables, which were the only possible source of starches or sugars, he could not have received more than 2 or 3 gm. of carbohydrate a day. It is improbable that he could have maintained a store of 400 gm. of glycogen in his body under the circumstances. The blood sugar did not fall enough to suggest that more than a small fraction could have been derived from this source, and the recent work of Palmer³⁰ proves, as far as is possible with animal experiments, that the quantity of sugar present as such in the tissues is insignificant. The results after the ingestion of whisky are also hard to interpret. It is known that alcohol requires a moderate amount of time, sometimes several hours, for its complete combustion, but it is impossible to tell how much alcohol is metabolized each hour, since the nonprotein respiratory quotient will not solve a problem with three unknowns. Alcohol has a quotient of 0.667, but it may possibly cause vasomotor and respiratory changes leading to an elimination or retention of carbon dioxide with resulting false quotients. But its action in normal persons or animals is to depress the quotient; in all the extensive studies concerning the utilization and effects of alcohol, a rise of the quotient after its ingestion has never been reported. In the earlier whisky experiments with Gerald S., there was a sharp rise in the quotient after drinking, followed by a corresponding fall in the second hour, the highest non-protein quotients for single hours being 0.764 on November 18, and 0.773 and 0.782 on November 20. This was not seen in control experiments in which the patient drank the same amount of plain water at the same temperature, or went through the movements of drinking without swallowing any liquid. Mild exercise, as above stated, had no immediate effect on the quotient. Finally, on Nov. 25, the whisky was given in such a way that there was absolutely no exertion on the part of the subject, and although the rise of quotient in the first hour was absent, the marked drop in the second hour was present. In this last observation there was no apparent increase in the combustion of carbohydrates, but in the first three the average quotient of the hours after whisky was slightly higher than before. There was thus an apparent increase in the carbohydrate metabolism, which would be even higher than calculated if alcohol with its low quotient were oxidized, thus tending to lower the total quotient.

Joslin has suggested that combustion of retained acetone bodies, with their high quotients (beta-oxybutyric acid 0.89, diacetic acid 1.00),

30. Palmer, W. W.: In press.

may account for some rise in the quotients of these patients. The suggestion is supported by the observation that on fasting the ketonuria falls and the quotient rises. Also, if it should prove true that alcohol diminishes ketonuria, as claimed by authors³¹ in the past, the rise of the quotient after ingestion of alcohol might correspond to an increased combustion of acetone bodies. The high quotients as described seem to be a regular or frequent phenomenon in patients with severe diabetes under the conditions described, and the possibilities may be discussed by comparison of the cases reported. The blood sugar, as stated, fell somewhat in the case of Gerald S., but rose during the development of the increased quotients in Geyelin and DuBois' patient (Cyril K.), and in the patient of Joslin.¹⁹ The above calculation in the case of Gerald S. requires the equivalent of 400 gm. of glycogen to explain the quotients observed. No patient could possibly retain enough acetone bodies to correspond to the whole of this requirement. The high quotients have generally been observed when the glycosuria and ketonuria were diminishing either during or after fasting, or on ingestion of whisky. An exception is present in the case of Cyril K. when receiving protein diet on December 16-17. Here the ketonuria was higher than on any previous day, namely, 75 gm. reckoned as beta-oxybutyric acid. The carbon dioxid capacity of the blood plasma had fallen to its lowest point, namely, 19.6 (the normal figures being from 40 to 45). The dextrose-nitrogen ratio was at its highest point, namely, 4.01. Under these circumstances it is difficult to understand what kind of material could be burned to give the observed nonprotein respiratory quotient of 0.743. This single result may possibly be due to some accident connected with the circumstances of this particular case. On the other hand, it may possibly be of some significance in connection with the fact that, although all the laboratory tests aside from the respiratory quotient indicated that the patient was in no wise better and in some respects worse on December 16-17 than on December 9-10, yet it was evident clinically that his condition was much better on the latter date and the symptoms of intoxication greatly diminished. This patient was receiving alkali during this period, but Gerald S. and Joslin's patient received none; therefore the quotients can scarcely be due to dosage with bicarbonate. It is conceivable that high quotients in one part of the twenty-four hours might be compensated by low quotients in another part. No respiration experiments were performed at night, but it is scarcely probable that any marked difference existed between

31. Neubauer, O.: Ueber die Wirkung des Alkohols auf die Ausscheidung der Azetonkörper, München med. Wchnschr., 1906, liii, 791. Benedict, H., and Török, B.: Der Alkohol in der Ernährung der Zuckerkranken, Ztschr. f. klin. Med., 1906, ix, 328. Stäubli, C.: Beiträge zur Pathologie und Therapie des Diabetes mellitus, Deutsch. Arch. f. klin. Med., 1908, xciii, 107.

day and night. Such a difference would in itself constitute an abnormality, for the day and night quotients have never been known to vary to such an extent in previous experiments on normal persons and animals. It is noteworthy that while the average divergence between the methods of direct and indirect calorimetry in the present series was only 2.3 per cent., and the agreement was close in the first experiments with Gerald S., yet beginning with the eighth day of his fast, November 18, when the period of high quotients began, there appeared minus errors of the direct as compared with the indirect calorimetry sometimes as high as 21, 14 and 16 per cent. Such discrepancies might in part be explained if the quotients were due to combustion of some other material, perhaps acetone bodies, instead of carbohydrate as assumed, for then the reckoning of the indirect calorimetry would be considerably altered. On the other hand, the divergence may possibly have been due to technical error in the measurement of the average temperature of the body.

4. *The Total Metabolism.*—In regard to the general question of heat production the present series of experiments agrees with the work of previous authors in showing the basal metabolism per kilogram of body weight to be increased in severe diabetes. But as above mentioned, the principal need in connection with this vexed question has been a satisfactory standard of comparison between diabetic and non-diabetic subjects. The linear formula devised especially to throw light on this subject is believed to afford such a standard, and the conclusions in the present paper are drawn on the basis of this mode of calculation. The summary in Table 8 shows that the surface area of thin diabetics is not so much smaller than that of normal men as would be indicated by Meeh's formula, and consequently their metabolism is considerably lower when compared with the normal average according to the linear or height-weight formula than when Meeh's less accurate formula is used. The difference between the results as expressed in terms of the two formulas in the case of Gerald S. is from 8 to 13 per cent. With William G. it is from 11 to 18 per cent., with Joseph U., 10 per cent., with John O'C., from 11 to 12 per cent. These were all very thin diabetics, and the differences with less emaciated patients would be proportionately smaller. With patients stouter than the average the metabolism would be higher according to the linear formula than according to Meeh's, but patients with severe diabetes are seldom stout.

Among the patients described in the present paper, it was noted that Gerald S. entered the hospital in a weak and exhausted condition. His metabolism at this time, November 9, was 2 per cent. above the average normal by Meeh's formula, but 8 per cent. below the average normal by the linear formula. William G. had been subjected to

prolonged low diet. Starting at 26 per cent. below normal on January 11, when glycosuria was absent, his metabolism rose, on increased diet and the return of active diabetes, to 20 per cent. below normal on January 15 and to 11 per cent. below normal on January 22. On the other hand, in the patient of Geyelin and DuBois²⁶ (Cyril K.), the diabetes was recent and acute, and here the metabolism was above normal. The respiration experiment on December 15 was after food, therefore the metabolism of 15 per cent. above normal does not represent a true basal value. The highest basal metabolism actually demonstrated here was 3 per cent. above normal on December 18.

The patient Edward M. never showed the true ravenous hunger of diabetics, but had been a heavy eater all his life and could dispose of a large diet exceptionally well, with no increase of his slight dyspeptic complaints. During most of September, weighing 58 to 63 kg. and leading the inactive life of a ward patient, he had enjoyed a high diet, the maximum being during the period September 21 to 26, with from 6,100 to 6,300 calories daily, consisting chiefly of fat, of which there was nearly 600 gm. daily. Instead of steatorrhea, there were small constipated stools, showing exceptionally high utilization by analysis. As stated in his history, the diet had been moderate but adequate preceding the first calorimeter tests. The body weight was about 60 kg., as opposed to his original "normal" weight of about 80 kg. But he felt well and strong at this weight, and, correspondingly, the basal metabolism on October 30 was found entirely normal, 3 per cent. below the average. On October 31 the metabolism was measured two to five hours after drinking 97 gm. olive oil. Table 8 shows the resulting increase of metabolism and lowering of the respiratory quotient. On November 3 the diet contained 5,300 calories with 483 gm. fat, and on November 4, 5,268 calories with 482 gm. fat. On the morning of November 5 the patient entered the calorimeter after taking 44 gm. protein, 38 gm. carbohydrate and 204 gm. fat. The metabolism two to five hours afterward is shown by Table 8 to average 17 per cent. above normal. Accordingly, the specific dynamic action of food, especially of fat, did not differ noticeably from the normal as respects its promptness or intensity in this patient, and there was no indication of an abnormally high metabolism ("Luxuskonsumption") on the excessive diet. The result with this patient under the conditions does not warrant a positive conclusion concerning possibilities in more severe cases, especially at the height of the diabetic process.

Since the last important discussion of the total metabolism in diabetes by Benedict and Joslin there have been several changes in the general point of view of the metabolism of normal controls and of diabetics as the result of work presented in previous papers of this series. In the light of these it has seemed advisable to recalculate the

cases of severe diabetes reported in the literature, and discuss the question in its most recent aspects. As we have shown, it is advisable to abandon comparisons made on the basis of cubic centimeters of oxygen per kilogram and minute and use instead the calories per square meter per hour. Recent work on the metabolism at different ages has emphasized the fact, first brought out clearly by Magnus-Levy and Falk,³² that metabolism changes with age. It must be remembered that a study of the surface area designed primarily to afford a basis of comparison between patients and normal controls has shown that Meeh's formula is not so accurate as the newly devised linear and height-weight formulas. Most important of all has been the study of a large number of controls by Benedict, by Means³³ and by the Russell Sage Institute staff, giving a normal basis of comparison which is not influenced by variations that might occur in small groups or by single investigators.

In Table 9 are given the results obtained in a large number of cases of severe diabetes. Since the height-weight formula was employed as a basis of comparison, the only cases that could be used were those where the height was given. This unfortunately has prevented the recalculation of the severe cases of Leo,³⁴ Nehring and Schmoll,³⁵ Rolly,⁷ and some of the cases of Magnus-Levy¹⁴ and Mohr.³⁶ The work of Leimdörfer¹⁷ has not been recalculated, since the abnormally low quotients make this impossible, nor has the work of Grafe and Wolff,³⁷ where it is difficult to reconcile the high respiratory quotients and high dextrose-nitrogen ratios. As will be seen, the large majority of cases was furnished by the careful work of Benedict and Joslin. For purposes of comparison, columns have been added showing the duration of life after the period of experimentation, the level of the nitrogen metabolism, the degree of emaciation, and the estimated degree of acidosis. If we study first the column showing the percentage variation from the normal, it will be noted that out of twenty-six cases thirteen are within the normal range of plus or minus 10 per cent. from the average. There are nine patients with an increase

32. Magnus-Levy, A., and Falk, E.: Der Lungengaswechsel des Menschen in den verschiedenen Altersstufen, *Arch. f. Physiol.*, 1899, Suppl., 314.

33. Means, J. H.: Basal Metabolism and Body Surface, *Jour. Biol. Chem.*, 1915, xxi, 263.

34. Leo, H.: Ueber den respiratorischen Stoffwechsel bei Diabetes mellitus, *Ztschr. f. klin. Med.*, 1891, xix, Suppl., 101.

35. Nehring, O., and Schmoll, E.: Ueber den Einfluss der Kohlehydrate auf den Gaswechsel des Diabetikers, *Ztschr. f. klin. Med.*, 1897, xxxi, 59.

36. Mohr, L.: Untersuchungen über den Diabetes mellitus, *Ztschr. exp. Path. u. Ther.*, 1907, iv, 910.

37. Grafe, E., and Wolf, G. L.: Beiträge zur Pathologie und Therapie der schwersten Diabetesfälle, *Arch. f. klin. Med.*, 1912, cvii, 201.

of from 11 to 23 per cent. and these deserve special attention. Two of these, V. and Cyril K., were studied after food, and if the stimulus of the recent meal were removed they might have come within normal limits. One of the subjects, G., was under intense nervous excitement during the experiment, and another, I., with a pulse of 120, had been described the year before as very nervous. This leaves us five cases in which there was a moderate but distinct rise in the metabolism, namely, Herr Mo., Frau Schm., Frau St., H., and U. To these we should perhaps add Cyril K. at the time of his first experiment, when after a breakfast his metabolism was 15 per cent. above the normal basal. To offset these there are four patients whose metabolism ranged from 14 to 19 per cent. below the average. Three of these, N., P. and Q., were children, and it is quite possible that the normal stimulus of the growing organism was checked by the diabetes. The fourth subject, Wm. G., was extremely emaciated. If we take the algebraic mean of the 26, we find that the metabolism in severe diabetes averages 3.3 per cent. above the normal, a figure which might be increased to about 5 per cent. by taking into account the fact that the average for the 89 normal controls of Benedict is 2 per cent. lower than the Sage standards.

Benedict and Joslin⁴ found that the average oxygen consumption of their diabetics per kilogram and minute was 15 to 20 per cent. above that of their twenty normal controls. Part of this difference was due to the fact that at that time few investigators realized the importance of the age factor. Part was due to the unusually low metabolism of the normal controls. In the twenty controls used by Benedict and Joslin for comparison with the diabetics, there are seven whose metabolism is 10 per cent. or more below the average normal described in the previous papers of this series. It so happens that these seven, A. F. G., T. M. C., Dr. P. R., Dr. S., H. F. T., E. P. C., Mrs. S. C., are used seventeen times in the total column of thirty-two, making the average of the column 8.6 per cent. below the standard. This is much greater than the divergence of —2 per cent. found in the total of eighty-nine normal controls. Their cases with severe diabetes, recalculated in terms of the height-weight formula, average only two per cent. above the Sage normal standard. It would appear that the metabolism of Benedict and Joslin's diabetic patients is within normal limits, while the large difference between their pathologic and normal cases is due chiefly to the low metabolism of the subjects selected for normal controls. It is quite possible that the low metabolism of these controls was due to the fact that they were poorly nourished and were selected because they resembled diabetics in this respect.

TABLE 9.—THE BASAL METABOLISM OF PATIENTS WITH SEVERE
SURFACE AREA AS ESTIMATED BY

Investigator	Subject	Sex	Age, Yrs.	Calories per Sq. M. per Hr. Height- Weight Chart	Normal Stand- ard Cal. per Sq. M. per Hr. for Same Age and Sex	Per Cent. Vari- ation from Normal Stand- ard	Respir- atory Quo- tient, Average
Magnus-Levy	Herr Mo.	♂	43	46.9	39.7	+18	0.70
	Frau Schm.	♀	35	41.2	36.9	+11	0.72
Mohr	Frau St.	♀	52	40.5	32.7	+23	0.71
Benedict and Joslin	A	♂	50	36.6	35.2	+ 4	0.71
	B	♀	40	26.0	36.9	— 2	0.73
	C	♂	28	40.1	39.7	+ 1	0.70
	D	♂	39	36.9	39.7	— 7	0.74
	G	♂	35	45.1	39.7	+14	0.73
	H	♀	38	40.9	36.9	+11	0.77
	I	♂	25	45.2	39.7	+14	0.73
	J	♂	20	43.6	39.7	+10	0.76
	K	♂	46	39.1	39.7	— 2	0.72
	L	♂	23	43.5	39.7	+10	0.73
	N	♂	14	43.0	49.9	—14	0.74
	O	♀	16	37.9	39.0	— 3	0.72
	P	♂	15	39.7	49.0	—19	0.69
	Q	♂	14	42.2	49.9	—15	0.77
	R	♂	47	43.6	39.7	+10	0.72
	S	♂	57	34.2	35.2	— 3	0.73
	T	♂	44	39.6	39.7	0	0.73
	U	♀	37	42.4	36.9	+15	0.73
	V	♂	36	45.8	39.7	+15†	0.73
Geyelin and DuBois	Cyril K. Dec. 15 & 16	♂	21	44.2	39.7	+11†	0.70
	Dec. 18	♂	21	40.8	39.7	+ 3	0.71
Authors	Gerald S. Nov. 9 & 12	♂	17	39.7	39.7§ (42.0*)	— 5 (—10*)	0.71
	William G. Jan. 15 to 22	♂	29	33.7	39.7	—15	0.70

* Using average normal for age of 17.

† Part of increase due to recent food.

§ Using average normal for ages 20 to 50.

DIABETES COMPARED WITH NORMAL STANDARDS ACCORDING TO THE
THE "HEIGHT-WEIGHT" FORMULA

Time Before Death in Months	Urine N per Day, Gm.	Emacia- tion or Per Cent. of Loss from Great- est Weight	Degree of Acidosis	Remarks B = Beta-oxybutyric Acid per Day
Coma 2		++	++?	
Coma 6		++	++?	
.....		Per Ct.	±	Moderately severe; Diac. 0 to +
Tb. 20	6-14	10-18	+	NH ₃ N 3.3, Diac. +, Active Tb. in lungs
Coma 6-1		9-18	++(?)	Diac. +++++
Coma 2	13-22	14-24	+++	B 14 to 61; NH ₃ N 2.6 to 5.6
Coma 3	13	15	0:+	Diac. 0 to +++++, urine alk. with 8 to 45 sod. bicarb.
Coma 15	17	+	+++	B 30, NH ₃ N 4.2, Diac. +++++, intense nervous excitement dur- ing experiment
Coma 4	9-12	14	+	B 8 to 11, Diac. 0 to +
15	14	30	±	B 4.8, NH ₃ N 2.2, pulse 120 (nerv- ous?)
36		15	±	Diac. + to ++, nervous tempera- ment
Coma 16-4	16-20	20-24	0:++	B 30, Diac. 0 to ++, NH ₃ N 3 to 5.8
Alive		20-16	±	Diac. 0 to sl. +
Coma 1½	5-10	9	+++	B 21 to 30, Alv. CO ₂ Hald. 16 to 28
Coma 3	8-11	14	+	B 13 to 14
Coma 1	5-18	20	+++	Diac. +++++, NH ₃ N 4.6 to 5
Coma 4	7-14	5	++	B 20 to 27, NH ₃ N 2.2 to 4.6, Alv. CO ₂ 31 to 40
Tb. 10	13-16	17	++	B 42 to 50, NH ₃ N 5 to 6, somewhat nervous, moved considerably
Coma 5	7-3	18	+	Diac. ++, NH ₃ N 1.2
Coma 1	9-12	28	+++	B 40 to 50, NH ₃ N 4.6 to 5.2, Boils
Coma 15-3	7-9.5	26	++	B. 18 to 22, NH ₃ N 3.6 to 4
Pneu. 11		6	0	Diac. 0. After light breakfast
Alive	36-37	27	+++	B 71 to 75, blood CO ₂ 19.6 to 20 After large breakfast
Alive	20	27	+++	B 58, blood CO ₂ 35, second fast day
Coma 4	11-15	31	++	B 3 to 14, NH ₃ N 3.4 to 4.7
Coma Tb. 2	14-20	42	+	Diac. ++, NH ₃ N 2.4, B 0.1 to 1.3

The profound effect of confinement and undernourishment on heat production has never received the attention it deserves. The reduction of metabolism in fasting has been shown in several experiments, the best being the recent work of Benedict,²⁰ whose subject L. fasted thirty-one days. On the first day of the fast he produced 40.3 calories per square meter per hour as measured while awake in the morning and as calculated by the height-weight chart. This figure is 1.5 per cent. above the normal average for similar conditions. On the tenth day of the fast the metabolism calculated in the same way was 16 per cent. below the average, and it remained between 18 and 22 per cent. below during the rest of the fast. A similar or even greater lowering of metabolism results from prolonged undernutrition. The figures of Svenson and others³⁸ for emaciated typhoid convalescents when compared with the normal standard indicate a metabolism considerably below normal in some instances. By similar calculation, the results of Magnus-Levy³⁹ with a neurasthenic youth who partially starved himself for a long period, are as follows:

TABLE 10.—METABOLISM EXPERIMENT ON MAGNUS-LEVY'S PATIENT *

Period	Date	Condition	Calories per Sq. M. per Hour Height-Weight Formula	Weight, Kg.	Relationship of Metabolism to Average Normal 39.7
I	Nov. 16 to 21.....	Very low diet.....	26.6	36.2	—33%
II	Nov. 23 to Dec. 9.....	Liberal diet.....	33.0	38.0	—17%
III	Jan. 26 to March 6.....	Fever from Tb.	43.4	48.4	+ 9%
IV	March 13 to May 8.....	Normal again.....	40.5	52.2	+ 2%

* Age 19, height 160 cm.

These figures are comparable to those shown in the present series of diabetic patients after treatment. The degree of elevation of metabolism due to the active diabetic process should be judged by comparison of such patients with equally emaciated and cachectic nondiabetics. It is also now possible to compare the same patient at times when active diabetes is present or absent, while the body weight and surface remain the same. Thus Gerald S., with intense diabetes, on November 9 had a basal metabolism 8 per cent. below normal. His fast ended November 18, and from then until December 7 he received a diet such that his

38. Recalculated in terms of surface area according to Meeh's formula, by Coleman and Du Bois, *The Influence of the High Calory Diet on the Respiratory Exchanges in Typhoid Fever*, THE ARCHIVES INT. MED., 1914, xiv, 168 (Fig. 4).

39. Magnus-Levy, A.: *Der Einfluss von Krankheiten auf den Energiehaushalt in Ruhezustand*, Ztschr. f. klin. Med., 1906, ix, 177.

weight on the latter date was practically identical with that on November 9; but the basal metabolism on December 7 was 22 per cent. below normal at a time when the urine was free from sugar. William G. weighed 43.2 kg. on December 11. In consequence of feeding high-caloric diet, the weight fell to 42 kg. by December 22, while the metabolism rose from 26 per cent. below normal on December 11 to 11 per cent. below normal on December 22. If we study Table 9 it is apparent that most of the diabetics with marked emaciation have a diminution in metabolism. In the children with diabetes and low metabolism the percentage loss from the greatest weight is small, but with a child that is growing taller even a stationary weight indicates emaciation. If "normal" adults and children were as emaciated as the diabetics, they would undoubtedly show a marked diminution in heat production.

Benedict and Joslin have ascribed an increase in diabetes to acidosis. This is usually associated with an increased protein metabolism, and it is often difficult to separate the two factors. It has long been known that increased protein metabolism causes an increased heat production. If we turn to Table 9 we can compare the increased metabolism with the degree of acidosis. There were nine patients whose metabolism was 11 to 23 per cent. above the normal. Of these two showed marked acidosis, namely, Cyril K. and the nervous patient G. Three others, Herr Mo., Frau Schm. and U., had severe acidosis. Patient H. had moderate acidosis, while the others, I. and V., had little or no acidosis, and the patient Frau St., with the highest metabolism of all, had very slight acidosis. In contrast to this, eight patients with severe or very severe acidosis showed a normal or decreased metabolism. These are B., C., N., P., Q., T., Cyril K. (December 18), and Gerald S.

Authors have erroneously attempted a direct comparison between dogs depancreatized or phlorhizinized at the height of their strength, and human patients who reach the stage of severe diabetes, generally after months of a slow cachexia. Accurate comparison demands equally acute human diabetes, or else the use of dogs with chronic diabetes or prolonged cachexia. The excessive nitrogen excretion of William G. and especially of Cyril K. (Geyelin and DuBois) is well comparable to that of the totally depancreatized dog, and in the latter the total metabolism was actually above normal in spite of four weeks of rapid wasting followed by five days of complete fasting. The alleged difference as respects increase of metabolism can therefore no longer stand as a distinction between clinical and experimental diabetes.

Theoretically it is to be expected that the metabolism will rise with the increase of the protein metabolism which accompanies the noncombustion of sugar derived from protein in the diabetic condition. Since the specific dynamic action is less in human beings than in dogs, it may

well be that the stimulus of an increased protein metabolism is relatively less pronounced in human than in experimental canine diabetes.

Recapitulating, one may state that the linear formula furnishes a more accurate standard of comparison than was previously available. According to calculation by this formula, an increase above the true normal metabolism is not demonstrable in the majority of patients with severe diabetes. Nevertheless, the diabetic process may be associated with a relative elevation of metabolism. In occasional instances the metabolism may actually exceed the average normal level of metabolism. In all cases the true increase appears only when one takes into consideration other factors incidentally present, some of them tending strongly to depress metabolism. For example, the percentage of increase may be fully as great as claimed by Benedict and Joslin, if the metabolism of diabetics is compared with that of other equally undernourished subjects, or if the same patient is compared at different times when active diabetes is present or absent. In practical application, the results indicate that diabetics generally have no higher food requirement than normal, and on account of undernutrition and lessened muscular activity will tend to maintain equilibrium on a smaller number of utilizable calories than normal persons. Because the diabetic is less active, as pointed out by Magnus-Levy, his actual consumption of energy as compared with normal controls is likely to be less. After treatment by fasting, even though the patient is gaining steadily in strength and well-being, a low level of metabolism has been observed, the lowest 36 per cent. below normal, and this indicates that a low diet will suffice for maintenance under these conditions.

SUMMARY AND CONCLUSIONS

1. Three patients with severe diabetes and three with moderate or mild diabetes have been studied in the respiration calorimeter. The effects of the oatmeal treatment and the fasting treatment have been followed in detail.

2. No special influence of oatmeal in diabetes or special readiness of oxidation of this form of carbohydrate was demonstrable in these experiments. The respiratory exchange fails to account for all the carbohydrate that disappears. The behavior of the respiratory quotient showed no important difference on the first day and on the third day of the oatmeal treatment.

3. The occurrence of "total" diabetes in human patients, with dextrose-nitrogen ratios approximating 3.65 to 1 and corresponding respiratory quotients, is here shown. Notwithstanding the extreme severity, neither the sugar excretion nor the gaseous exchange gives ground for assuming the formation of sugar from fat in any instance.

4. Even in the severest type of diabetes the active symptoms may

be eliminated completely by prolonged fasting. The observations in the respiration calorimeter prove that patients as a result of the fasting acquire the power of oxidizing sugar derived first from their own body protein and later from the protein and carbohydrate of a carefully regulated diet.

5. The respiratory quotients during fasting and after the glycosuria had ceased were in some such instances higher than can be easily explained by the oxidation of the materials supposedly available. Also the ingestion of alcohol was sometimes followed by respiratory quotients higher than would theoretically be expected. The data will be analyzed in a subsequent paper.

6. The specific dynamic action of food, especially fat, was apparently normal in a patient with moderately severe diabetes.

7. The results of two respiration experiments in a severely diabetic patient have shown that mild exercise slightly raises the quotient, and this suggests the possibility that exercise may improve carbohydrate utilization. Generalizations or positive conclusions from these experiments are not attempted.

8. According to comparisons of the surface area as calculated by the linear formula, increase of the basal metabolism above the true normal level in severe diabetes is generally absent or slight. The metabolism was shown to fall markedly during fasting, to 20 per cent. below normal. The level of metabolism in diabetes is the resultant of a number of forces; for example, increased destruction of protein and perhaps other processes tending to increase metabolism, and undernutrition, muscular relaxation (as in prolonged confinement in bed) and other possible conditions tending to diminish metabolism. According as one or the other of these groups of forces predominate, a higher or lower metabolism may be expected in any individual case of diabetes.