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OBJECTS AND METHOD OF DIET ADJUSTMENT IN DIABETES *

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In the dietetic management of diabetes we are engaged in the effort to correlate symptoms and signs shown by the patient with the kinds and quantities of food he consumes. The success of treatment, the average of results in all types of cases, depends on the truth of our concept of the relationship existing between symptoms or signs and the food supply. During the last few years the average of results obtained in the dietetic management of diabetes has been improved greatly through the work of Allen and Joslin, and the system they have developed is in some respects more logical and less empirical than any we have had heretofore. Yet the literature of the subject is still confused by a lack of unanimity among all writers as to the best manner of handling all cases. In a recent monograph, Falta [1] has again told the merits of his "cereal cure" (Mehlfrüchtekur), and endorsed methods of management that differ materially from that which has found so much favor in this country. Newburgh and Marsh,[2] failing to achieve practical results by their application of the principles of "total dietary restriction" and "undernutrition," resort to low protein high fat diets with striking success in the management of seventy-four cases. In the past, good results were obtained and may still be obtained in some cases by old fashioned "rigid" diets. The remarkable improvements that have sometimes been seen with the institution of a Donkin "milk cure," a von Duering "rice cure," a Mossé "potato cure," a von Noorden "oatmeal cure" or any one of several analogous procedures cannot be denied and have never been explained fully to the extent that one may predict with certainty just when one of these empirical procedures will and when it will not produce a result better than that attainable by a more systematic method. The present study was made in the effort to correlate some of these varying views of different writers, and, if possible, to clear away some of the confusion that they tend to create in the mind of the physician as to what method of procedure he may best follow in any specific situation.

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1. Falta: Die Mehlfrüchterkur bei Diabetes Mellitus, Berlin, 1920.
2. Newburgh and Marsh: Arch. Int. Med. **25**:647 (May) 1920.

Discrepancies in the clinical literature of diabetes arise from three main sources: (1) Confusion in the minds of writers as to the exact nature of the anomaly of the metabolism which characterizes diabetes. (2) A general tendency among clinicians to think of the food supply of the body too exclusively in terms of diet, to the neglect of endogenous factors, and (3) the almost universal custom of thinking of the food supply simply as so much carbohydrate, so much protein, so much fat and so many calories without further analysis.

It will be necessary to develop each of these points separately.

NATURE OF THE DIABETIC ANOMALY AND PRINCIPLES OF TREATMENT

(*a*) One single specific defect characterizes diabetes. This consists *in an inability on the part of the body to utilize as much glucose as may be utilized by the normal body when the supply of glucose exceeds certain limits.* The diabetic appears to be capable of utilizing a limited quantity of glucose as well as the normal individual, but fails to utilize a normal percentage of any glucose introduced into the body in excess of this limit. This limitation of the body's power to utilize glucose is present in every case of diabetes. In its absence we can not say that diabetes exists. In its presence alone, without any other accompaniment, one must say that diabetes does exist.

(*b*) The endocrine function of the pancreas, so far as we know it at all, is a single highly selective function having to do with the utilization of glucose and nothing else. All that we know of this function is deduced from our knowledge of the changes which occur in the diabetic metabolism and from the established relation between diabetes and the pancreas. Were it not for the occurrence of the metabolic phenomenon which is called diabetes, we would have no more reason to speak of a special endocrine function of the pancreas than we now have for speaking of such a function in the case of any of the organs which are not considered as endocrine organs in the usual sense of the word. No second metabolic disturbance besides diabetes has been found to occur with consistency after reduction of pancreatic substance. It is accordingly necessary to conclude that the work of the pancreas as an endocrine organ, so far as we know it today, has to do solely with the disposition of glucose, and that to lessen this work, one must lessen the quantity of glucose entering the metabolism. The pancreas is a glandular organ innervated from the celiac plexus. Vagus and sympathetic fibers pass into its substance. It is a nerve gland apparatus. Presumably it performs its function by secreting a substance having the power to dissociate the one specific sugar glucose into which all other carbohydrates that are capable of utilization on the large scale must first be converted before they can be oxidized, reduced or built up into glycogen. That such an apparatus should be stimulated by glucose to

provide for the disposition of glucose is a thought in keeping with many facts. That a weakened pancreas in the presence of a sufficient supply of glucose might be stimulated into a state of fatigue and decreased function, and that a sufficient diminution of the glucose supply might then lessen the stimulation, place the organ in a state of comparative rest, and permit it to recuperate up to a certain limit, is also quite conceivable and affords a logical explanation of many observed facts.

(*c*) The anomaly of the metabolism in which abnormal quantities of acetone, acetoacetic, and β hydroxybutyric acids appear in the tissues, blood and urine is not due directly to any impairment of the endocrine function of the pancreas. It is a secondary effect in the nature of a disturbed metabolic balance resulting from the withdrawal of oxidizing glucose, as, when one stone is withdrawn from an arch all the other members may settle to a new position. This anomaly is not peculiar to diabetes nor constantly associated with it. It occurs in other diseases. It may be made to appear in a normal subject by starvation, or a diet containing too low a proportion of carbohydrate and too high a proportion of fat, and when this is done it may be made to disappear again simply by the addition of more carbohydrate to the diet. It appears to be *the immediate result of the oxidation of certain fatty acids in the absence of a sufficient proportion of "oxidizing" (dissociated) glucose.*

There is for any given individual at any given time, *a definite ratio between the quantity of glucose oxidizing in the body and the maximum quantity of ketogenic fatty acids that can be oxidized in the same time without the appearance of abnormal amounts of the acetone bodies.* In other words, *the quantity of oxidizing glucose fixes an upper limit to the quantity of ketogenic fatty acid that can be completely oxidized at the same time.* As to the absolute magnitude of this ratio, and the degrees of its variation in different individuals in health and disease, it is too early to make a final statement. Some years ago, on the basis of chemical studies by Ciamician and Silber, and test tube experiments with acetoacetic acid, I suggested a certain type of reaction as the basis of "antiketogenesis" in which one molecule of acetoacetic acid would react with one molecule of an alcohol or glucose.[3] Zeller, working with normal individuals on ample diets consisting of carbohydrate and fat with very low protein contents, shifted the proportions of fat and carbohydrate without changing the total calories and saw acetone appear when the ratio of carbohydrate calories fell below 10 per cent. of the total, that is, when the ratio of *fat* to *carbohydrate in the diet* in grams was about 4 to 1. Recalculating Zeller's experiments, Lusk estimated the relative quantities of sugar and higher fatty acid

3. Woodyatt, R. T.: J. A. M. A. **55**:2109 (Dec. 19) 1910.

that might have been oxidizing together in the body. Allowing for the formation of sugar from the glycerol of the fat, and of glucose from the protein catabolized, and for some glucose from glycogen, but not for ketogenic amino-acids from protein, Lusk suggested that possibly one triose molecule was necessary for the complete oxidation of one of higher fatty acid, that is, one molecule of glucose to two molecules of higher fatty acid, or 3 gm. to 1 gm. P. A. Shaffer [4] has worked with test tube experiments and with diabetic individuals in which he conducted metabolism studies, including observations on the respiratory quotient at the time acetone first appeared. Shaffer calculated the ketogenic acids of protein on the basis of the quantities of leucin, tyrosin and phenyl alanin found by analysis in 100 gm. of ox muscle protein by Osborne, assuming that each molecule of these known acetone formers may yield one molecule of acteoacetic acid, or its equivalent. As a result of his work, Shaffer suggests that one molecule of glucose is necessary for the complete oxidation of one molecule of acetoacetic acid, or one molecule of any higher fatty or amino-acid that yields one molecule of acetoacetic acid (or equivalent). The molecular weight of glucose being 180, of oleic acid 284, of palmitic acid 256, and the average of the two acids 270, the ratio found by Shaffer, if expressed in grams would be about 1.5 gm. higher fatty acid to 1 gm. glucose. Working with diabetic patients on maintenance diets under conditions that made it probable that the proportion of food stuffs in the diets corresponded fairly with those actually catabolized in the body, and estimating the glucose and fatty acid as hereinafter indicated, we have also observed at the time acetone appeared, ratios of 1.5 or a little above or below this figure with considerable frequency in harmony with the work of Shaffer. Accordingly, even though it may prove necessary to correct this figure as data accumulate, and for individual cases, it would seem that for clinical purposes one will make no gross error if it is assumed that the ratio of higher fatty acids to glucose, which if exceeded will lead to acidosis, is likely to be close to 1.5 to 1. (in gm.). This refers to the materials actually catabolized and to the diet only under the stated conditions.

TREATMENT

It follows from the foregoing that the rationale of dietetic management in diabetes is *to bring the quantity of glucose entering the metabolism from all sources below the quantity that can be utilized without abnormal waste; and to adjust the supply of fatty acids in relationship to the quantity of glucose* so that in the mixture of food stuffs oxidizing in the body, the ratio of the ketogenic fatty acids to

4. Shaffer, P. A.: Proc. Am. Soc. Biol. Chem. Fifteenth Annual Meeting, December, 1920, p. 6; J. Biol. Chem. **46**:98 (March) 1921.

glucose shall not exceed limits compatible with freedom from ketonuria. When, as, and if, under these conditions of relative rest for the pancreas, the glucose using function improves, then the food supply may be increased gradually in so far as this can be done without disturbing the above relations.

ENDOGENOUS FACTORS OF FOOD SUPPLY, ILLOGICAL DIET RESTRICTIONS

When a man fasts he does not, of course, cease to produce heat. Normal men during a fast on light exertion have been observed to produce from 29 to 30 calories per kg. of body weight daily. For a 50 kg. man this would mean 1,500 calories per day. During the first four days of a fast, Cetti produced on the average 29 calories per kg. for a total of 1,618 calories per day, and catabolized 85.88 gm. protein for 329.8 calories and *136.72 gm. fat for the remaining 1,288 calories.*[5] In a case studied by F. G. Benedict,[6] on the second day of fasting there were produced 1,768 calories, or 29.9 calories per kg., and the individual was estimated to have catabolized 74.7 gm. protein, *147.5 gm. fat* and 23.1 gm. glycogen. These figures are by no means the highest that might be selected. Thus, a well nourished normal man weighing 50 kg., who during a fast produces 1,500 calories per day, may actually catabolize in the neighborhood of 75 gm. protein, 125 gm. fat and a little carbohydrate from glycogen. These well known facts are repeated simply to emphasize the magnitude of the food supply from the tissues in fasting, and to point out, in particular, that in fasting over 100 gm. fat may be thrown into the metabolic stream and catabolized daily. It has further been shown that the amount of fat in the fasting organism materially affects the amount of protein burned. In a critical review of the literature of the subject, Lusk has said: "Where there was much fat present, little protein was consumed; when there was little fat, much protein burned; and when there was no fat, protein alone yielded the energy for life." In a normal individual, the ingestion of fat will not prevent the death of the organism because there is a continual loss of tissue protein from the body which finally weakens some vital organ to such an extent that death takes place. *But the ingestion of fat may spare tissue fat and thus prevent the protein loss from becoming abnormally great.* It may be said that the ingestion of fat spares the individual any such protein loss as will occur if the tissue fat is allowed to become too much depleted. In this sense, the ingestion of fat by an emaciated individual spares protein for that individual. Voit found in a fasting animal that the ingestion of suitable amounts of fat scarcely influenced the protein metabolism. To one dog "which in starvation

5. Citation from Lusk, Elements of the Science of Nutrition, Ed. 3, 1917, pp. 86-89.

6. Benedict, F. G.: The Influence of Inanition on Metabolism, 1907, p. 194, Table 128.

burned 96 gm. fat, Voit gave 100 gm. fat with the result that it burned 97 gm." The fat ingested simply burned instead of the body fat, but the total amount of protein and fat burned remained the same" (Lusk).

Now, if a certain diabetic patient during a fast reacts essentially as a nondiabetic individual in the same state of nutrition; and if he weighs 50 kg., produces from 1,250 to 1,500 calories, and in doing so actually mobilizes and burns 100 to 120 gm., or more, fat, the ingestion of an equal quantity of fat should leave his metabolism in the same state as before. The supply of fat would come at one time from the tissues, at another from the diet, but the quantity thrown into metabolism—the quantity presenting itself for disposition in the cells would be the same in both cases. *If these premises are sound, why then should we ever use complete fasting for diabetes?* Granting that a diabetic patient may suffer from obesity as well as diabetes—that he may have two different metabolic defects; or granting that at times it might seem desirable to starve for other conditions besides diabetes. In such cases fasting would be rational, if it would improve the general condition. But for diabetes itself, and particularly for diabetes associated with undernutrition, why for the purpose of desugarization should the patient be compelled to draw from his tissues the fat that he might draw from a diet, especially if in drawing from his tissues he lowers his fat reserves to the extent that he increases his protein losses? The striking results that have been obtained by Newburgh and Marsh with fat replacement diets bear significantly on this point. The practice of starving, or virtually starving, a patient in order to render his urine sugar "free," and then building up the diet, first with carbohydrate and then with protein, with a particular avoidance of fat, would appear to be based on the supposition that if fat were administered it would increase the catabolism of fat. But this would be in disregard of the endogenous food supply, and illustrates the necessity of thinking in terms of the metabolism rather than of the diet. As the diet falls, the endogenous supply rises to take its place, and vice versa. The lower the diet, the less its significance in calculating the food supply from all sources. It is possible to maintain the normal body with a diet that contains only 10 per cent. more calories than are produced in fasting, and the differences in the catabolism of a man when receiving no diet and when receiving a 1,500 calorie diet may be slight.

(3). DEALING WITH THE FOOD SUPPLY IN TERMS OF CARBOHYDRATE PROTEIN AND FAT

Carbohydrate, protein and fat are as such three separate and distinct substances, no one of which can be expressed quantitatively in terms of another, and if we speak of food supplies or diets as made up of so

much carbohydrate, so much protein and so much fat, we simply name them in terms of three variables. Thus each particular combination or diet becomes a specific, and having learned by experience how one of them will affect a certain patient, we have no means of knowing exactly how a second dissimilar combination will affect the same patient, much less another, except by trial and experience. The number of possible combinations of three variables is infinite and the number of practical food combinations, no two of which will differ by less than 5 gm. of one ingredient or by less than 50 calories runs into the thousands. Accordingly, if we attempt to correlate symptoms and signs shown by the patient with the diet and follow the usual system of thinking of diets simply in terms of carbohydrate protein and fat, without attempting to resolve them into simpler terms, it will be necessary to establish by experiment the effects of each diet combination in every type of case. It would seem tedious and hopeless to proceed by this inductive method. A further objection to this method, and a clear advantage in using another, lies in the fact that protein, carbohydrate and fat as such are not in reality the substances that present themselves for the final oxidative attack in the body which results in the liberation of energy. These substances are resolved by the processes of digestion and intermediary metabolism into simpler substances before they can be burned in the tissues. It is not starch in the bowel nor glycogen in the liver and muscles that taxes the endocrine function of the pancreas, but the glucose into which these carbohydrates are resolved. Protein of the diet ceases to be protein and becomes a mixture of amino-acids before it can be absorbed from the bowel and these undergo deaminations, etc., prior to actual oxidation. Neutral fats, to be sure, may be absorbed in part as such, and may be deposited in the tissues as such, but before they can be oxidized and used as sources of energy, they must first be saponified into glycerol and higher fatty acids. Thus, as a matter of fact, carbohydrate protein and fat are not the actual food stuffs with which we are dealing when it comes to the final metabolic processes. In the management of the diabetic food supply, it is simpler and more rational to think in terms of the chemical metabolism. Falta devised a formula in which he added the carbohydrate of the diet to the urinary nitrogen times 2.8, or (following Lusk's suggestion) 3.65 to show the total quantity of glucose entering the body from carbohydrate and protein. Then, subtracting from this the quantity of glucose excreted in the urine, he obtained a figure for the quantity of glucose actually utilized. The quantity excreted, divided by the total quantity, supplied gives a fraction which multiplied by 100 was Falta's diabetic quotient. The latter has a limited value. The absolute quantity utilized is of more interest. The principle is important and can be developed further.

WHAT FOODS BECOME IN THE BODY

Of the carbohydrates of the diet and tissues that play a significant rôle in heat production, all that do not already exist in the form of glucose are converted into this form by the processes of digestion or intermediate metabolism or both prior to ultimate utilization. We may, therefore, say that 100 gm. utilizable carbohydrate in the diet, if all is digested and absorbed, introduce into the metabolism about 100 gm. glucose.[7]

Fats of the diet in the course of digestion and intermediate metabolism must be saponified into glycerol and higher fatty acid before they can be oxidized. Fats such as tristearin, or an oil such as triolein, when completely saponified, yield approximately ten parts by weight of glycerol to ninety parts by weight of higher fatty acid. Glycerol is capable of conversion into glucose in the body almost gram for gram. So we may say, for clinical purposes, that 100 gm. mixed fat in the diet, if completely absorbed and catabolized, will introduce into the metabolism about 10 gm. glucose and 90 gm. higher fatty acid.[8]

Protein of the diet, or tissues, is resolved into amino-acids, and in so far as these are absorbed and catabolized, they must be deaminized (and presumably at the same time oxidized) to yield oxy- or hydroxy acids. Of these, a part is convertible into glucose, another part into β hydroxybutyric and acetoacetic acids, while a third small fraction is destroyed in as yet unknown ways. According to the experiments of Lusk on phlorhizinized dogs, which have been repeated by others, and according to numerous observations in cases of maximal human diabetes, one may say that 100 gm. mixed food protein are capable of introducing into the metabolism approximately 58 gm. glucose. The same 100 gm. of protein also introduce a certain quantity of products which are quite the equivalent of products of the higher fatty acid catabolism in that they are capable of yielding β hydroxy and acetoacetic acids. The exact quantity of these substances formed in the catabolism of 100 gm. protein can be estimated only roughly. The amino-acids that are certainly known to yield acetone bodies are leucin, tyrosin and phenyl alanin. If we take the quantities of these amino-

7. In tables of food analyses all that is listed as carbohydrate is not necessarily utilizable carbohydrate.

8. If objection is made to the view that neutral fats may yield 10 per cent. of their weight in glucose on the grounds that ingested neutral fats have not been observed to cause the appearance of "extra" sugar in the urine of phlorhizinized dogs, it may be suggested that the ingestion of fat by a starving phlorhizinized dog would scarcely be expected to increase the fat catabolism for reasons already given unless special precaution had been taken to discharge tissue fat, etc. It is not improbable that the tissue fat that a fasting phlorhizinized dog catabolizes does produce glucose and that the glucose is then credited to protein.

acids found in 100 gm. ox muscle protein by Osborne and Mendel,[9] as Shaffer has also done, and convert the weights given into gram molecules, we obtain 0.16 gm. molecules of these ketogenic amino-acids. If we assume that each of these is capable of yielding one molecule of acetoacetic, or β hydroxybutyric acid, and accept the view that one molecule of a higher fatty acid such as oleic or palmitic acid also yields one molecule of aceto-acetic (or β hydroxybutyric acid, then the 0.16 gm. molecule of ketogenic amino-acids would be equivalent in respect of its ability to form aceto-acetic acid to 0.16 gm. molecule of higher fatty acid. If the acid were oleic (molecular weight 284), this would mean 45.44 gm. The nature of this estimation is such that considerable error is scarcely avoidable, but it affords a tentative figure that serves a practical purpose, even though it may require correction in the light of experience.

It will thus be seen that all of the foods of the diet, except a small fraction of the protein, resolve themselves in the body into two things; glucose, on the one hand, and higher fatty acid (or acetone forming equivalents) on the other. If we let G stand for the quantity of glucose, and F A for the quantity of higher fatty acids that may be introduced into the metabolism by a mixture of carbohydrate, protein and fat, then

100 gm. carbohydrate yields in the body	100 gm. G and 0 gm. FA
100 gm. protein yields in the body.....	58 gm. G and 46 gm. (?) FA
100 gm. fat yields in the body.....	10 gm. G and 90 gm. FA

These relationships may be expressed in the form of simple equations in which G is the total quantity of glucose introduced into the body by a given food combination; F A the total quantity of higher fatty acids (plus ketogenic amino-acids expressed in terms of higher fatty acid) C, carbohydrate; P, protein; and F, fat (neutral); thus

$$(1)\quad G = C + 0.58\ P + 0.1\ F$$
$$(2)\quad F\ A = 0.46\ P + 0.9\ F$$

If the ratio of F A: G which if exceeded leads to acetonuria is 1.5: 1, then when $\frac{F\ A}{G} = 1.5$ we derive from (1) and (2) the equation $F = 2C + .54\ P$, which for clinical purposes may be stated simply as

$$(3)\quad F = 2C + \frac{P}{2}.$$

DISCUSSION OF HYPOTHETICAL DIETS

Let us now consider four hypothetical diets: I, II, III and IV, and analyze them from the viewpoint of their possible effects on a certain diabetic patient weighing 50 kg. Let it be assumed that each diet is

9. Osborne and Mendel: J. Biol. Chem. **17**:366, 1914.

completely digested, absorbed and catabolized, and that each is sufficient to cover the maintenance requirements of the body, so that we may in discussing them waive endogenous factors. Were these diets not sufficient to maintain the body, foodstuffs derived from the tissues would add themselves to the combination actually being utilized in the body and these would have to be known and allowed for. Also if some of the fat were deposited in the tissues this would have to be allowed for.

Looking at these diets simply as so many different combinations of carbohydrate, protein and fat, and going no further, they appear to be quite dissimilar. Who could certainly judge their relative effects on a patient? Diet I is a fair example of the old fashioned "rigid" diet, with almost no carbohydrate and the protein at 3 gm. per kg. of body weight. Diet II is a high carbohydrate, low protein diet. It is the kind of a combination that might possibly be given in a von Duering "rice cure," or a "cereal cure." This diet would permit the patient to enjoy 350 gm.—almost a pint—of boiled rice or other cereal; or, he

TABLE 1.—ELEMENTAL ANALYSIS OF FOUR HYPOTHETICAL DIETS

	I.	II.	III.	IV.
Carbohydrate	10	77	60	51
Protein	150	30	85	70
Fat	84	108	91	125

could have 134 gm. white bread and butter—three slices—with each of his regular meals. Diet III appears to be intermediate between Diets I and II in all respects. It contains less carbohydrate than Diet I, but more than Diet II; and the fat is less than in Diet II and more than in Diet I. It contains nothing that is not contained in higher quantities by one of the other diets. Diet IV resembles Diet II, but might be suspected of having a higher caloric value because of its fat. We make a rapid estimation of calories and note that Diets I, II and III each represent 1,400, while Diet IV shows about 1,609 calories. On the basis of calories alone, if any of the diets is not to be tolerated, Diet IV would be the one to suspect. Now, if in each diet we add up the grams of carbohydrate plus 0.58 of the grams of protein, plus 0.1 of the grams of fat, we find that Diets I and II are alike in that each is capable of introducing 105 gm. glucose into the metabolism. They are not only isocaloric, but will yield the same quantities of glucose. If we assume that the patient is capable of utilizing from 105 to 110 gm. glucose per day, he might very well tolerate either of these diets. Of the two, he would be less likely to tolerate Diet I. Coming to Diet III, and estimating the glucose equivalent G, we found it to be

118. This harmless looking isocaloric diet will surely cause glycosuria in the patient who is capable of utilizing only from 105 to 110 gm. Diet IV, with 300 more calories than any of the other three, has the same glucose equivalent as Diets I and II and will probably be borne as well as either. The question arises in respect of Diet IV as to whether the high fat is permissible or in any sense objectionable. We estimate the higher fatty acid value of this diet F A by means of formula 2. Taking 0.46 the protein + 0.9 the fat, we find 32 + 113 or 145 for F A. As stated, G is 104. Then the ratio $\frac{F\ A}{G} = 1.4$. *As a general rule, we have found that acetone does not appear in the urine of an uncomplicated case of diabetes, or remain permanently if present when the ratio does not exceed this, provided, that* the diet is completely absorbed, and catabolized and sufficient for maintenance, so that endogenous factors of food supply do not complicate the calculation. Accordingly, we say that the quantity and proportion of fat in Diet IV are probably not too high for complete utilization in the normal manner and that there is probably nothing objectionable about it.

This leads us to the problem of calculating the theoretical optimal diet.

ESTIMATION OF OPTIMAL DIETS

If C = carbohydrate, P = protein, F = fat, G = glucose and F A = higher fatty acids (plus ketogenic amino-acids expressed in terms of higher fatty acid), we may say—as shown above—that the quantity of glucose which any given combination of foods may introduce into the metabolism is expressed by the equation: (1) $G = C + 0.58 + 0.1\ F$ and that the quantity of higher fatty acids (and equivalents) may be expressed as (2) $F\ A = 0.46\ P + 0.9\ F$. When the ratio $\frac{F\ A}{G}$ exceeds a certain value, ketonuria develops. Assuming that this ratio is 1.5, then $\frac{C + 0.58\ P + 0.1\ F}{0.46\ P + 0.9\ F} = 1.5$, when the ratio of fatty acids to glucose is as high as it may be without ketonuria. Simplifying this we obtain $F = 2\ C + 0.54\ P$, or, simply, (3) $F = 2\ C + \frac{P}{2}$. If it is agreed that the ratio F A : G shall not exceed 1.5 and that the relationships expressed in equations 1 and 2 are as given, then to estimate the optimal food combination or diet one may use equations 1 and 3. Given the quantity of glucose that the patient can utilize completely, assign this value to G in equation 1. Thus, if 100 gm. is the highest quantity of glucose derived from all sources that the patient can utilize, 100 gm. = C + 0.58 P + 0.1 F. In order to secure the maximal number of calories, the diet must clearly contain every possible gram of fat (at 9 calories per gram) that

the value of G and the relations expressed in 1 and 3 will permit, and consequently the lowest possible carbohydrate protein fraction (at 4 calories per gram). Also, as between carbohydrate and protein, the protein must be as low as possible and the carbohydrate as high as possible for 1 gm. carbohydrate yielding 1 gm. glucose and 4 calories provides for the normal oxidation of 1.5 gm. of higher fatty acid. On the other hand, 1 gm. protein having the same caloric value as carbohydrate yields less glucose to support fat combustion and besides this yields acetone itself. If the body weight of the patient be 50 kg. and 1 gm. protein per kg. is selected as a conservative minimum; then P becomes 50 gm. and $F = 2\ C + \frac{P}{2}$ becomes $F = 2\ C + 25$. We have already made G = 100 gm. Now, the glucose yielded by the 50 gm. protein will be 0.58×50, or 29 gm., leaving 100 — 29, or 71 gm., to be distributed between carbohydrate and fat. In other words, $C + 0.1\ F = 71$. From this we obtain $F = 710 - 10\ C$.

TABLE 2.—Showing Optimal Food Combinations When G = 100 Gm. (in the Equation G = C + .58 + .1 F); When FA: G = 1.5; and When the Protein Is 0, 25, 50, 75 and 100 Gm. (i.e. 0; 1.0; 1.5; and 2.0 Gm. Per Kg. for a Body Weight of 50 Kg.)

	P.	C.	F.	Calories	Difference in Calories
(1)	*0.000	83.333	166.666	1833.327	76.25 (2)-(1)
(2)	25.000	70.208	152.916	1757.076	76.26 (3)-(2)
(3)	50.000	57.083	139.166	1680.826	76.25 (4)-(3)
(4)	75.000	43.958	125.416	1604.576	76.25 (5)-(4)
(5)	100.000	30.833	111.666	1528.331	

*No. 1 is hypothetical and could only be considered as the nonprotein fraction of a larger combination.

But we also have from the above, $F = 2\ C + 25$. So $2\ C + 25 = 710 - 10\ C$, solving which C = 57 gm. (57.08). Substituting this value for C in $F = 2\ C + 25$ we find F = 139 gm. (139.16). Then, the optimal food combination that will fulfill the conditions and relations specified is: carbohydrate, 57 gm.; protein, 50 gm.; fat, 139 gm. = calories, 1,680. Proving this diet, we find the total glucose equivalent $G = 57.08 + (0.58 \times 50) + (0.1 \times 139.1) = 99.99$ as called for. Also $F\ A = (0.46 \times 50) + (0.9 \times 139.1) = 150.24$ and $\frac{F\ A}{G} = 1.50$ as required.

It is apparent, that any addition of any foodstuff to this diet will make G greater than 100. If, on the other hand, one added more fat—say, 10 gm.—and subtracted 1 gm. carbohydrate, G would remain

100 and the calories would be increased by 86, but this would make $\frac{F\ A}{G}$ greater than 1.5. The effect of changing the protein can be seen by comparing the caloric value of a series of optimal food combinations with the protein rising from 0 to 2 gm. per kg.

For each gram of glucose that can be utilized in the body there are 18 calories in the optimal food combination.

For each gram of protein in the food supply, subtract 3 calories from the optimal number.

For mental calculation, if one knows that a patient can actually utilize a certain number of grams of glucose, take this number times seventeen as the approximate number of calories that he will be capable of using at best without glycosuria or acetonuria if the diet is most favorably balanced. Then, knowing the patient's weight the severity or mildness of the situation becomes apparent.

REPORT OF CASE

To illustrate practical aspects of the principles discussed, the following case will be found of interest.

A Greek, aged 26, was admitted to the hospital as an emergency case. He was very weak, languid and emaciated; body weight 45 kg. There was a flush on the face, and the respirations were slightly increased when quiet in bed. The plasma carbon dioxid was 23.9 volumes per cent. by Van Slyke. The breath smelled of acetone and the urine contained large quantities of sugar and acetone bodies. He had the symptoms and signs which are commonly taken to indicate a very severe case of diabetes.

First Stage: He was put to bed with artificial warmth and placed on a diet of 400 gm. of 5 per cent. vegetables with clear broth and plenty of water. But after four days, he still passed 32 gm. sugar in the urine with acetone and 2.3 gm. ammonia. His temperature on the fourth day ranged from 96.4 to 97.6 F.; the pulse from 56 to 60, and he was so weak that it was not deemed safe to continue the effort to desugarize at that time. This ended the first stage of management.

Second Stage: He was then given for five days a diet containing 114 gm. carbohydrate, 45 gm. protein, 15 gm. fat and 760 calories. G for this diet is 142 gm. During these five days he excreted on the average 85 gm. glucose per day, so that he was disposing of about 67 gm. glucose per day from the diet alone. His general condition improved and he was then desugarized by two days of complete fasting. Having remained sugar "free" for one day, he was then given 400 gm. vegetables of the group that contains not over 5 per cent. of carbohydrate plus 1 liter of clear broth. This diet contained 12 gm. carbohydrate, 14 gm. protein and 104 calories, and G is 20 gm. But he promptly showed sugar in the urine and was again desugarized by one day of fasting. The patient had just manifested his ability actually to utilize at least 67 gm. glucose, yet the mere feeding of a diet that could yield but 20 gm. of glucose in the body induced glycosuria.

Third Stage: The urine was now free of abnormal quantities of sugar and acetone, and the patient was given a liter of broth and 200 gm. of the fresh vegetables, which he bore without glycosuria. Then he received 400 gm. greens, then 1 egg, and so on until the diet contained 314 calories, when the urine again showed sugar. Again, his condition was such that it was unsafe to continue

these tactics in the effort to maintain him in the sugar "free" state. Three weeks had passed and three successive attempts had failed, although at no time had the diet been capable of introducing into the body as much glucose as the patient had actually utilized on the 760 calories diet of the second stage.

Fourth Stage: He was given a diet that contained 92 gm. carbohydrate, 103 gm. protein, 70 gm. fat and 1,416 calories. G for this diet is 159. He was on this diet for two weeks and excreted on the average 50 gm. glucose per day. Thus, he was actually utilizing about 109 gm. glucose per day. His condition was much improved and he was then desugarized by two days of fasting.

Fifth Stage: He was now in the sixth week of management, free of glycosuria and acetonuria after his third desugarization, and the attempt was again made to build up his diet gradually. But at 780 calories glycosuria recurred. A fourth desugarization by fasting was followed by another attempt, but glycosuria developed with a diet of 1,000 calories. He was desugarized a fifth time and again broke over at 1,000 calories. Nine weeks had elapsed. He was then established on a diet of 953 calories, with which he remained sugar "free." The diet now contained 50 gm. carbohydrate, 67 gm. protein and 56 gm. fat, with G = 88. The plasma carbon dioxid was 60 volumes per cent. There was no abnormal quantity of acetone in the urine and the urinary sugar as measured by the method of Benedict, Osterberg and Neuwirth showed 454, 515, 486, 425, 494, and 400 mg., respectively, per day on six successive days (tenth week).

At 22 calories per kg., even with a subnormal basal rate, this was barely a maintenance diet and it was apparent that unless something better could be done, the outlook for the patient was hopeless.

Much has been written about the harmful influence of too much protein in the diabetic diet. Naunyn, von Noorden, Falta and others have emphasized the necessity of keeping the protein of the diet within limits. A new interest had been given this subject by the recent report of Newburgh and Marsh. We decided to test this idea to its limit. So the patient was placed as nearly as might be in a state of specific protein hunger.

Sixth Stage: The diet was made up exclusively of rice and butter to contain 24 gm. carbohydrate, 2.5 gm. protein, 102 gm. fat, and 1,024 calories. The calories were, therefore, a little higher than he had yet been able to receive without glycosuria. He was placed on this diet and remained sugar free with excretions of 305, 400, 370, and 392 mg. respectively, on the four following days. There was no acetonuria. Now, the diet was rapidly increased; first by additions of rice alone; then by butter and rice together. In ten days it contained 84 gm carbohydrate, 11.5 gm. protein, 162 gm. fat and 1,837 calories. The urine at no time contained acetone and during these ten days had contained 308, 359, 384, 317, 545, 335, 439, 330, 486 and 333 mg. respectively, of sugar. But the patient was not in nitrogen equilibrium. The urinary nitrogen was extremely low yet it alone was exceeding that of the diet by about 1 gm. daily. So two eggs were added to the diet which made it contain carbohydrate 84 gm. protein 25 gm. (or 0.6 gm. per kg.), fat 174 gm. and calories 2,000. On this (if the stools were neglected), the patient came into nitrogen balance. Thus, after nine weeks of trial, the ordinary practice of under-nutrition had failed to establish the patient in the nondiabetic state with more than 953 calories, whereas after two weeks of the rice-butter diet the calories had more than doubled and the carbohydrate had been increased to 60 per cent. This seemed like a miracle. The 84 gm. carbohydrate when served in the form of boiled rice made a mass of about 400 gm. which was all that the patient would eat.

The contrast between the trays that now came to him and those that he had formerly had aroused many remarks in the ward. Surely, it might seem that there were merits in protein deprivation.

This is the type of result that astonished von Noorden when he first used his oatmeal cure. It is the type of result that has made the reputation of the von Duering rice "cure," the Mossé potato "cure," the Falta cereal "cures." However, if we examine this diet according to the equation and take the grams of carbohydrate plus 0.58 of the grams of protein, plus 0.1 of the gram of fat, we find that G is 116 gm., and it will be remembered that in the fifth stage the patient had shown his ability to utilize 109 gm. glucose although at that time he had not remained sugar "free." He was not doing much more. The question arose as to what would have happened had the high protein diet of the fifth stage had a value for G less than 116.

Seventh Stage: A diet was composed to contain 28 gm. carbohydrate, 118 gm. protein (2.7 gm per kg. instead of 0.6 gm.), and 160 gm. fat. Total calories, 2,024 (as against 2,000). G for this diet is 112. The patient was given this diet and remained sugar free and free of acetonuria. He remained on it for eight days when it was increased to find his tolerance limit. This was from 119 to 120 gm.

INTERPRETATION

Clearly, the merit of the rice-butter diet had not lain simply in its low content of protein. Four times as much protein had not been incompatible with a result just as good. In retrospect it is clear that the patient had shown from the second stage on the inherent ability to utilize a goodly amount of glucose. His actual tolerance was probably higher on the last day than it was on the seventh but as early as the fourth week he had burned almost as much glucose as he ever did later, so it can not be held that the final result was simply made possible by a rising tolerance. Notwithstanding his manifest ability to burn glucose, he had repeatedly shown glycosuria on very low diets that were incapable of introducing into his body as much glucose as he was able to burn, paradoxical as it may seem. This tends to encourage speculation. Shall we say that because of the general emaciation the starved kidneys had become abnormally permeable to sugar, that the "renal threshold for sugar" was lowered, introducing an element of "kidney diabetes"? Or, shall we evade the issue and say that in such cases the attempt should not be made to maintain the patient in the nondiabetic state; that such patients should be fed and allowed to run sugar until they are stronger, in spite of all that we know of the power of an excess of glucose to diminish tolerance. Shall we entertain the idea that a diabetic may burn more sugar if he is given an excess than he can if he is given just the quantity that he can utilize

without glycosuria? I should say no, these ideas are based on misconceptions of the food supply of the diabetic. *It was clear in this case, from the events that followed, that the patient could be given every gram of glucose that he was capable of burning under any circumstances and still be kept from showing glycosuria, provided his food supply were suitably adjusted.*

Earlier in the paper emphasis was laid on the necessity of conceiving the food supply of the diabetic patient as coming from the tissues as well as from the diet, especially when the diet falls below the maintenance requirements of the body. In the present case, we are dealing with such a situation. All of the low diets that aroused wonder because they induced glycosuria, even though incapable of introducing into the body as much glucose as the body could burn, were diets that failed to meet maintenance requirements. Consequently, when these diets were being used, the patient was drawing a greater or smaller part of his food supply from his tissues. It is not only necessary to consider the supply of food from the tissues, but to consider the kind and quantities of foods that will be supplied by the tissues of the particular case in hand. When a patient is thrown back on his own tissues for food, he can only draw on the materials that are there. As emphasized by the quotation from Lusk, when in fasting the body contains much fat, much fat burns and little protein; when there is little fat in the body, little fat burns and much protein; when there is no fat, protein alone burns. But whatever the composition of the body, something burns while life persists. This patient had very little fat in his body, and the quantity of glycogen was certainly negligible. Therefore, when this patient fasted, he must have produced much of his heat from protein. He weighed 43 kg. If in fasting he had produced only 15 calories per kg., this would have totaled 645 calories, an amount of energy contained in 161 gm. protein. If he catabolized this weight of protein, he would liberate 58 per cent. of this weight, or 93 gm. glucose. Then, had he at this time the ability to burn 109 gm. glucose, the addition of 20 gm. from the diet would probably cause glycosuria. Unfortunately, in this case the basal metabolic rate and the urinary nitrogen were not actually determined during the fasting periods. But the literature contains many references to the "azoturia" of emaciated diabetics, and there can be no doubt that in such a case as this fasting induces a marked protein loss. Thus, fasting, in the case of a sufficiently emaciated patient, is the equivalent of a pure protein ration. In another case, with plenty of fat in the body, it is quite different as much tissue fat will burn and much less protein. It was pointed out earlier that the ingestion of

fat by a fasting individual who already has plenty of fat in his body has very little effect on the protein metabolism. If too much fat is ingested, it may increase acidosis and increase the protein loss but in the right quantities it simply replaces tissue fat. But, if the body fat is already depleted and if, as a result of this the protein breakdown has already become excessive, then the ingestion of fat will retard the prevailing protein breakdown and reduce it to a lower level. Thus in the emaciated individual, the ingestion of fat spares protein. In this diabetic patient, in this particular state, the feeding of enough fat should reduce the protein catabolism and thereby reduce the quantity of glucose thrown into circulation. When he was given the rice-butter diet he received at once 102 gm. fat for 918 calories, almost enough to replace his minimal fasting caloric requirements, and this put a rapid quietus on the excessive protein breakdown. The quantity of glucose from protein having thus been cut down, there was then opportunity to introduce more carbohydrate in the diet which further suppressed the protein breakdown. *The principal reason why this diet operated so well was because of its content of fat and because the body was so depleted in fat at the time when it was given. The patient was in a state of extreme fat starvation.* When in the sixth stage of management the patient did equally well on a low carbohydrate high protein diet this was because the combined carbohydrate and protein of that diet introduced into the body no more glucose than had formerly come from the combined carbohydrate and protein of the rice-butter-egg combination, and because this diet also contained enough fat to prevent endogenous factors of food supply from coming into action. Thus, it will be seen how the administration of a diet in excess of maintenance requirements may under certain conditions actually reduce the quantity of glucose in circulation in the body. Were the fat dropped out of these last two diets, more glucose would be thrown into metabolism by the increased breakdown of tissue protein induced by the lowering of the diet. This, I take it, is the explanation of a certain type of glycosuria which develops with prolonged undernutrition. I have seen a patient with diabetes similar to this one who could not be desugarized at all by fasting, but who cleared promptly when enough fat had been added to the diet with no other changes. This man, in fasting, catabolized so much protein that his protein sugar overtaxed this tolerance limit.