THE IMPORTANCE OF REGULATING THE FAT-INTAKE IN DIABETES MELLITUS.

BY

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THE dietetic treatment of diabetes mellitus has passed through three stages, progressing from a simple problem with one unknown quantity to its present position of a complex investigation involving the determination of at least two additional factors.

The first stage was initiated by the accidental discovery made by Rollo, in 1797, that glycosuria could be controlled by the exclusion of vegetable foods from the diet, but it was not until the relation between the digestion of carbohydrates and the formation of sugar was established by Gmelin and Tiedemann, in 1838, that the treatment of the condition by limiting the carbohydrate intake was placed on a rational basis. The discovery by Lépine and Barrah, in 1891, that sugar could also be derived from proteins paved the way for the second stage in the treatment, for their experiments and the clinical observations of Kolisch and Schumann-Leclercq (1903) showed that regulation of the protein as well as the carbohydrate is necessary if the progress of the disease is to be checked, especially in severe cases. Until very recently the third important constituent of the diet, fat, has been regarded as a comparatively innocuous food for diabetics; they have consequently been given it in large quantities and encouraged to consume as much as possible with a view to maintaining their weight and, if possible, increasing it. The most recent experimental and clinical investigations have shown, however, that control of the fat allowance is quite as important as regulation of the carbohydrate and protein intakes if a gradual failure of metabolism with ultimate return of the glycosuria and progressive acidosis are to be guarded against.

Diabetic Lipaemia.

When phlebotomy was commonly practised it was known that the blood in severe cases of diabetes occasionally had a milky appearance, and that on standing a creamy layer of fat separated out on the surface. Although such a condition of lipaemia is very rarely seen in any other disease than diabetes no great importance has been attached to it, save that it indicated a grave prognosis, and until recently no attempt has been made apparently to study the fat content of the blood systematically to discover the antecedent stages and ascertain whether an excess of fat, without obvious lipaemia, existed in all cases of diabetes. The first comprehensive series of cases in which such an investigation was carried out was reported in 1916 by Bloor,¹ who had previously studied the fat content and relations of the blood in a number of normal individuals and other pathological conditions by methods specially developed for the purpose, and so was in a position to make reliable comparisons. He found that out of the thirty-eight diabetics investigated a lipid value of the blood in excess of the normal average was present in thirty-six, and in all but three of these it exceeded the highest limit met with in healthy persons, in spite of the fact that a characteristic milky appearance was found in only two instances. A marked increase, up to 100 per cent. or more of normal values, was found in all the severe cases, but clinically mild cases also sometimes showed considerable abnormality. As a rule, however, the more severe and long-standing the diabetic condition the more marked was the abnormality in the blood lipoids.

From these results it would appear that an excessive lipid value of the blood is very common in diabetes, and that it may be regarded as an almost constant phenomenon of the diabetic condition. This being so the questions that arise are: What is the source of the excess of fat? and What is its significance? The evidence at present available suggests that it originates mainly in the fat of the food, and that the probable reason for its appearance in the blood is a partial failure of the mechanism for dealing with fat arising from the essential nature of the diabetic state, like the associated defects in carbohydrate and protein metabolism. The dependence of lipaemia on the fat content of the diet was well shown in Bloor's two cases of obvious lipaemia, which promptly cleared up when a fat-free diet was substituted for the fat-rich diet they

had been taking previously; and similar observations have been made by Allen, who has pointed out that dogs rendered diabetic by partial removal of the pancreas rarely show lipaemia unless precautions are taken to ensure good digestion, and that it then varies with their digestive powers, appearing readily on feeding them with fat and ceasing promptly on its omission. Allen has shown also that the excess of fat in the blood in diabetes is not due to hyperglycaemia, nor solely to removal of pancreatic tissue, and that absence of carbohydrate or loss of sugar from the body do not appear to be responsible for the condition, since maximal phloridzin poisoning followed by feeding with nothing but fat in dogs fails to produce anything resembling diabetic lipaemia. Bloor found that there was no definite relation between high blood lipoids and the occurrence of acetone bodies in the urine, although he points out that maximal lipaemia probably never exists without acidosis, because acidosis goes with the general severity of the diabetes. That diabetic lipaemia is not due to change in the reaction of the blood is indicated by the fact that the greatest possible reduction in its carbon dioxide capacity by acid poisoning produces no characteristic change in that direction. It would therefore seem that the tendency to the imperfect utilization of fat in diabetes is not dependent upon any other feature of the disease, but is a primary phenomenon of the condition which appears to vary independently of the other symptoms, although its extent corresponds roughly to the severity of the disorder.

Ketonuria.

The existence of an excess of lipoids in the blood in most cases of diabetes suggests that the mechanism by which fat absorbed from the bowel is taken up by the cells of the body is usually more or less at fault, but there is another point in fat metabolism at which failure frequently occurs also—namely, its oxidation in the tissues. This is indicated by the presence in the blood and urine of imperfectly oxidized products in the shape of the acetone bodies (acetone, aceto-acetic acid, and beta-hydroxybutyric acid), which have been aptly likened by Woodjatt to the smoke from a badly burning candle or fire. The work of Rosenfeld, Hirschfeld, Geelmuyden, Magaus-Levy, and others has shown that the principal source of the acetone bodies is fat, and it may be taken as proved that the presence of acetone and its associates in the urine and blood is mainly influenced by the amount of fat in the tissues, and hence in the food.

It is well known that the fasting human subject shows ketonuria, and that the available store of fat in the body is one of the chief sources of the condition under such circumstances was strikingly demonstrated by the experiments of Folin and Denis² with fasting obese women in whom marked acidosis and serious symptoms of acid poisoning corresponded to the rapid loss of weight resulting from starvation. Ketonuria likewise results from simple carbohydrate abstinence, and it would seem that a certain proportion of available carbohydrate is necessary for the complete and orderly combustion of fat by the tissues. According to Zeller,³ a molecule of sugar must be oxidized for each two molecules of fat, which would mean in a normal individual the ingestion of one part of carbohydrate for each four parts of fat. If carbohydrate is not available the sugar derived from the constituent amino-acids of proteins may be used, and it is for this reason that proteins are antiketogenic in normal persons. They are less efficient for the purpose than carbohydrates, for some amino-acids are themselves capable of giving rise to a considerable proportion of acetone bodies. In the diabetic subject the degree to which fat is completely utilized depends upon the relation between the power possessed by the tissues of making use of the sugar offered to them and the amount of fat taken in the diet, or stored in the body. If carbohydrate foods are comparatively well metabolized, a considerable amount of fat can be burned without "smoking" or giving rise to acidosis; if the defect is more pronounced and only a small quantity of carbohydrate can be made use of, a proportionately smaller quantity of fat can be taken without being imperfectly oxidized, while if the tolerance for carbohydrate is slight ketonuria and acidosis occur with even a small amount of fat in the diet, or with no fat at all, since more or less of the carbohydrate of protein

origin is probably also being excreted in the urine as sugar, and there may not be sufficient available to suffice even for the complete oxidation of the protein fractions that give rise to acetone bodies.

It may consequently be taken as a general working rule that fat unbalanced by an adequate available supply of other foods is poison to the diabetic, and it therefore follows that the craving for bread and other starchy foods shown by patients on a high protein-fat diet is rather an expression of a natural want hitherto misunderstood than an evidence of original sin that can be dealt with more satisfactorily by restoring a proper balance in the diet by reducing the fat than by increasing the carbohydrate, as is usually taught. Owing probably to a latent reserve power possessed by most people, diabetics can generally be trained to utilize gradually more fat, but their reserve power in this respect is not unlimited, and, like the tolerance for carbohydrates and proteins, is easily overstrained, with rapidly increasing acidosis and death from coma.

Fat and Sugar Utilization.

A third aspect of the fat problem in diabetes that has been reinvestigated lately is the influence exerted on sugar utilization. It has been contended by some writers that sugar can be formed from fat, since the addition of fat to a diet that has previously been well borne may increase the glycosuria in diabetes; but the experiments of Ringer, Allen and DuBois, and others are strongly against such a transformation taking place in animals or man, so that some other explanation must be sought. Recent experiments carried out by Allen⁴ appear to have solved the mystery. He found that if two dogs are made diabetic by removing corresponding portions of the pancreas from each, and, after their carbohydrate and protein tolerance has been determined, one is given only just sufficient fat to prevent loss of weight, while the other is allowed as much as he will eat, or is forcibly fed with fat, the former, although thin and always hungry, will remain sugar-free, whereas the other gains in weight, appears healthy and happy, but eventually develops glycosuria, with ultimately fatal results, unless the fat feeding is promptly stopped and he is starved until the glycosuria is controlled. Contrary to what might have been expected if fat were transformed into sugar in the body, examination of the blood of such dogs shows that the first effect of adding fat to the diet is to reduce the percentage of sugar. As the fat feeding is pushed and the weight of the animal increases, a parallel rise in the level of the blood sugar takes place, however, and finally glycosuria occurs. An abnormally high blood-sugar level may exist for some time before sugar appears in the urine, and persist for a considerable interval after all fat has been omitted from the diet, suggesting that an excess of fat reduces the permeability of the kidneys for sugar, and showing that its evil effects continue long after the cause has been removed, thus probably explaining the diminishing glycosuria, without a corresponding fall in the blood sugar, of chronic cases of diabetes kept for long on a diet with a high fat content.

These experiments have been repeated under such a variety of conditions and with such adequate controls, always with similar results, that it seems reasonable to conclude that the hyperglycaemia and glycosuria following excessive feeding with fat are due to a failure of metabolism consequent on the gain in weight above what the defective assimilative functions of the animal are able to cope with, and that any attempt to induce a high level of nutrition with fat results in an aggravation of the diabetic condition similar to that which follows a like attempt with carbohydrate or protein, although its effects are slower and more insidious.

Applications to Treatment.

The application of the results of the observations outlined above to the clinical treatment of diabetes mellitus obviously entails the forsaking of several cherished beliefs and standards. It will also involve very considerable modification in current methods of determining and regulating the diet, even the most modern. We can no longer consider that we have done our duty by our patients if we have merely rendered their urine sugar-free by limiting the carbohydrate intake or adjusted the protein allowance

to their metabolic capacity; we must now also ascertain the optimum amount of fat which will meet their needs, prevent acidosis, and avoid the onset of glycosuria, either immediately or in the future.

The prevention and control of acidosis is so often a matter of primary importance when patients come under observation that it will be well to consider it first. It has long been known that it is dangerous to change a severe case of diabetes suddenly from an ordinary mixed diet containing carbohydrate to one consisting of protein and fat alone, as serious acidosis may develop, but it does not appear to be generally recognized that it is often equally dangerous to deprive a patient of all food and adopt the fasting treatment without adequate preparation. In order to prevent acidosis occurring, and avoid increasing it when already present, the chief source of the acetone bodies, fat, should first be eliminated from the diet as far as possible. After a day or two on a fat-free diet the carbohydrate may generally be reduced with safety, but it is not wise to leave out all carbohydrate until the protein intake has also been brought down by at least half. Both carbohydrate and protein may then be gradually reduced until a diet of low-value green vegetables only is being taken, when, if the glycosuria still persists, actual fasting may be instituted without fear of grave complications developing. When the diet is being built up again and the patient's tolerance is being tested after the glycosuria has been controlled, fat should be introduced with equal care, none being allowed at all until a fair tolerance for carbohydrate and protein has been established. The fat content of the diet, like the carbohydrate and protein, must then be worked out each day and the effect of every addition be carefully watched.

Unfortunately the results of analyses of the urine do not afford information that is of much help in regulating the allowance in many cases, although variations in the total acidity, true ammonia nitrogen, calcium, and magnesium excretions, with increase in the total output of acetone bodies may give useful indications in some instances, and show that the fat is being increased too rapidly. As a rule the most reliable information is given by examination of the blood. Allen's experiments on dogs have shown that a rising blood-sugar curve with increasing weight when fat is being added to the diet indicates approaching failure of metabolism with eventual glycosuria, but earlier and more certain information that the mechanism for dealing with fat is being overloaded can be secured by estimating the lipid value of the blood by Bloor's method or, since it has been found that the cholesterol increases parallel with the fat, by cholesterol determinations. When the apparatus and time for blood analyses are not available, the fat allowance must be regulated by the patient's weight and the appearance of sugar in the urine.

It must be borne in mind, however, that weight is not necessarily a true index of the tissue mass of the body as it is influenced by accidental circumstances, particularly loss and retention of water, and that glycosuria is a late symptom of failure of metabolism due to excess of fat in the diet.

If sufficient care is taken, glycosuria can usually be avoided if the fat-intake is so adjusted that, while further loss of weight is guarded against, progressive gain is prevented. This ideal, which should be aimed at in all cases, is quite contrary to the older teaching, according to which increase in weight was, above all other things, the most desirable for a diabetic, since it was considered that gain in weight meant gain in strength also. That such is not really the case has been shown by the experiments of Williams⁵ with the Collin dynamometer. It appears from his results that, as a rule, diabetics are physically distinctly weaker than normal persons, owing partly to loss of musculature, but also probably in consequence of the diminished supply of energy furnished by the imperfectly utilized food to the muscular mechanism they possess so that it is incapable of functioning normally. There appears to be a direct relation between the food tolerance and the muscular vigour of the patient, and if the tolerance is depressed by the continued use of a diet beyond his metabolic capacity further decline in the physical powers takes place, whereas if the food tolerance is increased by the employment of a diet within the physiological limitations of the individual, even though it falls far short of the theoretical energy requirements of

the body, an appreciable increase in muscular tone occurs.

Overfeeding, therefore, is not only a cause of glycosuria in diabetes, but also results in a progressive failure in metabolism with loss of strength. It appears to matter little whether the excess of food is in the form of carbohydrate, or protein, or even fat—the outcome is the same; but as the effects of an excess of fat are more insidious and difficult to recognize in the early stages it is necessary that particular care should be taken in regulating the fat allowance. Since I realized that fact and applied it in my clinical work I have obtained much better and more permanent results than formerly. It has also enabled me to recognize and deal with cases of recurrent glycosuria that would otherwise have been puzzling. As an example I may quote the case of a boy of 14 who was brought to me in October, 1916, by Dr. J. Howard Cook.

When he was first seen by Dr. Cook he was passing about 100 grams (5.5 per cent.) of sugar a day, but when he came to me the sugar excretion had fallen to about 10 grams a day. The patient's carbohydrate and protein tolerance were worked out, and he was put on a diet on which he remained sugar-free for about three months. A return of the glycosuria then occurred, but on his carbohydrate allowance being readjusted the sugar disappeared, and it remained absent for about four months. As the glycosuria then recurred it was evident that his carbohydrate tolerance was steadily falling, and the prognosis appeared to be bad. A further readjustment of both the carbohydrate and protein allowance kept him sugar-free for another four months, when sugar was again found. I went into the case very carefully with Dr. Cook, and we came to the conclusion that as the boy's weight was increasing more rapidly than would probably be accounted for by natural growth and a considerable amount of fat was being taken in the diet, it would be advisable to try the effect of reducing it. This was at once done, and I hear that he has since remained free from any trace of sugar although more starchy food has been taken, and that he has improved in strength and general condition.

The importance of a strict control of the fat content of the diet has been impressed upon me by a number of other cases, including several which had been submitted to the fasting treatment with immediately satisfactory results, but with ultimate return of the sugar. In some of these that have come under my care owing to the recurrence, I have found that an excess of protein was being taken, but in others careful chemical examination has shown that the fat content of the diet was the difficulty, and when it was adjusted to the patient's metabolic powers the glycosuria promptly ceased and did not return.

Patients who are steadily losing weight, as most diabetics are, naturally desire to put on flesh as quickly as possible, and are apt to judge the success or failure of any treatment they may undergo by the extent to which their wish is gratified; but, although we may understand and sympathize with their longing, it must not be gratified, and we should explain that gain in bulk is a sign of failure rather than of success. A steady weight that can be maintained without overtaxing the patient's defective metabolic powers should be aimed at, and any attempt to improve a bad situation by overfeeding, or even feeding up to the theoretical caloric requirements of the body, must be abandoned. Gain in weight must be sacrificed to well-being and satisfaction of the appetite to length of days. Individualization of the diet, in which the allowance of carbohydrate, protein, and fat is regulated by the tolerance of the patient for each, and by his powers of dealing with the diet as a whole, is the line along which the treatment of diabetes is developing, and, although it is very likely that we have not yet reached finality and that other considerations, such as the mineral content of the diet and the amino-acid make-up of various proteins, etc., will eventually have to be taken into account, it is clear that the older standards and empirical methods employed for so long are doomed, and will have to give place to scientific dieting based upon exact modern chemical research and knowledge.

REFERENCES.

- ¹ *Journ. Biol. Chem.*, 1916, xxvi, p. 417. ² *Ibid.*, 1915, xxi, p. 183. ³ *Arch. f. Anat. u. Physiol. Phys. Abst.*, 1914, p. 213. ⁴ *Amer. Journ. Med. Sci.*, 1917, cliii, p. 313. ⁵ *Arch. Int. Med.*, September, 1917, p. 399.

THE American Women's Zionist Organization announces that Mrs. Peter J. Schweitzer of Brooklyn has given £5,000 for the building and maintenance of a model eye hospital in Palestine. A medical unit has left for Jerusalem.

AN OUTBREAK OF PHLEBOTOMUS FEVER.

BY

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AN outbreak of phlebotomus fever (sandfly fever) occurred in a squadron of yeomanry on outpost duty in mid-Egypt in the middle of the summer of 1917. The post was on the western edge of the cultivation, and I was in medical charge of the unit. Of the total strength 86.4 per cent. were infected. The first to contract the illness were the men, non-commissioned officers next, and officers last. The first case was discovered on the thirty-seventh day in occupation, and from this there were three or four fresh cases daily for a week, and an average of six daily in the second week. For medical reasons the unit then moved about a mile and a half to a new camp on fresh ground, and, although it was impossible to avoid carrying the infection, better conditions followed. For military reasons it was desirable to maintain occupation of the first position, and after taking preventive measures additional to what had already been followed, a guard drawn from another unit was placed in it. Four days had scarcely elapsed when the non-commissioned officers and men who formed this presented symptoms of infection, and the illness spread through all of them.

The accommodation consisted of a dwelling-house and offices which the officers and non-commissioned officers occupied, and shelters constructed of wood and canvas for the men. All were placed compactly on an elevated site adjacent to a pool which covered about an acre and contained more or less stagnant water. Agricultural drains of muddy water were in touch. The sanitary arrangements were satisfactory except the drinking water, which was bad; the latrines and horse lines were at a reasonable distance. Preventive measures were adopted in the form of cresol spraying throughout, and the use of paraffin oil on breeding places. Everyone, officers and other ranks, had a mosquito net, but this could not be counted on as the midge is so small that it can pass through the mesh. They were plentiful, very small and midge-like, with hairy bodies. They were found on walls and in rubble, but the breeding places must be moist.

The incubation period was from four to seven days. The onset was very sudden, accompanied with severe malaise, headache, and suffusion about the eyes and post-orbital pain. Pain in the lumbar region was generally intense, and pain and cramp in the limbs occurred. Constipation was nearly always present and profuse sweating. The temperature rose quickly to 102.5° or 103°, and on a few occasions to 105°. After twenty-four hours the pyrexia diminished, and at the end of three days fell to normal. The pulse was not correspondingly accelerated—it was seldom above 80; it became soft and weak and the cardiac condition required attention.

The suddenness of the onset was the marked feature. A man to all appearances in normal health was on duty at 9 a.m., and an hour later reported ill with giddiness and inability to carry on. His temperature was 103° F.; other symptoms developed in the course of an hour or two. One night another was found on horseback wandering up and down the road, unable to recall to mind the way he was accustomed to take to reach camp. He was feeling dazed and ill, and his temperature was 103.2°. An hour earlier, feeling all right, he had left head quarters of the regiment, two miles back.

Phlebotomus fever had not previously been prevalent, nor were contacts from outside found. One or two subjects of malaria were on the strength. From dengue the condition is differentiated by the suffused eyes, absence of rash and of secondary rise in the temperature after a few days running normal. In paratyphoid the pyrexia seldom runs so high, and has not the characteristic third-day drop to normal. Severity of the rigor and fall of the temperature in a matter of hours distinguish it from malaria; enlargement of the spleen is also to be remembered.

Most cases were evacuated to hospital. Those remaining in the lines were kept together apart from the uninfected; they were given a purgative and sodium salicylate, phenacetin, or opium for the relief of the pyrexia and aching limbs. Subsequent debility was a marked feature