Some Recent Views on the Trends, Characteristics and Treatment of Diabetes Mellitus

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In spite of the remarkable advances in our knowledge of diabetes mellitus during the last quarter century, the mortality from this malady has increased steadily throughout the civilized world. It has shifted proportionately, however, from a lower to a higher age group. While in 1900 diabetes ranked 27th among the causes of death in the United States, the latest statistics show that it now ranks 10th, taking a toll in the registration areas of continental United States of approximately 30,000 lives annually. Following the introduction of insulin in 1923, there was a slight recession in the rate, but more recently this gain has been entirely lost.

According to a recent report by Joslin, Dublin and Marks* on the "Characteristics and Trends of Diabetes Mortality Throughout the World," this astounding increase has been chiefly among older persons, and especially in women, in whom the increase over the rate in adult males during the five-year period ending 1930 was 76 per cent. In fact, it is now estimated that 26 out of every 1,000 girl babies born in the United States are expected to succumb to diabetes. This investigation also revealed a diabetes mortality in the United States for 1932 of 22 per 100,000 population, the highest of any civilized country in the world; while in Canada the rate for the same year was only 12.8. Such a rise in mortality, in the face of unquestionable improvement in the vital statistics of New York City show that the death rate from diabetes rose from 17.3 per 100,000 population in 1901 to 30.3 in 1934.

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An analysis by Lande2 of the mechanism of deaths from diabetes at the Mt. Sinai Hospital, New York City, from 1923-33 reveals a 12 per cent. mortality in cases of diabetic coma under 40 years of age in contrast to a rate of 54 per cent. above this age. Of the cases which were complicated by infections, 52 per cent. were fatal, with tuberculosis and the pyogenic infections taking the heaviest toll. Of all the deaths, it was found that only 33 per cent. were associated with other conditions which were fatal within themselves, and, therefore, unavoidable. In such cases, the coma is of secondary importance, and its control does not affect the outcome. In the cases of diabetic coma otherwise uncomplicated the mortality was 22 per cent. It is evident, therefore, that, in addition to defective carbohydrate metabolism and ketosis, there are other significant factors concerned in producing such a high death rate in this class of patients, and that an appreciable coma mortality is inevitable at best.

The acidosis, or alkali deficit, of the diabetic is due to a reduction in serum bicarbonate, and this means a low CO2 combining power of the blood with, in severe degrees, the consequent stupor and coma. It has been determined, however, that an acidosis of a greater degree than is found in diabetic coma may exist in other conditions without being attended by a similar syndrome. Also, there is no direct correlation between the concentration of ketones in the blood and the depth of coma. Hence, we see that the mechanism involved in the production of diabetic coma is not entirely understood. It is true that acetone bodies may produce mild anesthetic effects, but there is insufficient evidence to incriminate a ketosis to the extent of producing coma and unconsciousness.

An analysis by Atchley3 and Peters,4 is that the breakdown of carbohydrate metabolism causes a greatly increased
excretion of water and of sodium and potassium, and, with the onset of acidosis, the consequent excretion of ketone bodies further augments the loss of water and the electrolytes, sodium and potassium, thus producing the alkali deficit and tissue dehydration. At the same time, there develops an increased permeability of the capillary walls with a tendency to permit fluids to pass from the vessels to tissue spaces, and, in severe grades of acidosis, some of the proteins pass with fluids from the blood stream. Thus, during a state of acidosis there develops a marked depletion in plasma fluids, brought about by the diuresis above described, together with vomiting, hyperventilation, and the passing of fluids through the capillary walls. Such a process diminishes blood volume, lowers blood pressure, and causes a capillary stasis, all of which, combined, produce the syndrome of shock. The peripheral capillary stasis is responsible largely for the escape of fluids from, and their failure to return to, the vascular system. In this state, recovery is dependent, to a large degree, upon restoration of the fluid content of the blood and the ability of the organism to utilize such fluids in replenishing the serum volume. Therefore, when a state of shock exists, restoration of blood volume by the administration of fluids should be the aim of treatment. Even though the ketosis has been overcome, and the CO₂ combining power of the blood has been elevated to normal, patients frequently do not manifest evidence of clinical improvement until the plasma fluid has been restored. A 5 or 10 per cent. dextrose solution in normal saline, given intravenously, will usually restore the serum volume, provided the permeability of the capillary walls has not been so altered that it is impossible for the fluids to be retained in the vascular system. When this state is reached, the restoration and control of carbohydrate metabolism and the elimination of ketosis no longer suffice to effect recovery. It is obvious, therefore, that changes in the capillary walls which occur with advancing years render them more vulnerable to such conditions; consequently, the outcome of acidosis, coma, dehydration and shock becomes more unfavorable the older the patient.

Practically all of the conditions of a degenerative nature which develop as the result of diabetes—such as arteriosclerosis, angina, coronary occlusion, fibrous myocarditis, cataracts and zanthoma—are direct results of incomplete fat hydrolysis. These conditions do not seem to be related to the severity of the disease nor to the degree of glycemia, but are correlated with the duration of the disease and the age of the patient. In this connection, White found that out of 234 cases of diabetic children, 156—66 2/3 per cent.—ran normal blood cholesterol values upon repeated analyses; while 67—approximately 28 per cent.—ran values persistently above normal. And of the 156 who ran normal cholesterols, 1 per cent. subsequently developed arteriosclerosis; while of the 67 who ran high cholesterols, 15 per cent. later developed arteriosclerosis, 4 per cent. cataracts and 6 per cent. nephritis. Also, out of 25 patients in whom cholesterol values were found extremely high—above 300 mgm.—44 per cent. had developed degenerative changes.

The primary etiology of diabetes is still shrouded in mystery and theory. The disorder makes its appearance in the form of an altered function which, if sufficiently severe, produces the symptoms and secondary tissue changes characteristic of the disease. All of our findings are mere symptoms of this disturbed function and its consequent pathological changes, none of which seems to throw much light on the primary nature of the disorder. While it has been substantiated repeatedly by clinical, pathological and experimental evidence that a deficiency in insulin is an essential factor in producing the fully developed condition in at least a considerable proportion of the cases, a number of investigators now question the constancy of this deficiency in diabetes. Falta thinks that a high-grade resistance to insulin, in itself, produces diabetes, and that such a resistance is often due to a strong counteraction of the suprarenals. Likewise, he thinks that a deficiency in function of the suprarenals may result in an uncontrolled secretion of insulin by the islands of Langerhans, with a consequent high sugar tolerance or even hypoglycemia. According to von Noorden, the essential disturbance in diabetes is not an inability of the tissues to oxidize sugar, but an inhibition of glycogen decomposition. This inhibition, he finds, is effective chiefly in the liver and to a lesser extent in the muscles and other tissues. He emphasizes further that glycogenolysis is not increased by the administration of insulin.

In view of the inconstancy of demonstrable pathology upon which to explain the genesis of this disease, together with the close interrelationships of the islands of Langerhans with the other glands of internal secretion, and their different effects upon, and responses to, the two phases of the autonomic nervous system, it seems very probable that, at least in most instances, we are dealing with a functional disorder due primarily to an inherent biologic genotype which is prone to an endocrine and autonomic nervous system imbalance. Such a view is sustained by the greater prevalence of diabetes in Jews. Further support of the role of biologic and functional factors in the causation of this disease is found in the greater incidence and the increase in mortality which occur during the years of the
physiologic epochs. Also, the fact that after the age of 35 the mortality in women increases rapidly out of proportion to that in men strongly suggests a probable incrimination of the relative functional status of the sympathicus and parasympathicus in the etiology of diabetes. In order for a disturbance in function of the autonomic nervous system to be an appreciable factor in the etiology of diabetes, it must take on the form of a sympathicotonia, or relative sympathetic predominance over the parasympathetic—since stimulation of the vagus system increases the secretion of insulin, while sympathetic stimuli depress this function.

Upon these conclusions, it is obvious that diabetes may be classified fundamentally into two types: 1) insular, or a mere insulin deficiency, comparable in nature and etiology to dysfunctions of the pituitary, thyroid, or any other gland of internal secretion; and 2) insulin-resistant, in which enough insulin is produced, but it is rendered inert by opposing or inhibiting sympathico-adrenal influences.

In regard to the dietary phase of treatment, the Vienna School, headed by Porges, Adlersberg and von Noorden, has recommended diets of low fat and high protein and carbohydrate content for a number of years. In fact, since 1903, when von Noorden advocated his "Oatmeal Cure," there has been in Europe a decided trend toward a sharp restriction in fats and an increase in carbohydrates. Such a diet tends to prevent the lipemia and consequent acidosis which are so common with the diets of high fatty acid values, and avoids arteriosclerosis and its sequelae.

Since the advent of insulin, there is no longer any reason to subject diabetic patients to diets rich in fat. On the contrary, it is very important that they should have generous rations of carbohydrates. Whereas, until recently, the diet usually advocated for the diabetic was in the proportion of about 3 gms. of fat, 2 gms. of carbohydrate, and 1 gm. of protein, with an approximate caloric value of 30 calories per kgm. of ideal body weight (higher values for children), and a fatty acid:glucose ratio of not more than 1.5:1, the more recent trend is to allow from two to four times as much carbohydrate as fat in the diet, with the caloric values about the same. Of course, if the condition is sufficiently mild to enable the patient to take a diet moderately restricted in carbohydrates, and, thereby, control the glycosuria without developing a ketosis, such a diet is not only permissible but is strongly advised. If the diet contains adequate carbohydrates, and their metabolism is assured by the use of insulin, if necessary, the blood cholesterol is held down and arteriosclerosis is not prone to develop. Furthermore, it has been determined that while diets of high fatty-acid content may aid in lowering blood sugar, they tend to impair sugar metabolism; likewise, it has been found that a high carbohydrate diet tends to improve this function. In this connection, Gray and Sansum report an improvement in sugar metabolism in 42 of 70 cases of diabetes which had been on high-carbohydrate and low-fat diets continuously for seven years. The diets which they usually used for mild cases had a carbohydrate:fat ratio of 3:1 or 4:1, and such cases did well on these diets. Severe cases, however, did best on a carbohydrate:fat ratio of 2:1. Also, Porges restricts the fat contingent sharply in the diabetic dietary—50 gms. daily being the maximum allowance. In fact, he found that his patients did better on a diet of proteins and carbohydrates only, eliminating fats altogether; also, that their capacity for work was thereby increased. Von Noorden thinks that a resistance to insulin is largely overcome by a diet extremely low in fat, but that it is inadvisable to hold a diabetic patient on any strict form of diet. Stolte strongly advocates a free choice of food for all diabetics. He further emphasizes that diabetic children thrive on a "free diet," and that even an occasional carbohydrate excess does not disturb the "total" metabolism. Moreover, it has been noted by numerous observers that the diabetic who receives a dietary rich in carbohydrates requires less insulin than the patient who has the carbohydrates restricted and replaced by fats. In further corroboration of these views, Ellis found that by the hourly administration of glucose and insulin large amounts of dextrose—600 gms. daily—are well tolerated and utilized in advanced diabetes without requiring any more insulin than was necessary on an ordinary restricted diet. In 7 out of 8 cases so treated, the carbohydrate metabolism was improved to such an extent that there was a great reduction in the amount of insulin required. In one instance, the amount of insulin required was reduced from 192 units daily, before the administration of glucose, to 9 units on the 21st day of the treatment, the diet otherwise being unchanged. While an explanation of the exact mechanism of this phenomenon is not offered, these observations serve to cast an altogether different light on the theories of pathogenesis and treatment of diabetes.

In order to treat diabetes properly, the treatment and a course of training should begin simultaneously. The patient should witness the first urinalysis and be told the significance of the findings. He should be taught to examine the urine, not only for sugar, but of far more importance, for acetone or diacetic acid, and taught what types of foods tend to produce positive reactions for these substances. He should be taught, also, that the
presence of ketones in the urine is the thing to be concerned about most, and that in order to get rid of them he should first have a positive reaction for sugar, then take insulin, and thereafter diminish the fat content of his diet. Such knowledge and practice on the part of the patient will greatly simplify his entire regimen. It will elicit a better cooperation and enable him to take insulin more intelligently, thus maintaining a better carbohydrate metabolism, and thereby affording a greater assurance against the future ravages of imperfect fat metabolism.

If the urine is positive for sugar and negative for the ketones and there are no complications which make it urgent that carbohydrate metabolism be corrected as early as possible, the patient should be instructed to restrict the carbohydrate content of the diet, but not necessarily in terms of grams and calories. This regimen should be persisted in until either the sugar disappears from, or fatty acids appear in, the urine. If diacetic acid or acetone does not appear in the urine and the urine can be rendered sugar-free by the mere restriction of carbohydrates, the use of insulin is unnecessary. At this point a blood sugar or, better still, a carbohydrate tolerance, determination should be made chiefly for the purpose of determining the level at which sugar appears in the urine. This serves to establish a comparative relationship between the level of blood sugar and the renal threshold, thus enabling both the doctor and the patient to use the simple and practical test for sugar in the urine as a fair indication of the blood sugar level. However, even though the blood sugar should run considerably higher than normal when the urine is sugar-free, unless there is evidence of a ketosis or a persistently high blood cholesterol, there still is no necessity for the use of insulin. If the patient's urine gives a positive test for fatty acids, the carbohydrates should not be restricted, and insulin should be administered in whatever quantities and at whatever intervals necessary to render the urine free from the ketones. In severe cases of diabetes it is not advisable to endeavor to keep the blood sugar within the range of normal nor to render the urine entirely sugar-free, as neither a hyperglycemia nor a glycosuria, per se, unless extreme, is particularly harmful. Besides, in cases of true diabetes with a large insulin:dextrose equivalent, it is hardly possible to counteract the hyperglycemia and glycosuria by insulin without producing hypoglycemic conditions. Therefore, after the fatty acids have disappeared from the urine, if insulin can be discontinued without the reappearance of ketosis and with the maintenance of a normal blood cholesterol, the further use of insulin in such a case is unnecessary. If, however, such a state cannot be established and maintained, a normal and well balanced diet should be permitted and a sufficient quantity of insulin used to assure its proper assimilation and utilization.

In regard to work and exercise, there is no reason that the diabetic should not continue his or her usual occupation and activities. Such a view is substantiated by Collazo and Barbudo, who found that in diabetes muscular exertion produces a slight increase in the lactic acid of the blood and a decrease in the glyceria. These findings were interpreted as meaning that exercise develops in the muscles a greater capacity to assimilate and utilize dextrose, and makes the liver develop a greater avidity for the lactic acid of the blood which, once drawn to the liver, is used by it to form glycogen. Furthermore, the works of Mayor and Mann and Lukens prove conclusively that in diabetes glycogen formation in the muscles depends primarily on glucose concentration, while insulin, acting as a catalyst, serves only in an indirect manner to accelerate this process. Also, Lublin observed while caring for 400 diabetics on the Island of Rugen that work gave favorable results. He found that on the same daily diet the blood sugar fell consistently on working days, and rose on Sundays. Such observations and results are explained on the basis that the formation of phosphagen is dependent largely upon the glycogenic reserve of the liver and muscles, and a diminution of this reserve produces an abnormally low phosphagen content of the muscles. Consequently, an inadequate carbohydrate intake and assimilation results in a depletion of hepatic and muscle glycogen, thus restricting Nature's buffering process of glycogen storage and energy reserve. If, however, a normal carbohydrate metabolism is maintained, the phosphagen content of the muscles is, likewise, maintained and a better energy reserve assured.

It seems axiomatic, therefore, that the goal in the diabetic dietary should be toward a diet normal for the individual, merely avoiding excesses of carbohydrates, and that most of the inability of the organism to utilize carbohydrates should be taken care of by the use of insulin in whatever quantities necessary. Of course, just what happens to the sugar which disappears from the blood stream following the administering of insulin is not known. It probably goes to form some as yet unidentified substance of carbohydrate metabolism. The wonder, however, is not so much that the entire phenomenon has failed of elucidation by the mere use of insulin, but that we can treat, with even a fair degree of success, such a complex disease as diabetes mellitus while knowing only a small part of its exact mechanism and what actually occurs.
In view of the foregoing, it is very probable that the answer to a higher death rate from diabetes in the United States, as compared to other countries, lies chiefly in the fact that we have been too reluctant both in allowing liberal quantities of carbohydrates in the diet and in the free use of insulin. So, rather than subject the diabetic patient to a strict, monotonous, unpalatable, and detrimental diet, it seems more expedient, much more practical and now even scientific to advise him to take insulin, eat, drink and be merry, that tomorrow he may live.

Bibliography