EDITORIALS

*DIABETES CONTROL**

Active, progressive, and uncontrolled diabetes results in premature widespread vascular degeneration. The question of the role which insulin deficiency plays in the tragedy of arterial deterioration may well lead to solving the most important pathological enigma of the present day, namely, arteriosclerosis. It is logical to assume that the earlier the diabetes is identified and an adequate program of management established, the less likelihood for complications to develop. There is wide-spread agreement that satisfactory control is based on diet, insulin, and exercise.

During the last 25 years the science of nutrition has made great strides. The danger of overweight for young and old is now recognized. By long continued overeating the potential diabetic may cause exhaustion of the pancreas and frank diabetes with the ordinary clinical symptoms. Metabolic exhaustion has been demonstrated experimentally to be an important precipitating factor. Prolonged fatigue, likewise, predisposes to vascular complications in the older patient.

Pancreatic exhaustion reduces the amount of available insulin in the pancreas. Insulin deficiency, relative or absolute, is the basic cause of diabetes. It would appear that the younger the patient the greater the loss of insulin production by the pancreas. Wrenshall and his co-workers found that insulin which could be extracted from the pancreas of diabetics averaged less than 40 per cent that obtained from the pancreas in normal individuals. In childhood diabetes it is less than 10 per cent of the amount extractable from the adult diabetic pancreas.

Continual overeating tends to prolonged increase in the level of the blood sugar. This stimulates the pancreas to make more insulin to meet the increased demand. Temporary exhaustion of the beta cells of the islets may occur. From observations on alloxan diabetes in animals, the early evidences of exhaustion, increase in cell size, cloudy swelling, changes in cell structure, if not too long in duration, may return to the normal healthy state provided the insult to the insulin-producing cells has not been too long in existence. Prolonged fatigue aggravates the strain on the beta cells. The homeostatic mechanisms of the body carry on most satisfactorily with a minimum of strain on specific cell functions when overloading and exhaustion are avoided.

What constitutes control of diabetes? What is the dividing line between satisfactory metabolic balance and the early defections which if not controlled would lead to serious complications? The answer to this inquiry is important. The criteria of adequate control are not generally agreed upon. The two items about which no agreement has been reached are blood sugar levels and sugar in the urine. Some men with expert knowledge and wide experience discount the importance of high blood sugars and glycosuria in the absence of other findings indicative of marked metabolic dysfunction.

For practical purposes it would be exceedingly helpful if definite criteria could be established indicative of the limits of the excursion of the blood sugar level, the duration of the elevation and the amount and time interval of the duration of glycosuria. Obviously, and yet again it might not be so direct as it sounds, a blood sugar level within normal limits and the absence of urinary sugar indicates satisfactory control. Yet, thinking just a little further, it must be admitted that when the diabetic patient becomes the victim of various ailments, infectious processes, and what not, he may be in poor metabolic balance and still have a blood sugar level within normal.

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Industry, labor, and the general public look to our Association for enlightenment. If we find disagreement among ourselves it stands, whether justified or not, as an accusation. The lay public interprets our dilemma in an unfavorable light. Regardless of the difference in origin of the metabolic defect, maintenance of nutritional balance with complete utilization of foodstuffs represents the ideal control. Emphasis should be placed on how much of the diet is utilized. Determinations of excess blood and urinary sugar are helpful in estimating the efficiency of the metabolic fire.

Criteria of satisfactory control are the same from infancy through the years to old age. The margins of safety, however, vary with age. The child diabetic is known to be very susceptible to acidosis. His margin of metabolic reserve frequently is limited. It is practically impossible to hold the growing youngster in nutritional balance without some degree of glycosuria at times, unless he is subjected to frequent unpleasant episodes of insulin shock. The common practice is to maintain the growing child on a generous diet including the essential building materials for body growth and organ function, plus the exceedingly important factor of satisfactory emotional maturation. To a generous extent the management of diabetes is a family problem, especially when the patient is a child.

In calculating the total carbohydrate available in the diet and compared with the amount of loss in the urine in 24 hours, a helpful estimate is obtained. Long continued elevation of the blood sugar and sustained loss through the kidneys represents inadequate control. Long continued glycosuria without ultimate kidney damage rarely occurs.

The fatigue element has not been sufficiently stressed. The experiments of Lukens and co-workers have demonstrated that long continued overloading of the pancreas in laboratory animals leads to anatomical changes. These suggest functional exhaustion in the early stages. Pancreatic exhaustion produced by carbohydrate overloading, or toxic chemicals such as alloxan, produce a state of exhaustion. The same sequence of events probably takes place within the human body. Pancreatic exhaustion is a commonly occurring condition in the precipitation of diabetes.

When the basic initial condition favoring the onset of the diabetic state is thus visualized, it offers a working hypothesis for control. If Cannon's views on homeostasis are acceptable, the normal values for blood metabolites should represent the most favorable blood and tissue concentrations for body function. The further away the deviation from the normal pattern, the more the lack of adequate control.

It is understandable, therefore, why the most advanced lesions of diabetes are commonly found in those patients with inadequate control for long periods of time. Granted the exact mechanism of vascular deterioration is not as yet understood. The fact remains that the most prominent degrees of arterial degeneration have been identified in long standing diabetes. Some years ago when the high fat diets were tried, the clogging of blood vessels in the lower extremities with large fat globules was a common finding at autopsy. We are indebted to Root, Marble, and their colleagues for detailed studies on the relationship between various degrees of blood sugar control and the occurrence of degenerative lesions in young diabetics. Some observations have been offered which at first glance might tend to contradict their conclusions. It should be kept in mind that among nondiabetics, the hereditary factor of tissue stamina and predisposition to degenerative lesions exists. With this qualification the additional strain of poor metabolic control augments and accelerates blood vessel breakdown. Individuals with a strong hereditary background possessed of a rugged vascular system will be less likely to show premature vascular deterioration if, when diabetic, the blood sugar level is maintained within homeostatic balance.

An adequate amount of insulin is a requirement equally important to diet in control of diabetes. Sherrill has illustrated the role which insulin plays in maintaining a satisfactory nutritional balance in each body cell. As the body mass increases there is a correspondingly inadequate amount of insulin for each unit of body weight. Therefore, if a low calorie diet reduces the body mass, there is a relatively greater amount of insulin for each cell. This is seen clinically when exogenous insulin is frequently no longer necessary when the obese patient rids himself of excess body mass.

Theoretically, the diabetic will not lose his control if there is always a moderate amount of food available by eating small quantities at frequent intervals; and if the estimated insulin deficiency of his pancreas is compensated for by a continuing and frequent administration of exogenous insulin. Ketosis and reactions from insulin over dosage are preventable and for the most part inexcusable.

Exercise is the third requirement for diabetes control. Muscular activity even for the older patients conditions organ function. It has a tonic effect on the circulation, digestion, liver function, and elimination of the body

wastes. The exact part exercise plays in protecting or predisposing to excess wear and tear on body tissues, especially of the vascular system, is not known. The sedentary individual who is continually feeding into his blood stream a concentrated caloric flow must, thereby, expose the vascular walls to greater strain than if the blood stream is speeded up by physical activity. Exercise may exert an influence as a catalyst by shortening the time period during which a high caloric concentrate is bathing the vascular walls. The sense of well being experienced following exercise may be the result of speeding up the blood stream, improving the tonicity of the vascular walls and shortening the danger period of exposure to metabolic concentrates which are commonly found in the walls of diseased blood vessels.

Diet, insulin, and exercise with the avoidance of prolonged exhaustion are the requirements upon which diabetes control is established. The exact level of the blood sugar is but one measure of control. For a physician interested in maintaining control of the diabetic state, the available evidence emphasizes the importance of maintaining the level of the blood sugar not over 200 mg. for any prolonged period of time. Granted many individuals may carry on apparently in satisfactory fashion with blood sugar levels over 400 mg. and more or less constant glycosuria for a variable period of time. Acceptance of such distortion of normal body chemistry as a condition compatible with well being is a dangerous practice. There are still many angles of the diabetic problem for which no answers are yet available. Nevertheless, the more clearly the metabolites and electrolytes of the blood fall within the accepted normal range, the closer will the diabetic come to satisfactory control.

EDWARD L. BORTZ, M.D.

DIABETIC RETINOPATHY.

The characteristic vascular lesion of diabetic retinopathy consists of the presence of great numbers of minute saccular aneurysms in the retinal capillaries. Hemorrhages and exudates commonly surround the aneurysms, indicating that these are loci of weakness in the vascular wall. The aneurysms are often hyalinized. Capillary aneurysms in the retina are also seen in a variety of other retinal lesions involving tissue damage, venous occlusion, etc. but in these conditions the aneurysms are mainly fusiform or varicose, while in the diabetic they are mainly saccular.

The retinal lesions of the diabetic are closely related to the renal lesions described by Kimmelstiel and Wilson. The latter are often associated with capillary aneurysms in the kidney glomerulus, and the typical globular hyalin, glomerular nodule of Kimmelstiel and Wilson may, in fact, be a hyalinized saccular capillary aneurysm. Kimmelstiel[1] believes that the hyaline material in the glomerular lesion is laid down outside the capillary basement membrane, while I have suggested[2] that the hyalinization occurs inside the aneurysmal sac in the retina, but it is agreed that the retinal and renal lesions are joint manifestations of the same vascular disease. Neither these retinal nor these renal lesions, characteristic of the diabetic, are direct consequences of atherosclerosis or malignant hypertension. They are almost never seen in atherosclerotic or hypertensive nondiabetics and may occur in diabetics in the absence of both athero- and arteriolosclerosis. Patients with diabetic retinopathy and nephropathy commonly show increased capillary fragility suggesting the presence of a generalized capillary disease, but microaneurysms have so far not been demonstrated in significant numbers in organs other than retina and kidney.

The characteristic capillary lesion is most frequently seen in diabetics of long standing, but it is not directly related to the severity of the diabetes in terms of insulin requirement. Many patients show a decline in insulin requirement associated with the onset of the retinopathy. The relative frequency of episodes of acidosis in patients with and without retinopathy is disputed. Zubrode, Eversole and Dana[3] found a lower frequency of acidosis in adult diabetics with than without retinopathy and nephropathy. Wilson, Root and Marble[4] found a higher frequency of acidosis in juvenile diabetics with than without retinopathy. In extremely rare instances, retinopathy or nephropathy morphologically identical with those of the diabetic have been found in nondiabetics.

Rich, Berthrong and Bennett[5] discovered that renal lesions resembling those of the Kimmelstiel-Wilson nephropathy could be produced in rabbits in a period of 2 to 3 weeks by the administration of 7.5 mg. of cortisone in daily intramuscular injections. Rich[6] found typical Kimmelstiel-Wilson nephropathy in a nondiabetic patient who had been subjected to very prolonged corticotrophin (ACTH) therapy. Naquin[7] has noted the appearance of retinal capillary aneurysms in nondiabetics under corticotropin treatment. Friedenwald and Becker have found that alloxan diabetes in rabbits predisposes these animals to the capillary lesions elicited by cortisone and corticotropin. They have,[8] therefore, suggested that the retinopthy and nephropathy of the diabetic may be the consequence of an increased secretion of cortisone