American Association of the Advancement of Science. In this address he succintly described Rubner as having ". . . the power of arriving at great results through simple means, and of drawing correct conclusions from a few well-conducted experiments." Lusk considered Rubner the greatest man he had ever known.

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CORRESPONDENCE

To the Editor:

In an article which appeared in the November-December 1956 issue of DIABETES, H. S. Seltzer *et al.* state that glucose tolerance curves in which initial hyperglycemia is followed by a fall of blood sugar to hypoglycemic levels are diagnostic of mild diabetes mellitus, and that the hypoglycemia recorded in such curves constitutes an early manifestation of the diabetic state. Such interpretation of initially high glucose tolerance curves seems to me unjustified and fraught with the danger of making the diagnosis of diabetes mellitus in a number of nondiabetic subjects who may exhibit this type of blood sugar response to oral glucose loading.

The significance of glucose tolerance curves with an early excessive elevation of blood glucose and a secondary hypoglycemia has been a matter of concern for a number of years and, for the sake of proper historical perspective, it should be pointed out that such curves were first reported by Seale Harris in 1924.[1] Although he was aware that the curves may appear diabetic during the first three or four hours of the test he considered patients with this type of tolerance curve as potential, but not real, diabetics.[1, 2] A similar view was recently voiced by Skillern and Rynearson[3] who regard such curves as indicative of latent diabetes, while a position similar to that of Seltzer *et al.* was taken about a decade ago by Zondek et al.[4] who expressed the belief that such curves represent "joint occurrence of hyper- and hypoinsulinism."

In referring to my observations on glucose tolerance curves with initial hyperglycemia and secondary hypoglycemia[5, 6] Seltzer et al. make an entirely unfounded statement in saying that I have overlooked the existence of diabetes in such cases and have applied to them an erroneous diagnosis of functional hyperinsulinism. The fact, however, is that the diagnosis of diabetes in these cases was not overlooked, but simply ruled out for a number of reasons that were considered in great detail. Thus in my paper on "Clinical versus Laboratory Hypoglycemia"[5] in which thirty-three such curves were analyzed, I have brought out that: a. in seven curves the two-hour blood glucose readings were only slightly higher than normal; b. in nine the blood glucose values fell at first to 100 mg. per cent or less, and then rose to reach higher levels (so-called rebound curves); c. in none of the thirty-three tests did the peak glucose concentration in the capillary blood exceed the normal values; and d. in all thirty-three a fall to subnormal levels occurred in the second phase of the test. I have therefore concluded that "These findings do not support the diagnosis of diabetes, a condition in which the disorder of carbohydrate metabolism is reflected in a high, prolonged tolerance curve.

It is well known that hyperglycemia confined to the first two or three hours after administration of the loading dose may occur in various conditions unrelated to diabetes, such as the dumping syndrome, peptic ulcer, liver disease, hyperthyroidism, et cetera. For this reason, in absence of clinical manifestations of diabetes, an initially high glucose tolerance curve is not necessarily diagnostic of diabetes. A scrupulous search for the various conditions which may give rise to initial hyperglycemia in glucose loading tests was made in my material, but from the data presented by Seltzer et al., it appears that in their series only routine liver function tests were carried out with regard to the differential diagnosis of diabetes.

Another important point in the interpretation of initially high and secondarily low glucose tolerance curves is the fact that the curve pattern may vary in the same subject from one test to another. Seale Harris[2] stated: "one glucose tolerance test is not always sufficient to warrant a positive diagnosis of hyperinsulinism since there seem to be periods when the hyperinsulinism patient will have normal blood sugar readings, even though at other times he has shown marked hypoglycemia." My observations, on the other hand, show that the initial hyperglycemia of glucose tolerance tests

may also be replaced by a normal elevation of the blood glucose in a repeat tolerance test taken under identical dietary conditions. Lastly, Smelo[7] reported that in repeat tests carried out after a preparatory high carbohydrate diet there is a shift of the initial hyperglycemia toward or to normal values. It is therefore clear that the failure of Seltzer et al. to obtain repeat tolerance tests precludes any definitive statement concerning the diagnosis of diabetes in their patients.

In his early observations on hyperinsulinism, Harris suggested that prolonged excessive work of pancreatic islands may result in a deficiency of insulin secretion, that is, in diabetes.[1] The literature, however, records only one case[8] in which a patient with an initially high and secondarily hypoglycemic glucose tolerance curve developed diabetes within a comparatively short period of time (six months). According to Seltzer et al. several of their patients progressed to the stage of obvious diabetes, but long-range observations of Smelo[7] indicate that the development of overt diabetes in patients with such curves is roughly what it is in the general population. Clearly, it is highly unlikely that all patients reported by Seltzer et al. will one day become true diabetics.

As for the contention of Seltzer et al. that I have applied to my patients with an initially high glucose tolerance curve the diagnosis of functional hyperinsulinism, a glance at table 2 of my paper[5] will show that only four out of thirty-three such curves were recorded under the heading of spontaneous hypoglycemia and the remainder were diagnosed in relation to the clinical conditions which may be accompanied by spontaneous hypoglycemia or mimic the hypoglycemic syndrome.

The correction of statements made by Seltzer et al. about my observations is, of course, less important than the central point on which their own paper is based, that is, that their patients had at the same time both spontaneous hypoglycemia and diabetes. For reasons discussed above, I hold the view that they failed to establish the existence of diabetes in their patients, and I should like to present a strong plea against making the diagnosis of diabetes, a condition which stays with a patient for the rest of his life, exclusively on the strength of a transient hyperglycemia in but a single glucose tolerance test.

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To the Editor:

CONCERNING TRAUMA AND DIABETES

The more I think of the association of trauma with diabetes, the more I am concerned with it and, like Oliver Wendell Holmes, feel that "I am too much in earnest for either humility or vanity."

So far as I am aware, there is general agreement that trauma causes diabetes only when the pancreas is severely injured. The number of such cases which are accepted as reliable do not exceed a half dozen. However, the possibility has arisen that a latent diabetes might be accelerated and its appearance made manifest following an injury. No such instance has come to my attention among the 49,000 patients under our care since 1897, with sugar in the urine, of whom approximately 85 per cent are proved diabetics. I recall no such instance developing among their relatives, although constantly my colleagues and I are seeking to demonstrate an increased heredity in our patients, because we know at the first visit only about 20 per cent show a positive heredity, but after fifteen or twenty years of the disease this may be doubled and in the thirty-year duration cases of diabetes, trebled. Moreover, on our history sheets in two places we have the word "Trauma" printed, with the rule that a positive or negative finding should be recorded. I might also state we have many cases of trauma in connection with injuries to known diabetics and, because legal inplications frequently arise we take unusual pains to record details for use in court.

Believing all diabetes is hereditary, it can be accepted that latent diabetes occurs only in an individual who is hereditarily predisposed to it and has a diabetic gene even if the heredity is not proved. Overweight, pregnancy, an infection, involvement of thyroid, pituitary, adrenal glands or the liver are often precursors of dia-

betes. As time has gone on, fewer and fewer cases have been reported in which a doctor has thought an accident was followed by diabetes. Years ago, in order to be fair-minded to those who might differ with my own conviction that accidents do not cause diabetes, I stated the opposite side of the question in such a liberal fashion that it almost invited anyone to take it. Despite this it has not led to the publication of such instances.

In approaching the problem, I think one should remember that about 40,000,000 persons, one-fourth of the inhabitants of the United States, have a relative with diabetes and are thus hereditarily predisposed to it; that accidents are increasingly common and increasingly investigated; that no increase of diabetes was noted in Germany, France, England or the United States following and during the World Wars, either in the Armed Forces or in the civilian population (I personally saw but two cases at Mesves and after I left but one more was reported among these 35,000 soldiers who were within one day of the firing line); that no known diabetes has occurred following an injury in Harvard athletics; that Dr. Harvey Cushing, Dr. Gilbert Horrax and Dr. James L. Poppen have noted no case following operations upon the brain; that Dr. Donald Munro has seen no such case in accidents to the head coming under his observation. Indeed, so far as neurogenic diabetes is concerned, von Noorden said this was buried as a result of the first World War. It is not reported in suits for divorce and I have heard of no instance of a criminal awaiting execution who developed diabetes. Does a surgeon, doctor or a dentist put off an operation with the thought diabetes might appear?

Jacobsen demonstrated that trauma frequently led to glycosuria and increased sugar in the blood, but in his 140 cases this was always *temporary*. Therefore, a latent diabetic would not become a permanent diabetic because of trauma because diabetes would always revert to its former latency.

The mere fact that an individual has shown a trace of sugar in the urine one or more times in the past by no means proves it was due to diabetes. Probably if all specimens of urine of an individual were examined for a week, at least one of these would show a positive test for sugar. Furthermore, one must never forget that if individuals live on a low carbohydrate diet and after a week are given a glucose tolerance test, glycosuria or hyperglycemia or both temporarily may result.

Case No. 13,332, a 14-year-old Jewish boy, slept all night Christmas Eve in 1934 but the following night rose six times to void urine. When I saw him seventeen days later the urine contained 8 per cent sugar. No trauma, physical or emotional, occurred on Christmas Day.

I am writing this letter because I may have been overconsiderate in stating the opposite side of the question, although inspection of the context and conditions published in my original papers would make my position clear that an accident does not cause diabetes; second, my experience with diabetics is so great that I feel it my duty to report it; and finally, because of the handicap which would attach to one-fourth of the population of the country and all known diabetics and their relatives if it were considered likely that they would become diabetic if they underwent an injury.

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BOOK REVIEWS

DIABETES MELLITUS: HANDBOOK FOR PHYSICIANS. *By Howard F. Root, M.D., and Priscilla White, M.D. $7.00, pp. 346, Landsberger Medical Books, Inc., distributed solely by the Blakiston Division of the McGraw-Hill Book Co., New York, 1956.*

This new publication admirably achieves its objective in being an excellent book on diabetes with a detailed outline of the treatment both of the disease and the complications arising therein. It is clearly and concisely written so that "he who runs may read."

While the section on diet and diet therapy may be somewhat long the summary of the different types of insulin, their duration and mode of action is excellent.

The section dealing with acidosis and its management is clear and comprehensive.

Correctly the authors have devoted considerable time, thought and space to the management of complications of neuropathy, eye and skin. The results of their wide and varied experience are summarized and an evaluation made of the current best methods of management and treatment.

Since it has been estimated that one of three diabetics becomes a surgical patient sometime in the course of his disease, the surgical management of the diabetic is timely and well conceived.

The chapter on pregnancy in the diabetic is extensive and although there is considerable difference of opinion among experts now as to the value of hormone therapy in the pregnant diabetic, certainly Dr. White's statistics are very convincing.

The pages devoted to children born to diabetic moth-