Special Article

Diabetes in the Future

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Tennyson in *Locksley Hall,*

". . . dipt into the future far as human eye could see;
Saw the Vision of the world, and all the wonders that would be";

and it is as natural for us all to do the same even though our predictions will not be as perfect as his when he,

"Saw the heavens fill with commerce, argosies of magic sails,
Pilots of the purple twilight, dropping down with costly bales; . . ."

Indeed, Dr. Best only two years ago indulged in "Crystal Gazing: The Future in the Field of Diabetes."[1] In reading what he had to say, most of all I am impressed by the multitude of hints and opportunities for research which his paper contains. These actually run into the hundreds. The future is replete with problems and far more than we clinicians imagine. Even the incidence of diabetes is largely unknown. His ideas count far more than his prophecies, pleased as we are to learn what he predicts. It is a sobering thought to realize, as Dr. Best points out, that we have only to increase somewhat the severity of our tests for diabetes to discover that practically all of us are potentially diabetic. There is a limit to the quantity of sugar we can tolerate without its escape in the urine. Think of what this signifies for the prevention of diabetes and its prediabetic phase. Then he predicts insulin will be made synthetically; that an oral insulin is quite possible; and suggests how the absorption of the insulin molecule can be prolonged and also that a store of insulin which has accumulated in one part or another of the body may be drawn upon according to need. Especially does he urge research for the discovery of a stimulant to insulin formation. Attention is also called to the fact that many of the tissues may vary much in their need for it, just as now the brain utilizes carbohydrate without it. Dr. Best's comment on the pathology of the pancreas is noteworthy because a year or two ago one might have said that in 25 per cent of the cases of diabetes no histologic changes in the pancreas could be found; in another 25 per cent they were present and in 50 per cent indefinite. Today as a result of the work of Maclean and Ogilvie[2] and quite recently of others, especially Gepts[3] of Belgium, one feels assured that in all cases of diabetes, alterations in the islands of Langerhans exist and indeed there are hints not only that hyperplasia of these can take place but even regeneration, with all that implies. We certainly should give credit to Weichselbaum[4] and our own Dr. Cecil[5] who in 1909 and 1910 both reached much the same conclusion, although for years their work was passed over.

As for my own ideas upon diabetes in the future, they are more prosaic but they are facts I have been able to gather in a lifetime.

First of all, it is safe to say there are to be many more diabetics in the future than in the past simply because diabetics are living so much longer; indeed, between 1897 and 1914 my fatal cases had lived 4.9 years but at present the average for the group is eighteen years. Children with onset in the first decade of life survived 1.2 years but now twenty times as long, or twenty-six years, and by far the greater number of the children in our juvenile group are alive. Only last year I found that 131 of our patients had had diabetes over forty years. It was noteworthy in this group that there were more men than women, but this was partly to be explained because many of these were discovered by life insurance examinations, usually in an early stage and more males than females sought insurance. That group of patients always has lived longer than the average probably because its presence was discovered nearer its onset. Furthermore, there were many doctors and that has always been a cheering thought because it showed that a knowledge of the disease helped in extending longevity. The results are shown in table 1 and table 2. Here also in these tables are hints for the future because these 131 cases developed their diabetes two years before the discovery of insulin.

There will be more diabetics in the future because today so many diabetics conceive. Bouchardat,[6] the most noted diabetes clinician of all time, wrote in 1875 and again in 1883: "Women who have diabetes very rarely become pregnant. Among a very considerable number of diabetics who have consulted me, I do not remem-

TABLE 1

Duration of life subsequent to onset of diabetes among deceased patients in Naunyn era (1897-1914) and Best era (1956-1957)

	Naunyn era		Best era	
	Number of cases	Average duration	Number of cases	Average duration
	326	4.9 years	640	18.2 years
Ages				
0- 9	24	1.3	30	26.4
10-19	39	2.7	52	23.5
20-39	85	4.3	91	25.1
40-59	126	7.0	304	18.7
60 and over	51	4.4	159	10.2
Unknown	1	—	4	—

Tables 1 and 2 were prepared by the Statistical Bureau of the Metropolitan Life Insurance Company and aided by a grant from the Department of Health, Education, and Welfare, United States Public Health Service, National Institutes of Health.

TABLE 2

The changing average age at death and average duration of diabetes in two important eras of treatment

Era	Number of deaths	Average age at death, years	Average duration of diabetes, years
Naunyn:			
1897 to 5/31/14	326	44.5	4.9
Charles H. Best:			
1/1/50 to 12/31/55	4,376	64.7	15.6
1/1/56 to 12/11/57	640	64.7	18.2

ber to have seen a single pregnant woman." Today in our series we have approximately 2,000 pregnant women. Of this number, Dr. Priscilla White with her colleagues at the Faulkner and Boston Lying-In Hospitals have studied 1,225 meticulously. At first there were only about fifty-five mothers in 100 who delivered living children but now the number has risen to eighty-seven in 100. Abortions and miscarriages were common early in this century but today are rare. Indeed, this last year Dr. White tells me that during 1959 no patient was advised to have an abortion. Even those diabetics who formerly were considered in too serious condition to go on with their pregnancy now are allowed to do so. Class F, the severest group of her series of patients, once included 5 per cent of all the diabetic pregnancies but today it has doubled to about 10 per cent. In January 1960, one pregnant woman, thirty-one years old, with diabetes of twenty-nine years' duration, blind and with impaired kidneys, was delivered at the Boston Lying-In Hospital of healthy twins who are living today. She was carried to the thirty-fourth week of her pregnancy. Another woman who was also blind, in February 1960 also was delivered of a healthy baby. The pregnancy in each of these two cases did not appear to have any deleterious effect on the kidneys of the patient.

We are all learning much from the pregnant diabetic. Years ago it was noticed that the offspring of pregnant diabetic women were often large. Furthermore, it was observed that the babies of such women had large islands of Langerhans in which there was evidence of regeneration. The earliest case of a huge baby was that reported by Bennevitz[7] in 1824 in which was the sentence, "It appeared as if Hercules was the father." With ninety-five depancreatized male rats in Houssay's laboratory it was shown that injections of female hormones would delay the development of diabetes. Dr. White has observed that those of her cases who have taken hormones throughout the pregnancy require somewhat less insulin than before delivery and less than in the control group which took no hormones.

Realizing that diabetics today conceive and bear many children, the question arises whether they will pass on to their descendants a diabetic heredity. How important this is in a patient like Mrs. D., a diabetic who has fourteen living children and forty-five grandchildren. Think of the growing number of individuals with an hereditary condition, and with their increasing duration of diabetes, thus favoring their passing on the disease.

Frankly, I think all diabetes is hereditary. My reasons are: 1. That when I questioned each case of a hundred seeing me in succession at the office during 1959, I found that sixty patients knew of a diabetic heredity. These patients supposedly would live five or ten years or longer, and during that period thus furnish the possibility for a higher percentage of this manifestation of heredity. Among our Quarter Century Victory Medal diabetics with their diabetes now over thirty-four years' duration, the evidence of heredity of diabetes also amounts to more than 60 per cent.

With our series of identical twins, 48 per cent of the number developed diabetes in both twins whereas among the dissimilar twins only 3 per cent. Dr. White, in a study of the relatives of diabetic children, found five times as many cases of diabetes as were present in the relatives of a nondiabetic control population.

Inherited patterns take time to show themselves. Dr. N. developed his diabetes in 1900 and in 1908 I found no evidence of its inheritance in his family and indeed it did not appear through his lifetime ending in 1920. Last year, his son developed diabetes approximately sixty years after his father. When I read in a history which has obviously been taken quite casually,

"no diabetic heredity," I often think of Dr. N. and how after waiting nearly sixty years heredity was demonstrable.

Another factor responsible for the increase of the number of diabetics in the future is the aging of our population. Diabetes occurs most commonly between forty and sixty years of age. In 1870 the average age at death in the United States was twenty-five years but now is 61.8 years and the expectation of life is 69.8—reaching a peak in 1959. This is important because three fourths of the diabetics have their onset after forty years of age.

Women who have children were recognized long ago to have a greater chance of becoming diabetic than single women. Indeed the frequency of diabetes in married females has increased to twice that of single women between forty and sixty years of age. The incidence for single women is about the same as for males. Perhaps a part of the reason may be that married women weigh more than single women but that is not the whole explanation. New data are needed on this point.

Another observation made in the last year—although not directly bearing on this point—was that I ran across twenty-eight women who had given birth to one or more babies weighing twelve or more pounds. All of these women later developed diabetes. Among them, Mrs. B. had fourteen children, twelve of whom are now living. Her diabetes was discovered twenty-nine years after the birth of her twelve-pound baby. In four other mothers the interval was twenty-five to thirty-three years. The average number of children born to each of these mothers before they developed diabetes was five. Three had ten or more children and three had 13, 15 and 34 grandchildren respectively. The average duration of diabetes in the mothers was sixteen years and the average age at which it developed was forty-seven years. The weights of the mothers in this series were high, thirteen of the twenty-eight exceeding 200 pounds. Only one of the entire number was underweight. Inheritance of diabetes for twenty-four of the twenty-eight mothers in which it was known was 66 per cent.

Boulin had the right idea when he inaugurated his prediabetic clinic in Paris. To this came those who were overweight and were lacking in exercise—the cases described by Katsch as "civilization" diabetes; patients with marked heredity; those who were pregnant.

Overweight is the one factor which stands out so prominently in diabetics. When I studied 1,000 cases of diabetes and calculated their weights compared with standard weights and heights, I found that even with patients with onset in the third decade, only 10 per cent were ever underweight; in the fourth decade, 5 per cent, in the fifth decade, 3 per cent and in the sixth (between fifty-one and sixty years of age) of the 252 patients there was only 1 per cent whose weight was below standard. In one way or another this table is duplicated. Today we know that with the new calculations of the Insurance Actuarial Boards, that our population in general is approximately 15 to 20 pounds overweight. This applies not only to men but to women. The one factor which all doctors can emphasize in the prevention of diabetes is the avoidance of overweight, particularly in the families of diabetics during pregnancy and also in the Jewish population. It is striking today to see how this idea is spreading. How rare it is to find a young Negress who is overweight in contrast to a few years ago when statistics showed that Negro women in New York City had a higher percentage of diabetes than white women. It is fortunate that one is safe in urging reduction in weight because not only is it advantageous for diabetes but for vascular disease as well. A century ago, Bouchardat recognized this by telling his patients to earn their bread by the sweat of their brow. One patient between the ages of ninety and 100 who feared she would fall on the slippery streets in the winter, solved her problems by a stationary bicycle which she uses three times a day.

A revolution has taken place in the causes of death of diabetics. In the last century and even in large city hospitals in the first part of the present century, tuberculosis caused half of the deaths of diabetics. In the years 1897 to 1914, 64 per cent of our patients died of diabetic coma. Today tuberculosis in our group has practically disappeared (0.2 per cent), and death from coma among our patients has declined to 1 per cent although among hospital patients admitted in coma the mortality is nearer 3 per cent. Gangrene has fallen from 8 to 2 per cent and infections from 14 to 4 per cent. In contrast, disease of the blood vessels in the kidneys, heart and brain has risen from 18 per cent to 78 per cent. Renal disease has advanced from 3.4 to 11.3 per cent and cardiac diseases have risen from 6 per cent to 50 per cent; cerebral arteriosclerosis from 2.8 to 12.5 per cent. On reviewing the past and present it is certainly not logical to believe that the causes of death which are prevalent today will be the same in the year 2,000. Complications in the eyes are spectacular. Of the 874 individuals certified for blindness by the Commonwealth of Massachusetts between July 1,

1958, and June 30, 1959, diabetics numbered 148, exceeding all other groups. A hint that it can be avoided is shown by our ninety Quarter Century Victory Medal cases because in these patients, even after twenty-five years of diabetes, there was no involvement of the eyes when examined by specialists.

Our methods for the prevention and early discovery of diabetes in its preclinical stages should be greatly expanded. We should enlist all state medical societies, all doctors, all hospitals in the task. There should be a concentrated effort upon the relatives of known diabetics, particularly upon those above thirty years of age and especially upon all fat individuals. If each doctor would examine the urine of ten additional patients, and better still, secure analyses of the blood, consider how many new cases of diabetes would be found. Perhaps the most practical way would be to subsidize our private and public laboratories so that the tests would be free to all.

Having discovered the diabetic and prediabetic then one can treat and protect him. Today we know that control of the diabetes pays.

As yet no one has met our criteria for the Quarter Century Victory Medal whose diabetes was not controlled, particularly in its first year. These Medal cases were the reason for our Hospital Teaching Clinic where patients can be taught control of the disease and prevention of complications and by self-service at greatly reduced hospital expense.

REFERENCES

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EDITORIAL

HYPOGLYCEMIC INSULIN REACTIONS WITHOUT WARNING SYMPTOMS

Hypoglycemic reactions due to the administration of insulin in diabetic patients, although usually harmless, may pose a major problem in patients who have unstable diabetes of long duration. The physician accustomed to combating hyperglycemia with keto-acidosis may well say, "A plague on both your houses," since unconsciousness occurs in this state as well as with hypoglycemia. However, the serious feature of hypoglycemic reactions recently stressed by Balodimos and Root* arises from the fact that these reactions sometimes occurred without the patient being aware of the usual warning symptoms. Patients of this group had learned to know the characteristic warning symptoms such as tremor, sweating, hunger or diplopia through many years of insulin administration. However, a stage was reached in which none of the usual symptoms was recognized. Patients continued to work automatically or became irrational, pugnacious, or even unconscious. These changes often occurred with striking suddenness. A series of sixty males and fifty-six females was reported among patients with long duration of diabetes treated with insulin. The average duration was eighteen years. The insulin dose varied from less than 20 units daily to 60 units. The series did not include patients who had reactions during sleep.

It did not seem that either the error of taking extra large doses of insulin or simple inattention to symptoms provided an explanation. The blood sugar levels were not strikingly different from those in other patients who had ample warning of approaching reaction.

Retrograde amnesia for periods varying from three minutes to one hour before the actual reaction was a feature in most of the patients. Electroencephalographic studies did not usually give any characteristic findings although some changes were observed in the tracings. The possibility that these reactions are actually epileptic

*Balodimos, M. C., and Root, H. F.: J.A.M.A. *171*:261-66, September 1959.