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A HALF-CENTURY'S EXPERIENCE IN DIABETES MELLITUS*

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In the last fifty years the duration of life of my diabetic patients has trebled, and in the next fifty years I believe it can be doubled even if there are no new discoveries. To attain this end it is essential that at each visit of a patient to a doctor the diabetic treatment and control of the disease be reviewed, revised, and improved and a careful search made for complications, diabetic and non-diabetic, which, if found, should be corrected.

The results of treatment of 10,673 of the fatal cases, among more than twice as many proved diabetics of the 35,597 who have consulted our group for sugar in the urine between 1897 and April 27, 1949, are shown in Table I. It is apparent that the average duration for all ages has advanced from 4.9 years in the Naunyn era, 1897–1914, to 14.4 years in the Best era, 1944–9. During this period the average age at death has risen from 44 years to 64 years and the life expectancy for each age group of all cases, fatal and living, is approximately three-fourths that of the general population of similar age.

TABLE I.—*Average Duration in Years of Life of Diabetics from Onset of Diabetes to Death in Successive Eras of Treatment*

Age at Onset (Years)	Naunyn Era, 1897–1914	Allen Era, 1914–22	Banting Era		Hagedorn Era, 1937–43	C. H. Best Era, 1944–9
			1922–9	1930–6		
All ages ..	4·9	6·1	8·0	10·4	12·5	14·4
Under 10 ..	1·3	2·9	2·8	7·3	10·3	18·3
10–19 ..	2·7	2·7	3·4	7·5	11·5	15·6
20–39 ..	4·3	4·9	8·9	14·4	16·9	18·7
40–59 ..	7·0	8·0	9·5	11·7	13·8	15·6
60 and over	4·4	6·4	5·5	7·1	8·8	9·4

Table I shows that the longest duration of life in the present era has been 18.3 and 18.7 years for those in whom the onset occurred under 10 years of age and between 20 and 39 years respectively. But the most important figure in this column is that for the group with onset in the second decade of life, because here the average duration was only 15.6 years, which relatively for their expectation of life is the lowest of all. There is little reason to suspect that diabetes is most severe in the second decade, and my only explanation for the short duration of life of our fatal cases in this period is the reaction of the adolescent to the method of treatment he has received. It constitutes an indictment of us doctors for not making it better.

Duration of Life of Diabetics Can Double

May I now submit reasons to explain why the duration of life of the diabetic can be doubled in the next fifty years? This is indicated, first, by a compilation of the statistics of our fatal cases by the Metropolitan Life Insurance Company, which has shown that already 24.1% have lived over 20 years; secondly, that 2,000 of the 30,000 diagnosed diabetics have already attained their full life expectancy; indeed, a few have attained twice their life expectancy.

Thirdly, other evidence has recently been accumulated by Dr. Ruth Reuting, of our group, who has followed up a series of 50 of our patients who had been diabetic for five years, originally studied by Dr. H. Clare Shepardson (1930): 19 of these patients died, with a duration of life of 17 years, and 31 are alive, with a duration already of 27 years. Reports from the living indicate that they have many years of health ahead. It will be difficult to double the duration of life of patients in whom the onset occurred above the age of 61, because it will mean that at the very least they must not only live longer but twice as long as they would have done had they been non-diabetic. On the other hand, to offset such handicaps we have 2,145 patients whose diabetes began when they were children. As an illustration of this possibility I would cite the fact that already 12% of these have lived 25 years, 4% 30 years, and a moiety even 35 and more years with their diabetes.

Fourthly, convincing proof of the possibility of doubling the present duration of life of diabetics is furnished by the 14 living instances of patients—recruited with one exception from those in whom the disease began at under 20 years of age—who have had the disease for 25 years and on meticulous examination are physically sound, free from eye complications as certified by ophthalmologists and from degenerative changes in the arteries as certified by radiologists.

Causes of Death of Diabetics

The causes of death have greatly changed in a half-century. Diabetic coma has been almost abolished. In a recent article, Duncan *et al.* (1949) record that for two years no death from coma has occurred at the Pennsylvania Hospital, in Philadelphia. At the Massachusetts General Hospital, I understand, only one death has occurred in two and a half years. We recently had a record of 92 successive cases of coma treated without a death, but I confess that since that time several fatalities have occurred, but we are trying to better this.

Among the 10,673 total deaths, the fall in diabetic coma as a cause is striking (see Chart and Table II). At first two-thirds of our patients died of it—and that proportion

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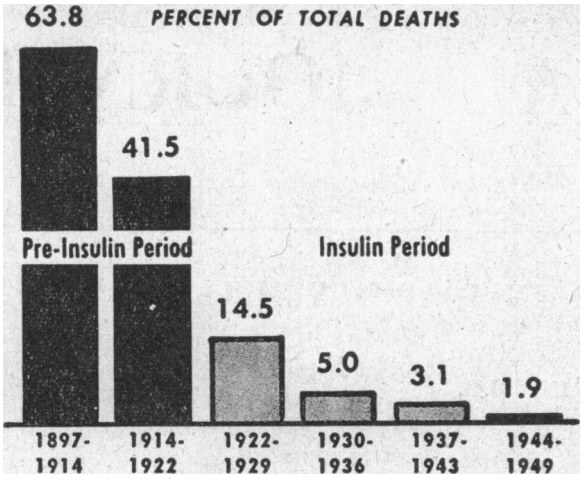

Chart showing decline in coma as a cause of death. (Experience of George F. Baker Clinic. Analysis by Metropolitan Life Insurance Company.)

TABLE II.—*Causes of Death*

	1897–1914	1914–22	1922–9	1930–6	1937–43	1944–9
All causes	100·0	100·0	100·0	100·0	100·0	100·0
Diabetic coma	63·8	41·5	14·5	5·0	3·1	1·9
Cardiovascular–renal diseases	17·5	24·6	46·8	58·3	65·0	70·1
Gangrene	3·7	4·2	8·6	7·6	5·1	3·1
Pneumonia and influenza	4·0	7·2	7·6	5·9	5·5	3·6
Other infections	3·4	5·5	8·6	6·4	5·4	3·1
Tuberculosis	4·9	4·9	5·5	3·4	2·5	2·1
Cancer	1·5	3·8	7·4	9·4	8·8	8·9
Other and unknown	4·9	12·4	9·6	11·6	9·8	10·3

was essentially the same as that recorded by von Noorden. Now, of the 2,299 deaths between 1944 and 1949, only 1.9% were from coma. This attainment reflects the change in treatment, but, to me, still more does it demonstrate the general practitioner's advance in knowledge, because almost without an exception, as Petrén observed some 40 years ago, diabetic coma originates outside rather than in the hospital, and it is the general practitioner who by his alertness, accuracy of diagnosis, and promptness in giving initial treatment has done so much to bring about this decline. My colleague Dr. Howard Root pointed out that our death rate in patients arriving in diabetic coma was to a large extent so low because the family doctor had given insulin before the patient was placed in an ambulance. Coma still occurs, but it is avoidable and usually amenable to treatment.

Tuberculosis now causes only 2.1% of our deaths ; indeed, it never caused more than 5.5%. However, tuberculosis still exists, as was recently shown by an analysis of the Shepardson group mentioned above, in which 14% of the 50 patients, 10% of the fatal cases, and 4% of the living showed it, the two living cases having been successfully operated upon and being now at work. I was told last summer that tuberculosis caused nearly 50% of the deaths in public hospitals in Paris and Birmingham, but the drop in tuberculosis in the general population in Europe has been so rapid in the last two or three years that I expect that it will soon be reflected in diabetes. Tuberculosis in our group has been most common in the patients recovering from coma. At one time, one out of five such patients developed it within three years, but here again it may be largely due to the fact that the individual who develops coma is the underprivileged, undiagnosed, and neglected diabetic, and so the one most likely to succumb to tuberculosis. To-day we are recognizing tuberculosis in our old and long-duration diabetics. Our most recently detected case was that of a patient aged 77 with diabetes of 20 years' duration. Her husband had died from it.

Infections once claimed 8.6% of our diabetics, but the proportion is now only 3.1%. Years ago, because of a remark of a well-known clinician that he had never seen one diabetic with pneumonia get well, I published the cases of a series of diabetics who had so recovered. To-day recovery is the rule, but a man aged 40 who had had diabetes for eight years and who entered our clinic in diabetic coma on December 15, 1949, died with massive bilateral pneumonia. Under infections I include not only general infections such as pneumonia but local infections such as appendicitis with its insidious and unobtrusive development, carbuncles for which an operation is almost obsolete, and many others.

Deaths from cancer have risen from 1.5% to 8.9%, and with good reason, because the patients are exposed to it for three times as many years and because they die at 64 instead of at 44. Cancer in a diabetic should be recognized earlier than in a non-diabetic, and the mortality from cancer in diabetics should be lower than in the non-diabetic population. No class of patients consult doctors over so long a period and so often as the diabetics. The routine visit of a diabetic takes time and thought if the doctor wishes his average patient to live more than 14.4 years.

The mortality from arteriosclerosis and cardiovascular–renal diseases has replaced and exceeded that from diabetic coma, and in the recent survey it reached 70.1%. Arteriosclerosis is not hopeless. First, we have our long-lived cases ; secondly, we have our patients with gangrene, which has decreased from 8.6% to 3.1%. Recently Barach (1949) referred to a mortality for amputations above the knee of 47 and 45% in a large city, but McKittrick *et al.* (1949) and his group in Boston have lowered this to 6%. Dr. Priscilla White's (1949) series was suggestive for those who had had diabetes for 20 years after an onset in childhood, and her figures have been corroborated by Root (1949), who studied an older series in which the disease started at between 15 and 30 years of age. Both agreed in showing that patients whose treatment was lax are most likely to develop arteriosclerosis, but among those who have been carefully treated it was far less common.

These statistics indicate that research in the prevention of arteriosclerosis should be carried out primarily in diabetics with a premature tendency to it, and especially in those in whom diabetes began before the age of 25, so that they can be followed up until they reach that period in life when arteriosclerosis begins to be routine in the general population. Here again the emphasis is on the success of treatment of the young diabetic, because in this group one can measure results.

Follow-up

In the follow-up of our 2,145 living child diabetics at the beginning of 1949, 33 deaths were reported. The causes of death in five cases are not yet known to us. Three (9.1%) of these deaths were caused by tuberculosis, showing the necessity for annual *x*-ray examination of diabetics and bringing up for discussion the possibility of B.C.G. prophylactic treatment of those with tuberculin-negative reactions. Please notice that this incidence of tuberculosis is high among the fatal cases, the neglected cases. Five (15.1%) of the deaths were from coma, indicating the irresponsible course of life of these young individuals. Two (6.1%) were due to accidents, not to hypoglycaemia.

The overwhelming cause of death was the cardiovascular–renal diseases, which accounted for 18 (54.5%) deaths. This shows the chief enemy which the young diabetic must face and the enemy you and I as general practitioners must combat. These young patients must in some way or other be told that if they do not keep their diabetes controlled they are liable to serious complications in their eyes, their kidneys, their hearts, or their brains. We can always offset this serious advice by emphasizing that those who are perfect after 25 years are in general those who have followed treatment the best.

Treatment

It is for the general practitioner to-day to make treatment of the patient as safe in his home as it is in hospital. This cannot be done unless the patient is under supervision. Whether one should say that the patient must report every three months or get another doctor is something for us to consider. Patients get tired of us doctors. We do not always give them something new at each visit, and, if we are holding a diabetic in bounds, that must be done. It means hard work, time, and interest. In treating diabetes in the home the family doctor has a great advantage over those who treat in hospital. At home the patient can have an early breakfast and a late supper, and not be under eight-hour labour rules—breakfast at 8 to 8.30 a.m. and the evening meal at 5 to 5.30 p.m. In the home he can have the advantage of exercise, and that is so difficult in hospital. At home one can plan for continuity of treatment and enlist the support of the entire family. To do this the doctor must more and more secure the help of the less expensive nurses' aides who can be taught to carry out minor duties and assume a part of the teaching.

The treatment of diabetes to-day is by no means as puritanical as at the turn of the century or in the Allen era, 1914–22, when we literally starved a diabetic to let him live and later were rewarded for so doing; but it is still puritanical. I venture the thought that no one would now like to keep the carbohydrate in the diet of a diabetic under 150 g.; all would maintain fat at a level which will prevent overweight, and protein at from 3 to 1 g. per kg., according to the patient's age. All recognize that the diet must be spread out from an early breakfast to a late evening meal, and generally with a little carbohydrate lunch in the forenoon, afternoon, and on retiring, to promote utilization and avoid insulin reactions.

I have profited much from watching Dr. Priscilla White's diabetic girls who are pregnant. They are so anxious to have a baby they would not deviate from the prescribed diet one iota. They maintain weight, keep sugar-free, and live on 180 to 200 g. of carbohydrate, cheerfully taking insulin as needed, one, two, three, or four times daily. By subtracting from this diet the carbohydrate, protein, and fat which the foetus needs, we can find on what carbohydrate an inactive young woman can live happily and efficiently.

Insulin is needed for far more diabetics, as I see them, than is reported by some physicians. Far, far more than 60% of our cases depend for their lives on insulin, and even this figure is low for our diabetics above the age of 40.

Education of the Patient

Education is everything for the diabetic, and I cannot support too heartily the article by Dr. Russell M. Wilder, jun. (1949), of the Mayo Clinic. If possible, the patient should be under observation in a convalescent home or a hospital in the first few days, but if that cannot be carried out—and we have great difficulty in doing this ourselves—then one must pay frequent visits to the clinic for instruction and control during the first week. After the first week the patient's interest begins to wane. Strike, therefore, while the iron is hot. We must tell the truth and be sure that our patients know what they face.

Recently I have been receiving replies in answer to a follow-up of those whose onset occurred in childhood, and these are revealing. One who has had the disease 25 years writes that she does not want to go to a diabetic doctor in her large city, but wishes to have a general practitioner who will be interested in her general condition. Another dislikes a diabetic doctor who sends her to a laboratory some miles away without her breakfast in the morning for a blood-sugar estimation and telephones the result at night. She wants a family doctor. Another wants a grant to study abroad, but she has had no family doctor, and came to the clinic, without having been seen by us for several years, with a blood sugar of 464 mg. A young man whose family doctor had died came recently with two teeth in the upper jaw and six in the lower, retinitis, a liver four fingerbreadths below his costal margin, 200 mg. of albumin in his urine, and a story of ten beers a day. He was a dwarf in stature, and although 25.3 years of age and a diabetic of 19.9 years' duration he did not know how many units of insulin his faithful mother was giving him.

Another college boy replies that he feels well, has not seen a doctor for seven or eight years, asserts that his desire is for happiness, and wishes to complete his college course and get married. I wrote him: "Would you advise your sister to marry a diabetic who had not taken stock of his condition in the last ten years?" You see, the general practitioner truly has the future of the diabetic in his hands, and it is only through him and his detailed and continual emphasis upon controlling the diabetes that the duration of life of diabetics can be doubled. Diabetes cannot be treated over the counter. Cases like those I have cited cannot be handled by wholesale socialized medicine. The only hope for such people is the individual personality of the doctor integrated into the individual life of the young diabetic patient.

Increase in Diabetes

The appalling increase in diabetes which has come to our attention in the last year or two continues. I understand from the reports which will be published in a forthcoming issue of *Diabetes Abstracts* that the number of diabetics is steadily growing in the U.S.A. What is especially significant, however, is the lessening of the difference in incidence between the high mortalities reported in the North and the low mortalities in the South. In Oxford, Massachusetts, and Jacksonville, Florida, practically the same frequency of diabetes in the general population was discovered—1% in Massachusetts and 0.9% in Florida. We must remember that diabetes is universal and the distribution approximately the same if one makes allowance for sex, overweight, age, and the percentage of the Jewish race. Along with all the energy spent upon the detection drive, we should remember that it is of no use discovering new diabetics unless we are in a position to treat them.

We must ask for publication of methods of treatment, but care should be taken in stating how many of the cases have been followed up. As frank and helpful as are the results of Fanconi *et al.* (1948), the fact that 49 of 136

cases were untraced is a great disappointment. We hope that they were their best cases, but are we justified in drawing that conclusion ? It may cost a considerable sum per patient to secure information about these 49 cases, but it is more than worth while. Perhaps in sending out letters and trying to secure replies we should call to the attention of these young people that when they ask us to recommend them for jobs we cannot do so unless we know how they are getting along.

I am more sympathetic in completing follow-ups this year than heretofore. At the beginning of 1949 we had 2,145 known subjects living who had been diabetic from childhood. By September 1,258 had been traced. Despite our first, second, and third letters, 2,365 in all, there still remained 50 untraced, but I believe it is only fair to these people and to all of us doctors to learn whether the treatment recommended has been good or bad and to discover whether it could be improved. (By April 1 of this year there were eight untraced.)

Apollinaire Bouchardat, who was born in 1806 and died in 1886, was the first doctor to give hope to the diabetic. He prescribed a palatable diet, taught diabetics, even before Fehling's test was printed, to examine the urine after they ate and thus find out whether a food was beneficial or not. He urged them to take exercise and demonstrated its advantages. Yet Bouchardat (1883), in offering hope for the diabetics, qualified his statement so as not to include children, and wrote that he had never seen a pregnant diabetic woman and, indeed, hardly gives us a hint that he recognized diabetic coma. But he laid the foundation for the treatment we are practising to-day. How pleased he would be to see the advances made, and I can imagine he would agree with me that the next fifty years hold more of promise than the last.

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A special uniform is being produced by the Ministry of Health for the trained women members of the National Hospital Service Reserve to wear when on duty in hospital. The uniform is of white drill, and different coloured epaulettes and belts will be worn—dark blue for a State-registered nurse, maroon for a State-certificated midwife, green for a State-enrolled assistant nurse, and white for a nursing assistant class 1. The State-registered nurses and midwives will wear caps of the veil type, and the State-enrolled assistant nurses and nursing assistants class 1 will have white close-fitting caps with a turned-up brim in front. Male trained members will wear coloured epaulettes on the white coats provided by the hospitals. The Reserve also includes a section for auxiliary members, whose training is undertaken by the St. John Ambulance Brigade and British Red Cross Society. They wear the indoor uniform of these organizations while taking hospital training or refresher courses. The Reserve is open to women aged between 17½ and 60 and to men between 30 and 60. There are already over 200 trained members and 2,300 auxiliary members in England and Wales.

PROCAINE PENICILLIN: CHOICE OF PREPARATION

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The production of depot or repository preparations has been an important development in penicillin therapy. In view of the rapid excretion of penicillin after the injection of aqueous solutions, the usual method of administration has been by injection at frequent intervals. This is a tedious procedure, causing much discomfort to the patient and a heavy strain on the nursing and medical staff.

Many attempts have been made to overcome these objections. These have involved quite different principles : one scheme is to give large doses (up to 500,000 units) of aqueous penicillin at intervals of 8–24 hours ; another is to delay the renal excretion of penicillin by means of *p*-aminohippuric acid or caronamide ; a third scheme is to delay the absorption of penicillin from the tissues by means of depot or repository preparations. The last method has been mainly adopted in this country for prolonging the blood levels.

The original depot products contained a mixture of beeswax (4–5%) and arachis oil ; with doses containing 300,000 units of penicillin, effective blood levels could be maintained for 8–12 hours. These preparations, being very viscous, were not only difficult to inject but also tended to produce local pain and discomfort. In view of these serious objections the production of procaine penicillin was an important advance (Salivar, Hedger, and Brown, 1948). This preparation is an equimolecular combination of crystalline penicillin G and procaine hydrochloride ; it is a relatively insoluble compound and was originally suspended in arachis oil. Procaine penicillin causes little pain and is easier to inject than the beeswax products ; with the standard dose of 300,000 units, effective blood levels are maintained for 18–24 hours (Jones and Shooter, 1948). It was later found that the effect could be further prolonged by incorporating 2% (w/v) aluminium monostearate in the oily procaine penicillin (Buckwalter and Dickison, 1948) ; Boger and Flippin (1949) claimed that, after an injection of 300,000 units, effective blood levels were present for 4–6 days.

Young *et al.* (1949) tested various procaine penicillin preparations and considered that the monostearate product was superior to the watery or oily preparations for delaying absorption ; they considered that the particle size of the penicillin crystals should not be too large (5–20 μ), and recommended that for the treatment of severe infections the procaine preparation should be combined with a soluble salt of penicillin. Emery *et al.* (1949), using a monostearate preparation with a particle size of 5 μ, obtained satisfactory levels in children for 24–48 hours, but experienced some difficulty in administration owing to the oily nature of the preparation. Wayne *et al.* (1949) confirmed these results, and found that by increasing the dose to 600,000 units assayable blood levels were often obtained after 72 hours.

There is no doubt that procaine penicillin with aluminium monostearate is superior to previous preparations in its capacity to prolong the blood levels, but two important