DIABETES MELLITUS—A REVISED CONCEPTION OF ITS STANDARDISATION

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THE number of diabetics is increasing every year. The increased span of life of the diabetic—at least three times as long as a quarter of a century ago—the propagation of individuals with a diabetic heredity, as well as the more frequent diagnosis of the mild type of the disease, have all led to an increase in the total number. At the present rate of increase we shall, within the next ten to twenty years, be presented with a social problem that must eventually be boldly faced.

"Before 1914, both von Noorden and I each saw approximately two-thirds of our patients dying of diabetic coma, and even with the introduction of the theory of under-nutrition by F. M. Allen this mortality was only lowered to 40 per cent. by 1922." This was the experience of E. P. Joslin in America. The isolation of insulin in 1922 immediately lowered the appallingly high mortality rate of those diabetics who could not be standardised on diet alone. The hypothesis that diabetes was primarily due to defective production of a pancreatic hormone had been suggested by some investigators. Banting and Best brilliantly provided the proof and converted hypothesis into fact. Accordingly, it was hoped that simple replacement therapy would solve the diabetic problem. The aim of treatment was to imitate physiology as closely as was humanly possible. In order to achieve this, the common practice at first was the advocacy of a low carbohydrate diet; insulin was used unsparingly, if necessary, to lower the blood sugar as closely as possible to normal levels throughout the twenty-four hours and to prevent anything but the slightest trace of glycosuria. The low carbohydrate diet therapy has become universally obsolete. Insulin, however, is still used to keep the urine sugar-free as far as possible and so lower the blood sugar to strictly normal limits. A period of hospitalisation is advocated by most physicians, *e.g.* three to four weeks by Sir Edmund Spriggs in *The Practitioner* of May 1939. In some cases the patient is taught to construct his diet from charts showing the composition and caloric values of various foods. For those who are not able to undertake the calculations needed to make

up and vary the diet in this way, various schemes of fixed rations and half rations have been devised. One of the best is that of the line rations of R. D. Lawrence (1939). Careful weighing is considered essential by most authors. " Unless his case is a very mild one he is not wise to leave his scales behind when leaving home " (Sir Edmund Spriggs). The patient is also taught to examine his urine for sugar and acetone. It is considered that the urine should be tested regularly by the patient or a relative in mild, and night and morning in moderately severe cases which are under control. The practitioner should arrange for any departure from a normal urine or from a slight reduction to be reported. The insulin dosage has to be adjusted according to the urine sugar. Diabetic coma and other alarming consequences, from gangrene to blindness, are threatened if the instructions are not obeyed implicitly. Frequent blood sugar tests are performed to ensure the accuracy of this standardisation. The closeness of the control required, however, even if the patient is sufficiently intelligent or conscientious to juggle with urine sugar and insulin, is by no means always easy to obtain, especially in young insulin-sensitive diabetics who readily swing to and fro between acidosis on the one hand and hypoglycæmia on the other. In any event, a precarious balance in the hospital ward by no means always stands up to the strain of working life. To make things more unpleasant for the diabetic he is taught to be constantly on the alert for the emergency of hypoglycæmic coma. We have seen young diabetics crippled in outlook by the kind of treatment outlined above. They have become " diabetically minded," have been regarded as invalids by their families and learned to consider themselves as such. Not only handicapped in their work, they have often also become quite incapable of leading a normal, healthy social life. Indeed, we have seen patients who have been kept in hospitals for months at a time, on discharge only to return in one or other type of coma.

A method of standardisation was devised some fifteen years ago, the results of which have appeared so gratifying as to be worthy of mention. Clinics have been established along the lines to be described, and so far some 1500 patients in this country have been observed undergoing such a method of standardisation and control. The following criteria were laid down as the standard to be constantly aimed at :—

(1) No acidosis.
(2) General fitness.
(3) No loss of weight.
(4) No active complications.

The maximum attention is focused on the patient's feeling of well-being and ability to do work. He must not be losing weight once what is regarded as his ideal weight is attained. There must,

of course, be no acetonuria and no evidence of any reversible complications. If these standards are achieved standardisation is ensured irrespective of the blood sugar level. Absence of glycosuria is not requested nor is it considered desirable. On the contrary, it is looked upon with mistrust as the possible forerunner of hypoglycæmia. In short, a margin of hyperglycæmia is allowed.

On his first visit the patient is weighed and reminded to attend next time similarly clothed. He undergoes a thorough clinical examination to exclude the possibility of extra-diabetic factors. Young patients are screened whether coughing or not. The diet is explained in a matter of a few minutes. The basis of the diet is a 2000 caloric diet consisting of 200 g. carbohydrate, 90 g. protein, 80 g. fat, which is adjusted according to the age, sex and occupation of the patient. For instance a heavy manual labourer is allowed 5000-6000 c. daily and generous carbohydrate allowances are made to children and pregnant women. The diet is extremely simple and is presented to the patient in the form of a small booklet. It is explained in terms of tablespoons, average helpings, slices, etc. It is of sufficient simplicity to allow him to eat in a restaurant at any time. Within the last few years the views of diabetic specialists have been inclining more and more towards a normal diet, to re-create the physiological state and meet physiological needs. Thus, cheating is not encouraged. On the other hand, complete licence to eat *ad lib.* and cover with insulin cannot be granted at the present stage of knowledge. In the first place it would rob the physician of one of the scales of the balance he has to maintain and place the onus on the patient to standardise himself; nor do we know at present how the diabetic organism would respond to the constant dietetic insults that would inevitably follow. Insulin is prescribed, if it is necessary, in order to achieve the standards laid down. One injection of P.Z.I. or G.I. is given daily (or P.Z.I./G.I. plus soluble insulin) whenever possible, or twice daily soluble insulin in those cases which do not react to the slow-acting type. Above all, there is no need for hospitalisation, except in very rare and most severe cases. Indeed, a worker can only be satisfactorily standardised while actually engaged in his normal working routine. He is not asked to calculate his diet according to complicated diet charts, or weigh his food or test his urine which a severe diabetic, who for instance works in a shipyard and eats in the canteen, would find virtually impossible to carry out. The responsibility for his health and well being is almost entirely taken over by the physician, and in return for this comparative freedom he is asked to pay a visit to the clinic every three or four weeks, especially if a severe diabetic. At each subsequent visit there is a general review and assessment of his condition. The first few visits will need to be at weekly intervals while standardisation is being achieved. Afterwards, the average moderate diabetic attends once in five or six weeks. He is always advised to attend at any time if he does not feel well, but up to now,

patients have not had to take advantage of this. Similarly, no patient has suffered a hypoglycæmic attack, nor would this be expected in view of the hyperglycæmia permitted. A few examples from records of the present clinic may help to show the type of check-up that is made. It will be seen that blood sugars are recorded for the sake of completing the clinical records according to modern standards, but it must be re-emphasised that treatment is not dictated by the figures obtained. At the same time treatment is not dictated by the amount of urine sugar excreted in twenty-four hours. Even though a patient excretes an appreciable amount of glucose in his urine in twenty-four hours, if he has no acetonuria, no symptoms, no loss of weight or complications and is able to do his work, his metabolism is considered to show a positive balance in terms of health and efficiency. If this is attained on diet alone, no insulin is required to lower the blood sugar and prevent the glycosuria. On the other hand, a patient who excretes only a small amount of glucose, but who continues to lose weight and complains of symptoms, is not well balanced but will require some insulin. For the purpose of the clinic, urine sugar is only recorded as trace, 1 plus, 2 plus or 3 plus. The indication for giving insulin is a simple one, namely when a diet adapted to the individual's needs does not achieve the desired standards of efficiency, so that he still does not feel well or fails to maintain the weight considered necessary or presents signs of acidosis or complications. The amount of insulin to be administered remains a matter of trial and error in each individual patient and is guided by the particular clinical picture of the patient concerned and not by his blood sugar level alone. Scott and Dotti wrote in 1932 that despite the multiplicity of papers on insulin research our knowledge of the deeper significance of insulin is still disappointing. About its pharmaco-dynamics we still remain largely ignorant up to the present day. " The most important reference books and current texts on the subject of diabetics do not provide the answers. Although every conceivable aspect of insulin is summarised and reviewed, we have been unable to ascertain from the mass of material any formula by which the physician can be guided." This is the conclusion of Collens and Boas in their recent textbook, *The Modern Treatment of Diabetes Mellitus*. The severity of a diabetic cannot be expressed in terms of insulin required, for this varies according to the great individual variation of insulin sensitivity. Himsworth has devised an insulin-glucose sensitivity test and he goes so far as to state on the basis of this test that " insulin sensitive diabetics tend to be younger, thin, and to have a normal blood pressure and healthy arteries, in them the disease is sudden and severe at onset; they easily develop ketosis and react to a slight excess of insulin with a hypoglycæmic attack. The insulin-insensitive diabetics, on the other hand, tend to be older, obese, to have hypertension and to exhibit arteriosclerosis; in them the onset of the disease is insidious. They rarely develop ketosis and can tolerate over-dosage of insulin without showing

symptoms of hypoglycæmia." From the practical standpoint, we sub-divide diabetics into three main types :—

(1) Mild—standardised on diet alone.
(2) Moderate—standardised on diet and insulin.
(3) Severe—difficult to standardise on diet and insulin.

The latter we have encountered mainly among the younger diabetics who appear to resemble closely Himsworth's insulin-sensitive type.

A few examples from present clinic. There is nothing of especial interest about the figures shown below. They are inserted merely to indicate the type of supervision considered necessary and it must be emphasised that it is carried out at a single session. This time-saving is an important factor from the point of view of an employee.

1. Miss M., aged 24 years. History of diabetes of twelve years' duration including 9 known diabetic comas. At one time she had been completely hospitalised for a period of three years. She had recently left hospital with the advice to inject 20 units sol. insulin t.d.s. She said she " did not understand " her diet as it had been changed so repeatedly. She complained of not feeling well. On examination, she was obviously below average weight and her breath smelt strongly of acetone. She had never had a job and was unable even to go out alone.

Date.	Urine Sugar.	Acetone.	Blood Sugar Fast : mgm./ 100 c.c.	Weight St. Lbs.	Treatment.		Remarks.
					Diet.	Insulin.	
26. 8.47	+++	++	285	7 10½	Standard diet +200 cal.	Sol. insulin 25 u.a.m. 15 u.p.m.	Complaining of lassitude, headaches, some thirst.
2. 9.47	++	Nil	200	7 11¾	Standard diet +200 cal.	Sol. insulin 25 u.a.m. 15 u.p.m.	Feeling better.
16. 9.47	++	Nil	194	8 0	Standard diet +300 cal.	Sol. insulin 25 u.a.m. 25 u.p.m.	Diet and insulin increased.
23. 9.47	+	Nil	170	8 2	Standard diet +300 cal.	Sol. insulin 20 u.a.m. 25 u.p.m.	Improving.
30. 9.47	+	Nil	165	8 3	Standard diet +300 cal.	Sol. insulin 15 u.a.m. 20 u.p.m.	Improving.
7.10.47	Trace	Nil	155	8 6½	Standard diet +300 cal.	Sol. insulin 15 u.a.m. 15 u.p.m.	Further insulin reduction made.
14.10.47	++	Nil	170	8 6¼	Standard diet +300 cal.	Sol. insulin 15 u.a.m. 15 u.p.m.	Feels and looks well.
28.10.47	++	Nil	170	8 6½	Standard diet +300 cal.	Sol. insulin 15 u.a.m. 15 u.p.m.	Feels and looks well.
7.11.47	+	Nil	160	8 4	Standard diet +500 cal.	Sol. insulin 20 u.a.m. 20 u.p.m.	No gain in weight for three weeks. Diet and insulin increased.
25.11.47	+++	Nil	195	8 7¼	Standard die +500 cal.	Sol. insulin 20 u.a.m. 20 u.p.m.	Patient pleased with extra carbohydrate.
16.12.47	+++	Nil	168	8 6	Standard diet +500 cal.	Sol. insulin 20 u.a.m. 20 u.p.m.	Reports that she has a job.
6. 1.48	++	Nil	200	8 8	Standard diet +500 cal.	Sol. insulin 20 u.a.m. 20 u.p.m.	Condition maintained.
27. 1.48	+	Nil	170	8 12¼	Standard diet +500 cal.	Sol. insulin 20 u.a.m. 20 u.p.m.	Considered stabilised at this weight.

2. Mrs B., aged 43 years. Referred from doctor with past history of severe diabetes.

Date.	Urine Sugar.	Acetone.	Blood Sugar Fasting mgm./ per cent.	Weight. St. Lbs.	Treatment.		Remarks.
					Diet.	Insulin.	
9.10.45	++	Nil	210	11 12	Standard diet	P.Z.I. 34 u.mane.	Complains of headaches and giddiness. B.P. 180/125.
16.10.45	++	Nil	170	11 8½	Standard diet	P.Z.I. 30 u.mane.	Quite well, B.P. unchanged.
23.10.45	++	Nil	175	11 9	Standard diet	P.Z.I. 30 u.mane.	Occasional symptoms thought to be consistent with hypertension.
6.11.45	++	Nil	190	11 13	Standard diet	P.Z.I. 26 u.mane.	Diabetes under satisfactory control.
27.11.45	++	Nil	200	11 13	Standard diet	P.Z.I. 26 u.mane.	Diabetes under satisfactory control.
4.12.45	++	Nil	170	11 13	Standard diet	P.Z.I. 26 u.mane.	Diabetes under satisfactory control.
8. 1.46	+	Nil	190	11 13½	Standard diet	P.Z.I. 26 u.mane.	B.P. 195/115.
22. 1.46	+	Nil	220	12 1½	Standard diet	P.Z.I. 26 u.mane.	Mild bronchitis, some dyspnœa and headaches.
12. 2.46	+	Nil	195	12 1	Standard diet	P.Z.I. 22 u.mane.	Improved again.
5. 3.46	+	Nil	166	11 13½	Standard diet	P.Z.I. 22 u.mane.	Condition unchanged.
19. 3.46	+	Nil	200	12 0	Standard diet	P.Z.I. 22 u.mane.	Condition unchanged.
9. 4.46	+	Nil	188	11 13½	Standard diet	P.Z.I. 18 u.mane.	Condition unchanged.
30. 4.46	Trace	Nil	173	12 0	Standard diet	P.Z.I. 16 u.mane.	Condition unchanged.
From this time patient has been seen at intervals of four and five weeks. No change has had to be made in diet or insulin.							
Latest Attendance							
6. 2.48	+	Nil	205	12 0½	Standard diet	P.z.I. 16 u.mane.	B.P. 190/115.

3. Miss H., aged 28 years. Referred by doctor suffering from loss of weight and thirst. Glycosuria and diabetic blood sugar curve found.

Date.	Urine Sugar.	Acetone.	Blood Sugar mgm./ 100 c.c.	Weight. St. Lbs.	Treatment.		Remarks.
					Diet.	Insulin.	
22. 4.47	++	+	370	7 11½	Standard diet +150 cal.	P.Z.I. 20 u.mane. S.I. 20 u.mane.	...
29. 4.47	++	Trace	240	7 11¾	Standard diet +150 cal.	P.Z.I. 20 u.mane. S.I. 20 u.mane.	...
13. 5.47	++	Nil	220	7 12½	Standard diet +150 cal.	P.Z.I. 20 u.mane. S.I. 20 u.mane.	...
10. 6.47	++	Nil	200	7 9½	Standard diet +150 cal.	P.Z.I. 20 u.mane. S.I. 20 u.mane.	...
24. 6.47	++	Nil	230	7 8	Standard diet +500 cal.	P.Z.I. 25 u.mane. S.I. 25 u.mane.	...
1. 7.47	Trace	Nil	155	7 9	Standard diet +500 cal.	P.Z.I. 25 u.mane. S.I. 25 u.mane.	...
29. 7.47	+	Nil	180	7 11½	Standard diet +500 cal.	P.Z.I. 20 u.mane. S.I. 20 u.mane.	...
10. 9.47	+	Nil	180	7 11½	Standard diet +500 cal.	P.Z.I. 25 u.mane. S.I. 20 u.mane.	...
30. 9.47	+++	Nil	200	7 13½	Standard diet +500 cal.	P.Z.I. 25 u.mane. S.I. 20 u.mane.	...
23.10.47	+	Nil	164	7 13½	Standard diet +600 cal.	P.Z.I. 25 u.mane. S.I. 20 u.mane.	...
4.11.47	++	Nil	185	7 13½	Standard diet +600 cal.	P.Z.I. 25 u.mane. S.I. 20 u.mane.	...
11.11.47	++	Nil	180	7 13¾	Standard diet +600 cal.	P.Z.I. 25 u.mane. S.I. 20 u.mane.	...
2.12.47	+++	Nil	185	8 2	Standard diet +600 cal.	P.Z.I. 25 u.mane. S.I. 20 u.mane.	...
23.12.47	+	Nil	175	8 0	Standard diet +600 cal.	P.Z.I. 25 u.mane. S.I. 25 u.mane.	...
6. 1.48	++	Nil	170	8 0	Standard diet +600 cal.	P.Z.I. 25 u.mane. S.I. 25 u.mane.	...

In his follow-up visits, if the patient does not have enough to eat, moderate additions are made to his diet. Unjustifiable loss of weight in a standardised diabetic is immediately investigated for extra-diabetic causes. The diabetic is just as prone to malignant disease as anyone else. Continual alertness to detect early phthisis in a curable stage demands that every cough be thoroughly investigated, as the condition responds quite well if the diabetes is adequately controlled. In the event of active complications the diabetes is more vigorously treated until the condition is halted or eradicated, and insulin is either given or increased in dosage even though not required for standardisation purposes. For instance, cases of pruritus vulvæ, so common and often the only symptom of the menopausal diabetic, respond rapidly to this additional insulin which can be later withdrawn. Retinitis and cataract are more rigorously treated in consultation with the eye specialist. Prophylaxis against gangrene is strongly urged in cases of corns and calluses, and patients referred for careful chiropodist attention. In such conditions as boils and colds the insulin dosage is increased and the patient seen again in one week.

Many gaps remain to be filled in our knowledge of the causative factors of diabetes and its associated diseases. Agreement has not been reached with regard to the pathological changes to be found in the pancreas and their significance from the aetiological standpoint. In actual fact, there is no evidence at present as to whether insulin secretion in diabetic patients is decreased, unaffected or increased in amount; there is no doubt, however, that it is less effective than normally. Recent work suggests that diabetes mellitus is not simply a disease of the pancreas. The work of Houssay and his associates in South America since 1937, followed by that of Young, has gone far to establish the view, at any rate in the experimental animal, that a diabetogenic hormone is produced in the anterior pituitary gland which is antagonistic in its action to that of insulin. Himsworth asserts that "the anti-insulin factor of pituitary extracts has the property required to produce the state of insensitivity to insulin characteristic of one type of diabetic patient, and it was found that after injection of such an extract into a normal animal the previously normal insulin-glucose curve was changed to an abnormal insulin-insensitive type." Young was able to induce hydropic degeneration of the islands of Langerhans in animals injected daily with large doses of anterior pituitary extract. Haist, Campbell and Best in repeating the experiments of Young observed that the production of permanent diabetes by the injection of large doses of anterior pituitary extract is accompanied by a marked depression of the insulin content of the pancreas. When, however, the animals were injected with anterior pituitary extract at the same time that they were either starved or fat fed or given insulin, they were able to prevent the development of diabetes and the insulin content of the pancreas was not seriously affected. Hydropic degeneration of the islands of Langerhans had been produced formerly by

Allen in the remainder of the pancreas after partial pancreatectomy in dogs. When seven-eighths of the pancreas was removed, these dogs were overfed and developed diabetes. He conceived the theory that degeneration of the islands resulted from their exhaustion through overwork. In the same way it has been suggested that the prolonged hyperglycæmia induced by the repeated injections of anterior pituitary extract causes the cells of the islets of Langerhans to undergo functional exhaustion and degeneration and that control of the hyperglycæmia before the pancreatic changes have advanced too far, can prevent the development of permanent diabetes. Further, it has been suggested that this might have important clinical implications. In practice, we have encountered quite a number of diabetics, usually of the later age-groups, who in spite of a persistently high blood sugar level have required gradually diminishing insulin doses for their standardisation as the years elapsed. Collens and Boas are of the opinion that resting the pancreas by creating smaller demands for endogenous insulin production appears to be only a transient form of relief.

Hyperglycæmia has always been suspect of exerting a noxious influence in some way or other. In the past it has been considered responsible at one time or another for certain of the diabetic complications. For example, it was thought that the increased sugar content of the blood and tissues seen in diabetic patients favoured the growth of bacteria, particularly staphylococci. Present-day opinion does not favour this explanation. There is by no means agreement that an increase of sugar in the blood predisposes to diseases of the skin. It seems certain that diabetic neuropathy is not the direct result of hyperglycæmia or ketosis, it may be seen in patients whose diabetes is well controlled by diet and insulin, whereas other patients who were free of neurological signs before treatment have developed symptoms and signs shortly after treatment has been started. The factors involved in bringing about certain degenerative changes in the diabetic are far from being elucidated. There has frequently been a tendency to fasten a greater part of the blame on to the diabetes or even on to the hyperglycæmia *per se*. Wilder, although recognising the great incidence of arteriosclerosis in diabetes and the importance of its treatment as a complication of diabetes, doubts that the vascular lesions are due solely to diabetes. Retinal changes occur predominantly in adult diabetics who have hypertension but may also be present in the juvenile diabetic. Wilder separates the arteriosclerotic retinal phenomena from the so-called true diabetic retinitis. In the former the lesions do not appear to be influenced by the severity or degree of control of the diabetes. On the contrary, they appear to be progressive in spite of every form of therapy. Similarly, there appear to be two distinct types of cataract—a true diabetic type said to be reversible by Wilder and the senile cataract. Russell Richardson and his colleagues have published in the *American Journal of Medical Sciences* (1945) the first of a series of studies of 100 patients with diabetes of ten or more

years' duration in one clinic. Subcapsular flocculi occurred in 5 of the 100 cases, and it is stated that the progress of such a cataract can often be arrested by correct treatment of diabetes. Collens and Boas, on the other hand, have not observed the disappearance of this type of cataract, having once developed, no matter how well the diabetes was controlled. It has, in the past, been the practice to ascribe indiscriminately all the misfortunes of the diabetic in the shape of so-called complications, to faulty control of his disease. It must, however, be conceded that certain of these degenerative processes which occur quite commonly in the non-diabetic and deteriorate progressively, are likely to follow a similar course when occurring in the diabetic. Recent investigations are helping to separate those complications which are due to the severity of the disease process and which may be reversible with adequate treatment from those which are not primarily or not entirely due to diabetic factors and which are not influenced by treatment of the diabetes. In the cases we have seen, the incidence of diabetic complications does not appear to have borne any strict relation to the severity of the disease or its degree of control but appears to have arisen in a completely haphazard and fortuitous manner. Genetic factors may be invoked to aid our explanation of the relationship of diabetes to its commonly associated diseases. "That one or more factors may be involved in diabetic heredity is suggested by the high incidence of obesity, of congenital defects especially of mesenchymatous tissue (first reported by Priesel and Wagner), possibly such degenerative lesions as cataract and arteriosclerosis in diabetic patients and the appearance of congenital anomalies, especially of the mesenchymatous tissues in the offspring of diabetic mother." However, there are matters nearer of solution from the standpoint of practical medicine. The hypothesis of a pancreatic hormone stood for many years before Banting and Best provided the proof. We feel that the position is similar to-day in relation to the anterior pituitary gland and that the answer will come from the physiologists and biochemists. Some recent work has carried us further in this belief. Work on the experimental animal will not always bear direct reference to the human subject but an interesting counterpart to the latest experimental work has unexpectedly come to light from studies on pregnant diabetic women. The first suggestion of a possible hormonal imbalance was made by Murphy (1933). He reported that the prolan excretion of two diabetic women exceeded the normal. This work was carried further by Smith and Smith who, estimating hormones in pre-eclamptic toxæmia of pregnancy, quite naturally turned to diabetics as material to study this problem from early to late pregnancy, since the incidence of pre-eclamptic toxæmia in diabetes is more than 30 per cent. These investigators confirmed in diabetics their earlier observation that an excess of serum prolan precedes, predicts and perhaps causes pre-eclamptic toxæmia. White and Hunt subsequently studied this problem in pregnant diabetics.

They confirmed the observation of Smith and Smith and in a large series were able to predict pre-eclamptic fœtal accidents by the finding of an abnormally high concentration of gonadotropins in the blood serum after the fifth month of pregnancy. White has carried this work further. On the advice of Smith and Smith a group of patients, whose values for serum prolan were supernormal, received massive doses of œstrin and, in addition, progestin. In 17 cases so treated the serum gonadotropin level dropped, and 15 of them delivered successfully. It would appear that White has made a significant contribution to the successful management of the pregnant diabetic. It has furthermore been suggested " that since in diabetes hypertension, albuminuria, retinitis and sclerosis occur, and since in our pregnant diabetics one half have demonstrable hormonal imbalance which if untreated is associated with pre-eclamptic toxæmia, and since the long-duration case with the most marked signs of sclerosis has been of an endocrine type, hormone studies should be carried out and substitutional therapy administered if indicated."

Whatever the future may disclose, the facts remain that we are in possession of two effective weapons in our treatment of diabetes mellitus, viz. diet and insulin. Are we making the best possible use of these ? We feel that the answer is not an unmodified affirmative. Recent research developments indicate that the static conception of the pancreas in diabetes can no longer be upheld. The evidence points to a continuous struggle between antagonistic factors of which the anterior pituitary factor or factors may prove to be the most important. Insulin counteracts the diabetes-producing factors. How it achieves this we do not know. It would appear possible that diabetes can arise in one of two ways : either the islets of Langerhans are incapable of producing an amount of insulin to meet the requirements of the diabetic organism, or the islets are able to produce sufficient insulin but some other mechanism interferes with its action. Either mechanism may prove to be the correct one or even they may both exist and account for the different clinical types of diabetes. It remains, however, for the physician to make the best use of insulin as far as its activity is understood at present. This requires the close observation and supervision of each individual patient. Each diabetic is a law unto himself. It is agreed that for therapy to be regarded as completely successful, the patient should be allowed to lead a perfectly normal life both from a working and social point of view. If we do not make the diabetic a completely normal and useful member of the community our therapy is not an absolute success. For this reason we advocate that the diabetic should be freed as far as possible from the restrictions that have encompassed him in the past.

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