

# CALIFORNIA AND WESTERN MEDICINE

VOL. XXIII

OCTOBER, 1925

No. 10

## SPECIAL ARTICLE

### REMARKS ON THE PRACTICAL TREATMENT OF DIABETES

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(*Delivered before the San Diego Medical Society, November 18, 1924*)

**D**OCTOR ALLEN'S method of handling the subject of diabetes, by refuting many of the erroneous views that creep into the discussion of any new subject is particularly pertinent. Following promptly in the wake of any scientific discovery is a stimulated crop of all kinds of pseudo-scientific views bearing more or less closely upon the subject; and even we physicians are not above espousing them for a time. A direct negation, given by an authority we recognize, to the more plausible of these errors clears our vision and strengthens our practice wonderfully.—EDITOR.

rather defending my position against their attacks, and the question as to who is right will simply have to be decided by experimental evidence.

The treatment of diabetes is today practically twofold: by diet and by insulin. I shall consider the subject under these two heads, and shall begin under each heading by stating certain things which, in my opinion, are not true.

**I** SHALL speak informally on the subject of the practical treatment of diabetes.

Many advances have been made in this subject, as you all know, and as in most subjects, many fads come and go. Sufficient time has now elapsed, I believe, for us to judge some of the recent movements in this subject, and I shall speak rather frankly and freely of my own notion of these movements. You are in no way obligated to believe what you hear.

In 1914 I set up certain innovations in diabetes in the form of a treatment based on something new in diet, namely, the limitation, not only of carbohydrate, but of total calories, the idea being that the tolerance is governed not only by the carbohydrate, but by the fat intake and body weight. In criticizing some of the ideas that have come up since that time, I am not attacking other individuals in expressing my opinion freely, but

#### DIET TREATMENT

First of all, it is not true that insulin diminishes the need for accuracy of diet. Diet is just as live a question as it ever was, if not more so. Accuracy of diet is needed as much as ever, if not more, because formerly there was greater leeway in treating diabetes on lax diets; now if a diabetic takes insulin he is almost compelled to have a weighed diet. For that reason many physicians who never studied diets before are studying them now in order to treat diabetes intelligently with or without insulin. A very striking suggestion in that connection has been put forth by Gray, who, in a recent paper, raises the question: "Is insulin more important to the diabetic than food scales?" The point brought out is that, from a practical standpoint, food scales may be considered more important than this wonderful discovery, because most diabetics do not, after all, need insulin, but they all need diet, and those who do need insulin cannot be treated satisfactorily with insulin unless they have accurate diet. That is one way of expressing the importance of diet in diabetes. Now we still have deaths in patients treated with insulin. We still have deaths from old-fashioned diabetes, because those patients do not follow diet, and any idea that one can use insulin successfully simply by planning the dosage of insulin and disregarding everything else is contrary to fact. Diet, then, maintains its full importance.

Second. It is not true that any form of diet can take the place of undernutrition. There are various forms of reduced diet, the strictest of all being total fasting. The more you undernourish the patient the more you raise his tolerance. To feed him with the number of calories he is burning is not equivalent to fasting; that can be shown experimentally.

Third. It is not true that the respiratory metabolism can furnish a guide to the diet. Perhaps such remarks may unfavorably impress persons who do respiratory metabolism. I appreciate their work very highly and its importance for theoretical and practical purposes, but tonight I am speaking of a practical subject to practitioners. A large proportion of writers on this subject now speak of taking the basal metabolism and figuring the basal diet of the patient, and then building up a diet from that, giving him first the basal requirement. This may be very interesting if you are doing research work on the subject,

or perhaps if you have a new machine and like to play with it or to impress patients. But for actual practical benefit I see no advantage in taking observations of the respiratory metabolism. It does not guide one in the treatment, and it does not tell how many calories the patient needs. Whatever his basal metabolism is we must guess at his active metabolism, and it is just as easy to guess at the whole thing in the first place.

Fourth. Another point bearing closely upon this whole subject is the question of protein. It is not true that protein has any specific injurious action on diabetes. A number of older writers have argued that it has some influence as a special toxic food injuring the pancreas somehow or other. More recent writers have speculated that it may be injurious through its specific dynamic action, raising the metabolism, and that for this reason protein should be especially restricted. The only answer is that it is not true in actual practice. If you think otherwise, try it. Protein makes somewhat less tendency to glycosuria than the equivalent in preformed carbohydrate. If there were any special toxic action in protein, or if it especially influenced the tolerance through its raising of the total metabolism, it would create more of a demand for insulin than carbohydrate. The contrary is true. Carbohydrate creates more of a demand for insulin than its equivalent in the form of protein. Therefore, protein is not to be particularly dreaded in diabetes.

Fifth. The total calories of the diet cannot be ignored. This means in particular that fat cannot be ignored. The tolerance or the diet cannot be figured solely in terms of carbohydrate, assuming that all diets are the same if they contain equal glucose values in the form of carbohydrate as such, or protein, counting it as 60 per cent carbohydrate, or with allowance for any supposed carbohydrate value of fat. You cannot figure diabetic diets as equivalent on that basis, but must consider also their total caloric value. This principle is largely ignored in recent writings on diabetes, but is just as valid as ever.

Sixth. As a continuation of this idea, the high fat diets, so-called, which have been the most recent of the diabetic fads, and which are very extensively used today, in my opinion do not represent any valuable new step in the treatment of diabetes. They are practically a reversion to the old treatment with low carbohydrate and protein and high fat. They are a negation of the principle of the influence of total calories. The basic principle of the high fat diets is that carbohydrate is all that counts; that if we restrict the carbohydrate enough, and also restrict protein, the more calories we give in fat or perhaps alcohol the better. That is untrue. I have published the proof, and some others have also published confirmations. Until these experiments are overthrown the principle of total calories cannot be ignored. As a matter of fact, Newburgh and Marsh, whose names are associated with high fat diets, have not ignored this principle in actual practice. If one will look up their papers he will find that, although their cases on the average are mild, the total calories in their diets are not high. Men like Petré in Europe have used actually high fat diets, running these diets as high as possible, often

above 3000 calories. But Newburgh and Marsh have done better. After an initial undernutrition with about 900 calories, they have limited their milder cases to about 2400 calories. Also, if you look up their original papers, you will find that their severe cases have received final diets only as high as 1500 calories. In other words, their diets were on the whole not higher in total calories than the diets of Joslin, myself or others for similar cases. They were not able to take thin diabetics and make them fat; nobody ever succeeded in doing that until insulin came. The reason is that the emaciated patient suffering with severe diabetes cannot assimilate high calories in any form.

Seventh. It is not true that the practitioner need go to the trouble of calculating ratios of the ketogenic and anti-ketogenic substances in the diet. That is again one of the fads that have complicated diet unnecessarily. In the first place, if we give a patient any ordinary combination of foodstuffs we are likely to use, we shall find that we have nothing to fear from acidosis provided glycosuria is kept absent. Newburgh and Marsh are perfectly correct in that principle, which is not new. If we keep a patient sugar-free we can give him huge quantities of fat in proportion to carbohydrate and protein, and not get serious acidosis. Wilder has published recently some very narrow ratios of carbohydrate and fat in the diet, allowing the patient to show some ketosis and finding that no apparent harm was done. It need not injure the patient if he does show a little acetone in the urine. It is extremely important theoretically to know what combinations of materials make acetone in the body and how and why ketosis arises. But even from a theoretical standpoint it is hard to tell where ketosis begins, and whether we should be guided by the first bare trace of acetone or only by a large increase. Practically no two authors agree as to the amount of ketogenic and anti-ketogenic materials a diet should contain. On the practical side I would say that we are interested only in making the patient safe and evidently various ratios are safe, but the main point is that they all fall within any diet we are likely to choose. Some people prefer higher fat, some lower fat, some higher carbohydrate and some lower, but I do not know anybody who can make any palatable combination of foods that would produce any serious acidosis in a patient who is sugar-free. Therefore, physicians need not worry too much about the scientific phrases.

Eighth. It is not true that there is any valid ratio of tolerance for different foods on the basis of their glucose value. It has been argued that in figuring the diet we must count the glucose available as 100 per cent for the carbohydrate, at 56 or 60 per cent for the protein, and at 10 per cent for the fat; and that thus diets can be planned which will prevent acidosis and at the same time supply high fat and high calories. The purpose of these calculations is to give the patient as many calories as possible. High caloric diets are what these authors have aimed at; their fundamental principle has been that only glucose need be considered, and that if you exchange other foods for fat you can give more calories in the form of fat, and therefore a higher fat diet is better. That is where the mistake lies. It is

not true that you can exchange 10 grams of carbohydrate for 100 grams of fat and have it mean the same to the patient. If you do that you are subtracting 40 calories and adding (with your 100 grams of fat) 900 calories; but they are not the same. If you could do this you could soon run up to a diet of 4000 calories, in return for taking away perhaps only 180 calories. What actually happens if you exchange glucose for fat is at first perhaps an apparent increase of tolerance or decrease of the insulin need. If a patient is on, say, 1500 calories, and you subtract 20 grams of carbohydrate and add 200 grams of fat, the first effect may be a lowering of the insulin dosage for at least a few days. Afterward you will find that the insulin dosage will creep up and the slow delayed effects of the fat will become more evident as the weeks and months go by. We have had plenty of examples of the harm resulting from adding calories in that fashion. One patient could be kept sugar-free on 40 units of insulin a day, but by substitutions which doubled his calories without changing the theoretical glucose value he reached a point where he was taking 140 units of insulin and still excreting 90 grams of glucose. It is easiest to see this result in the severe cases; therefore, they are the best for tests. But in all cases total calories must be considered, and food-stuffs cannot be interchanged on a mere basis of glucose content.

Ninth. It is not true that any special or artificial kinds of food can evade this law. Levulose, caramel, intarvin, glycerol, and other artificial or unusual forms of food have been introduced as things which might not form glucose in the metabolism, thus returning to the old notions of diet. These foods may not impose the same strain that carbohydrate does. Foods differ in this respect. The greatest strain on the pancreatic function is imposed by carbohydrate, the next by protein, and the least by fat. But even if the artificial foods may perhaps impose less strain than carbohydrate, they do not escape the law of total calories, and it is not true that you can give any food to diabetics without taking account of its caloric value.

Tenth. It is not true that the influence of body weight and obesity is yet explained by any known metabolic laws. We do not know why obesity predisposes to developing diabetes. Joslin especially has shown the fact statistically. Obesity or gain of weight also has a marked effect on the tolerance of diabetics. The tolerance is greatly increased by reducing the weight. Of course, as we increase the weight we increase metabolism, but as far as known the increased strain on the pancreatic function is out of all proportion to the increased metabolism. If you increase a patient's weight by ten, fifteen, or twenty pounds, you increase his metabolism appreciably, but in some cases you may increase the insulin requirement four or five times. The tissue he puts on is likely to be almost pure fat, and adipose tissue is not known to increase the metabolism greatly; but it seems to be this very adipose tissue which chiefly increases the insulin requirement. When a patient begins to lay on fat his insulin requirement goes up. The reason may be figured out some day in terms of metabolic laws, but up to the present the explanation seems not to have been found.

#### INSULIN TREATMENT

Turning to the subject of insulin, I shall mention a similar list of things, which, according to present evidence, are not true.

First. Insulin is not required in the majority of diabetic cases. It is easier and simpler to get along without it, and most cases are mild enough that you can get along without it.

Second. It is equally well known that insulin does not cure diabetes. We have tried maximum dosage in children with very mild or early cases, and have not succeeded in curing them; these children, like all other patients, have remained diabetics. In a few cases the tolerance does rise tremendously, so that insulin may be greatly reduced and sometimes stopped altogether. There is always the hope that in some rare cases the diabetes may come to an end, particularly if there is an acute or subacute pancreatitis underlying the diabetes. It is theoretically conceivable that if the pancreatitis gets better the patient may recover. But ordinarily the rule is, once a diabetic, always a diabetic; and that rule has not been broken by insulin.

Third. It is not true that insulin has any specific curative effect upon diabetic complications. If we become too optimistic on this subject we are likely to be disappointed. It was always true that if we controlled the diabetes the complications became better. We thus obtained good results in gangrene, without insulin. Insulin furnishes a quicker and surer means of arresting all complications; but if a patient has deep gangrene he still, as a rule, loses his foot. We saved some feet before we had insulin, and we do not save appreciably more of them nowadays with insulin, because there is the same basis of arteriosclerosis. We save some lives we could not save before, because patients can be kept sugar-free more readily, but insulin has no specific action on the gangrene. Sugar freedom obtained by insulin is no more important than sugar freedom obtained by diet in its effect on complications.

Fourth. It is not true that there is any practical method of giving insulin except by injection subcutaneously or intravenously. There has been interesting work done experimentally with the administration of insulin by various other ways, especially in animals. But from the practical standpoint it does not work, and if any absorption were obtained it would be too uncertain and irregular for practical purposes. Also, no other pancreatic preparation has been shown to have any effect. Pancreatic substance taken by mouth in any form, or proprietary remedies alleged to stimulate the pancreas or to act in some way other than insulin, have not sustained their claims and have no scientific basis.

Fifth. It is not true that any diabetic cases are refractory to insulin. It is interesting to watch the literature for reports of that kind. I felt pretty sure they would come from people who use high caloric diets and who do not recognize certain principles in diet. Those reports are coming in. One of the most noteworthy was published by Falta last July. He reports a case in which he gave insulin, as high as 160 units a day, and it did not affect the blood sugar when given either subcutaneously or intravenously. Therefore, he claims that this case is re-

fractory to insulin and assumes that it is not due to deficiency of insulin or of pancreatic function, and must be due to some other cause. If you study this case you will observe that, although during a few hours following his doses he did not find much fall of blood sugar, yet he admits that the total sugar excretion on insulin days was less than without it. Then, too, the patient is described as being of medium height and weighing approximately 200 pounds, decidedly obese. That kind of a result can be duplicated any day. By fattening a severely diabetic patient, you can get him into a condition where insulin can be poured in almost like water, and the largest doses will have minimal effects. If Falta's patient were brought down to a reasonable weight, it would probably be found that the case not only can be controlled by insulin, but is not very severe. Such difficulties are going to be encountered by a number of people who give fats and other foods in such quantities as to keep their patients obese. I mentioned our own experience where a patient took 140 units a day and still excreted as much as 90 grams of sugar a day.

Sixth. Following up the point just mentioned, it is not true that there is evidence of disturbance of any gland other than the pancreas in typical cases of diabetes. Insulin prepared from the pancreatic islands does control diabetes in every case, and no preparation from any gland other than the pancreas has the slightest influence on diabetes. Yet in spite of this discovery, the pluriglandists base an argument on the fact that you can give insulin to lower the blood sugar, and give adrenalin to bring it up. One lowers, the other raises; therefore, is there not an antagonism? and the answer is, no, there is not. In the first place we have no evidence that adrenalin is ever thrown into the blood stream in such quantities normally in the living body. Furthermore, there is no evidence of a true antagonism. Adrenalin tends to produce glucose from glycogen and thus throws sugar into the blood stream, but it does not cause inability to use glucose, which is the essential feature in diabetes. Furthermore, there is recent evidence that insulin does not serve specifically to build up glycogen, and under some circumstances actually reduces it. Therefore, no true antagonism exists between adrenalin and insulin, and there is no proof of any glandular antagonism in the body. Diabetes is purely a pancreatic disease.

Seventh. It is not true that the mechanism of insulin action is yet known. The theory of Winter and Smith that there is something peculiar in the character of the glucose, that the blood sugar in diabetes is chemically different from that of the normal organism, is not apparently gaining support. One of the most interesting future possibilities is that we may learn how insulin is related to the carbohydrate metabolism, or to the total metabolism. Even the toxic effect of insulin is not yet explained. One of the brilliant observations of the Toronto school was found in the symptom complex of hypoglycemia—the effect on the body of too little blood sugar. But insulin poisoning is not due strictly or solely to hypoglycemia. Your patient may show severe symptoms of collapse, or even unconsciousness or convulsions, and yet not have an extremely low blood sugar. We do not know what makes the

intoxication in such a case. We do know that glucose relieves it, regardless of the blood sugar level.

Eighth: It is not true that the insulin requirement is governed by the total metabolism. Exercise is a very powerful means of raising the total metabolism, but it rather lowers the insulin requirement. The patient taking heavy exercise does not need more insulin than before; he needs less. Whether insulin is related to the basal metabolism is not clearly proven. There is partial evidence in favor of the conception of basal metabolism being a deciding factor. In fasting, glycosuria is reduced, the insulin requirement is reduced and the basal metabolism is reduced. We do not know whether the fall in metabolism is the essential reason for the relief of the strain upon the pancreas. In the majority of cases when the basal metabolism is raised (e. g., by gain of weight, by hyperthyroidism or by fever) the tendency to glycosuria and the need for insulin is increased. But this suggestive evidence is not conclusive.

Ninth. It is not true that either the diet or the urine furnishes any uniform basis for calculating the insulin dosage. In the early days many conjectures were made that if there was a certain quantity of glucose in the urine or in the diet a certain number of units of insulin would be needed. That is not true. The only way to find out the insulin dosage is to try it. For instance, there is a difference according to the source of the glucose. If a patient shows glucose in the urine from adding carbohydrate to his diet, that is one thing; if he shows the same amount of sugar in the urine from adding high calories in the form of fat, that is very different. The latter form is much harder to clear up, and takes more insulin. Also the effect of complications is well known. Acidosis, for some reason, multiplies the insulin requirement. There is also an observation from Toronto which seems to be correct, that each unit of insulin becomes less effective as the total units are increased. If you give a patient 100 units of insulin, each unit is less effective per gram of glucose than if you give 10 units. There are other factors, but certainly there is clinical proof that only by testing the individual case can one decide how much insulin is needed.

Tenth. It is not true that there is any specific progressive pathological process in diabetes if the pancreatic function is saved from functional overstrain. Several years ago I put forward this doctrine, and I doubt if anybody believed it at that time. Now with insulin at hand, probably everybody will believe it, because with insulin we can relieve the strain upon the pancreatic function more easily and more thoroughly than could previously be done by diet. In severe cases it was formerly very difficult to keep the blood sugar down and clear up obvious signs of overstrain of the pancreatic islands. Now that this is done on a wide scale with insulin, everybody can see that the progressiveness of diabetes can be halted. The reason for progressiveness is found in the hydropic degeneration of islands of Langerhans, photographs of which you have seen passed around in this meeting. Hydropic degeneration is the vacuolation, swelling and destruction of the island cells, which results from functional overstrain. The islands get it only when they try to

work beyond their capacity. When that process is checked either by diet or by insulin, diabetes apparently does not progress.

#### PRACTICAL DETAILS

Altogether twenty points have been mentioned as not true, and it may be asked, "What is true?" There remains much room for individual judgment as to the method actually used, if a few basic principles are observed.

In the first place we prefer beginning with institutional treatment, which means that the patient generally remains in the hospital for two or three weeks. We believe the case can be studied better and the patient taught to care for himself better by being in an institution, and the period should not be too short or he loses the full benefit.

Then, using the same two headings, diet and insulin, I shall take up first, diet.

The first requisite is a doctor's ability to calculate a diet. If he cannot figure a diet in carbohydrate, protein and calories, he ought not to treat diabetes. Anybody can be a specialist if he will simply familiarize himself with the primary principles of diet, but if he will not take that trouble, he ought to send his diabetic patients to somebody else. But if he goes to this trouble he can treat diabetes more easily and also more successfully than can be done by following any hard and fast set of rules.

As regards proportions of the different foods, we believe that 60 to 80 grams (or more in mild cases) of carbohydrate and about the same of protein makes the most satisfying diet, is most conducive to comfort, strength and fidelity, and gives the widest margin of safety against acidosis. In a few cases lower carbohydrate and protein may be useful for reducing the dosage of insulin or avoiding it altogether. In all cases it is a matter of preference, not a choice between right and wrong, as to whether the diet contains high or low proportions of carbohydrate or fat, provided the total calories are suitably restricted. If you believe in carbohydrate and protein rations as low as 30 or 40 grams per day you may treat diabetes very efficiently with them, but comparative tests will show you that in the long run little insulin is saved and the patients are distinctly less comfortable than with the more normally balanced diet above mentioned.

As regards total calories, our diets are such as to keep the patients not above the normal average weight. Sometimes they are fully up to the normal, and frequently five or ten pounds below the normal average, because in this way less burden is placed upon the pancreas, and on the whole the patients do better. The influence of the total calories and body weight far exceeds the influence of a few grams more or less of carbohydrate or protein.

Then, as regards insulin, we use it when there are severe complications, or when the patient cannot gain tolerance for an adequate diet without insulin. Blood sugar determinations are desirable. Some persons have tried substituting other tests, particularly the new quantitative methods for sugar in normal urine, but I believe the consensus of opinion is that the best method is that of blood sugar tests. They may not be absolutely indispensable, but they

are extremely valuable and are generally the best basis of treatment.

The dosage of insulin is that which will keep the patient completely free from glycosuria, and the blood sugar as nearly normal as possible. It cannot always be normal. But the patient with glycosuria or extremely high blood sugar is liable to infections, and is more apt to develop acidosis and perhaps die suddenly. With existing glycosuria, even though the patient is on high insulin dosage, there is very serious danger of a sudden outbreak of acidosis, causing death within forty-eight hours.

The total daily dosage is divided into a number of injections, according to the size of the total dose. We practically never give more than 20 units in one dose. We seldom give less than two doses per day, even if the total number of units of insulin is low. Insulin may be given with meals; that is the commonest way, but in some of the severest cases we have published a method of giving it about one hour before breakfast for the first dose, and an hour or two after supper for the third dose, as that plan shortens the night period. This reduces the tendency to fluctuation in the blood sugar, and there is no particular reason why every dose should be given with a meal.

Also the plan is to keep the total insulin as low as possible. If it rises too high, for example, above 100 units, it is almost impossible to keep the patient free from glycosuria or hypoglycemia, one or the other. The only remedy is to cut down the insulin dosage. The way to do that is to reduce the patient's weight. Therefore, as far as possible, we use a low caloric diet to keep the body weight somewhat below normal, and in that way ordinarily we keep the insulin dosage down, so as to allow the case to run smoothly. The patient who can use the least insulin is the best off in the long run.

The special treatment of complications cannot be gone into in detail, partly because it has been covered so often before.

The point I would emphasize, in conclusion, is that all the evidence, theoretical and practical, indicates that if patients are handled properly in these two respects—diet and insulin—every case of diabetes can be controlled, and this control can be maintained without downward progress and without any deaths occurring on account of diabetes.

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**Some Causes of Ageing**—"We doubt if we can ever discover means of greatly lengthening life," concludes Malford W. Thewlis (Medical Journal and Record). "There are many factors," continues this author, "at play in the production of premature senility, such as an abnormal mode of living, and the excitement and worry of modern life. Normal old age seems to be a mystery, as far as its actual cause is concerned. There seems to be a law of Nature which brings about old age just as it brings birth in a given length of time, and puberty at another. If Rolleston is right, there is a more or less definite cycle during which cells multiply and after which they cease to do so. It seems to be the best explanation we have of the cause of normal old age. As for the causes of abnormal old age, to repeat, numerous factors must be considered."

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"... There is no greater power in the realm of man today than the printing press, and it would be infinitely more powerful and productive of results if those whose thoughts go out to millions through it would write in a spirit of service and in the sense of stewardship."—Edward W. Bok.