

The Canadian Medical Association Journal

VOL. VI.

AUGUST, 1916

No. 8

THE TREATMENT OF DIABETES MELLITUS

BY ELLIOTT P. JOSLIN, M.D.

Boston

RATHER more success is achieved by surgeons in the treatment of general peritonitis than is attained by physicians in the treatment of diabetic coma. In neither condition are the statistics flattering to the profession; but the successes obtained by our surgical colleagues in the prevention of general peritonitis make the failure to prevent coma as a cause of two out of every three diabetic deaths mortifying to say the least. We physicians should begin to regard diabetic coma in the same light as your British brother, Mr. Moynihan, has taught the medical fraternity to look upon the late stages of a neglected gastric ulcer—namely, as an emergency which should not have been allowed to arise.

With this issue of the prevention of diabetic coma plainly to the fore as the cardinal point in the treatment of diabetes, it is pertinent to inquire what diabetic patients are most susceptible to coma? And your own experience will enable you to anticipate that the answer, which an analysis of my own fatal cases shows, will be children. Of the sixty-two diabetic children under the age of fifteen who have died under my care, coma was the cause of death in all, and the significance of this melancholy fact is this: that where diabetes appears in its most severe type, as in children, coma is its expression. The propositions are simpler to state than to execute—first, that the best way to avoid coma is to prevent the progress of a case of diabetes from the mild into the severe type, and second, to protect the patient from all those agencies such as infections, anæsthetics like chloroform and ether, undue exertion (mental or physical), which tend toward intensifying the severity of the dis-

Address delivered before the Ontario Medical Association, June, 1916.

ease. For if the diabetes is kept mild or moderate the coma need not be feared.

Next to the children in the frequency of death from coma, strange as it may appear, were those of my cases who succumbed during the first year of the disease. The cause of death in 87 per cent. of these was coma. But diabetes is a chronic disease and the first year of its course should be mild rather than severe, and in mild diabetes coma should find no place.

Just as the health officials of a city, zealous to lower its death rate, concentrate their efforts on those sections of the city with the highest mortality, so should we, in the treatment of diabetes, concentrate our efforts where mortality is also greatest—on the children and on those patients who have recently developed the disease. To-night attention will be directed upon the treatment following immediately upon the detection of the disease, for this is where the highest mortality in diabetes now exists.

Reference has just been made to a mortality of 87 per cent. from coma among diabetics who die during the first year of the disease. Is the term "first year of the disease" quite accurate? It is meant to be accurate. I have most conscientiously tried to fix a definite date for the onset of diabetes in all of my cases. But honestly would it not be more truthful to say the first year of the recognition of the disease? And herein lies a vast difference which gives rise to serious reflection, for it is in the first year of the *recognition* of the disease that treatment is begun, and the highest mortality occurs. Disagreeable as such an implication is to hear, some support for it is afforded by the fact that with the increase in the knowledge of the treatment of diabetes, the mortality for the first year of the disease has decreased. It is significant that whereas between the years 1824-1898, of those cases of diabetes dying at the Massachusetts General Hospital, the duration of the disease was under one year in 68 per cent., for the subsequent fifteen years ending November, 1913, Dr. Brigham and I are able to say, thanks to the courtesy of the hospital authorities, that the mortality during the first year of the disease had fallen to 41 per cent. My friend Professor Naunyn, whom all of you will recognize as a master of diabetes, though his cases must have been treated during a generation previous to ten years ago, showed a mortality of only 28.2 per cent., which was the same, as far as I can determine, for the city of Boston for 1915. The period of my own activity has been later, and so more favourable; perhaps my cases have been less severe, and this may explain first, why but 17 per cent. of my own cases

have died during the first year of the disease, and second, the more encouraging feature that 95 per cent. of those living have already gone beyond this period. In fact, my own experience is against the idea that properly treated diabetes runs an acute course. Such figures, while they afford reason for gratification at the improvement in treatment, also furnish proof that the high mortality in the first year is unnecessary, and in what follows will be indicated how the development of acid poisoning during this period may be avoided and how to conquer it before coma results.

The prophylactic and etiological treatment of diabetes will surely play an important rôle in the future, and it is already plain that progress will be along two lines; first, towards the early detection of the disease in those susceptible to it. The whole trend of Naunyn's teaching favours the energetic treatment of the slightest evidence of diabetes. The importance of the early treatment of pulmonary tuberculosis is not greater than that of the early treatment of diabetes.

The only way in which an early diagnosis of diabetes will ever be made is to search for it. The favourable results in fifty-seven of my cases of diabetes revealed by life insurance examinations cannot be explained by the mildness of the diabetes discovered. It is a hopeful sign that the insurance companies are offering to examine the urines of their policy holders gratis at frequent intervals. Everyone should have the urine examined upon his birthday.

Diabetes should be sought in the families of diabetic patients and in order to allay anxiety from urinary examinations, it is a good plan to have these made with such frequency that they will become simply a matter of routine. Such individuals should be taught to regulate the quantity of food eaten by the body weight, and never to indulge in unusual quantities of carbohydrate.

No præxistent abnormal condition has occurred more frequently among my diabetic patients than has obesity, and it affords a splendid opportunity for the physician in which to practise preventive medicine. Patients should be cautioned against suddenly gaining weight at any period, but particularly after infectious diseases. The development of diabetes following infectious diseases and in the course of pregnancy always should be borne in mind. Finally, anything which tends to promote the mental and physical welfare of the patients will tend to prevent the onset of diabetes.

Surgery may find a field for treatment in the future more than it has in the past. I recall eight cases of diabetes associated with gall stones which ran an unusually favourable course so soon as

the symptoms of the gall stones had subsided, either as a result of medical or of surgical treatment.

That temporary periods of under-nutrition are helpful in the treatment of diabetes will probably be acknowledged by all after these two years of experience with fasting. In no other way can one so readily keep the urine free from sugar and this is the foundation of all diabetic treatment. With a sugar-free urine there is seldom any opportunity for coma. The inauguration of the treatment and the prolonged continuance of the same are problems which present the most difficulty. Practically the only danger associated with the former is the possibility of acid poisoning at the beginning of the fast, though it can be emphatically stated that it is the rule for acid poisoning to decrease rather than to increase as the fast continues. But on account of the few cases where it does increase it is safer to prevent acidosis than to allow it to develop. This is the reason for what might be called a preparatory treatment for fasting, for it can be assumed that a method of treatment which approaches or embraces fasting is the best method we possess. It is a sound rule of all treatment that patients coming to the physician in an endurable state must not be made worse or have their lives jeopardized by the therapeutic procedures adopted.

Treatment is simplified, if acidosis is prevented, because no urinary tests will, as a rule, be required save a qualitative test for sugar and the simple ferric chloride reaction for di-acetic acid. Such simplification of methods is necessary when we realize that most physicians do not have more than five or ten cases of diabetes a year and therefore cannot devote to these a proportionately large share of their time.

Individuals predisposed to acidosis are those in whom the disease is of long duration. These are the patients who, after having lived in a fairly comfortable condition for years, finally succumb to active treatment within a few days of its commencement. All complicated cases, especially those in which the complication involves the kidneys, heart or thyroid, demand preparatory treatment, for they are especially susceptible to acidosis. In this group are also included elderly patients, because of their vulnerable kidneys. Very fat diabetics could appropriately be included, and so too, patients about to undergo surgical operations. Finally, all patients showing signs of acid poisoning demand this preparatory treatment before the fast, unless the physician is in a position to watch quantitative changes in the acidosis from day to day.

The principle upon which preparatory treatment is based is

simplicity itself—the exclusion of the source of the acid poisoning. Since the chief source of acid poisoning is fat, this constituent of the diet is prohibited before any further change is made. If this rule is adopted, the opportunity for the patient to develop acid poisoning is greatly reduced, and for two reasons: first, the chief source of acid bodies is removed, and no fat is then available for the formation of acid bodies except the fat of the body; second, in consequence of the partial fast, which is thereby initiated, the possibility of oxidation of some of the carbohydrate which the patient is eating is afforded, and if this should fortunately take place, acidosis is sure to decrease. So strongly have I been impressed by the stormy career of the diabetic patients in whose diet carbohydrates have been suddenly restricted and fat increased, in contrast to the placid course which those pursue from whose diet fat has been excluded and the carbohydrates left unchanged, that whenever I am asked to see a new case of diabetes I beg the physician either not to change the diet at all, or simply to omit the fat until the consultation takes place, and when the patient actually comes for treatment I first omit all the fat in the diet, after two days the protein as well, and then halve the carbohydrate on successive days until 10 grams are reached unless the patient is already sugar-free, and thereafter fast.

The days of preparation for the fasting are also advantageous in that they allow opportunity to examine into the general condition of the patient. It would be absurd to feed a patient without teeth with coarse vegetables, or to give these to another patient who has diarrhoea. The bowels must be thoroughly opened, but I do not believe in free catharsis. Gain enough is obtained if a movement is produced once in twenty-four hours when it has only been taking place once in three days. In other words, do not upset any patient who is in a tolerable state. Furthermore, allow the patient to continue his regular routine, avoiding excess in any direction. Remember what happens to an old man who is suddenly confined to bed, and the discomfort which follows confinement following a fracture. Do not force a temperate man to drink against his will.

An advantage which the omission of fat from the diet affords is the rest which is given to the digestive tract. Former treatment, which increased the fat in the diet, was the converse of this, and frequently led to vomiting, with the result that patients on the verge of coma fell into it. In every way seek to prevent worry on the patient's part, and from the start give them to understand that they are at school rather than at a hospital.

After the preliminary measures have been taken to prevent the appearance of acidosis one may proceed with fasting. Fasting is never so rigorous as doctors or patients expect. Patients are more ready to undergo it than physicians to prescribe it. Quite as often it is as much a relief to the patient as it is a discomfort. This is in part due to the gradual decrease in polydipsia and polyuria. Headache occurs less frequently than I expected, and is usually dispelled by a cup of coffee. Nausea almost never occurs unless a patient is given alkali or alcohol. Children bear it more easily than adults. Case No. 899 with onset at eighty-three shunned it and rightly, but she became sugar-free and her family, at first reluctantly, but now emphatically, agree, with distinct benefit. In fact, it is always desirable to avoid fasting in the old, and this can ordinarily be accomplished by the help of preparatory treatment because the simple omission of fat and reduction of protein and carbohydrate will usually suffice to make the urine sugar-free.

Fasting does not seem like fasting to the patients when they receive coffee, tea, cracked cocoa and broths, and are given an unlimited supply of water. If the quantity of urine, as it often does, falls to less than normal, the patients are urged to drink water freely. Clear meat broths are a great satisfaction. Contrary to my experience with digestive cases, broths do not stimulate the appetite in fasting diabetics; they relieve it. The advantage of broths is probably due in part to this, but to a considerable extent to the patient receiving salt by which he may maintain the equilibrium of the body fluid. It is possible that the salt is a more important factor in the treatment than has been supposed.

Patients should not be kept abed during fasting, neither should they be forced to be up all day. They should be afforded diversion by visits from friends, walking short distances, easy handiwork, playing games, letter writing and reading. In general they are glad to rest for the greater part of the first day of the fast, but upon each succeeding day I have noticed that they are desirous to increase the amount of exercise, and the exercise appears to lessen the necessity for a prolonged fast. Case No. 765, a trained diabetic, who returned to the hospital in order to become sugar and acid-free, at the end of three and one-half days of fasting, enjoyed, without fatigue, going to the theatre. I confess this was not with my advice, for I have endeavoured to prevent exposure to any infectious disease of all diabetic patients during fasting. However, Case No. 938, a child of two and a half years, underwent fasting

treatment successfully in the presence of a mild infection of the upper air passages.

It is surprising how variable is the period required to render the urine sugar-free. Frequently a urine which contains 7 per cent. of sugar becomes sugar-free after four meals of fasting, and conversely a urine with only 3 per cent. of sugar may still retain traces after the patient has been deprived of food for three or four days. In general cases seen soon after onset become sugar-free promptly, whereas the reverse is generally true for those of long duration. Children showing large quantities of sugar have also become sugar-free very promptly when the duration has been only a few weeks. I have a suspicion that cases of long standing will actually become sugar-free more quickly if they undergo preparatory treatment than if they are fasted immediately. This may be due to the avoidance of even a slight acidosis. Even a slight acidosis must be conquered.

The observation of Folin and Denis that an obese individual, though otherwise normal, developed marked acidosis upon fasting but went through a second period of fasting with less acidosis than the first, and the practice, observed by many clinicians of the old school, who advantageously fasted their diabetics one day a week, have given the cue to intermittent fasting.

For a good many months none of my patients have been subjected to a fast of more than four days. A prolonged fast is unnecessary, and even if the fast is carried out, it is doubtful if the patient would always become sugar-free. The apparent reason for the persistence of sugar in Case No. 610, who fasted for nine days, was the presence of a vulval abscess, and inquiry among my friends shows that an infection of some kind is usually present when glycosuria persists after a fast of a few days' duration. This is not always the case, for the difficulty in rendering the urine sugar-free may be due simply to the extreme severity of the disease.

Alternate feeding and fasting are adopted when it is found that the glycosuria persists after a preliminary four days' fast. The method which I have found most successful has been to allow, following the first fasting period, 20 to 40 grams carbohydrate—not far from half a gram per kilogram body weight—and about one gram of protein per kilogram for two days. The sugar promptly increases in the urine, but if one averages the excretion of sugar in the urine of these two days with the two days at the beginning of the fast, the result is encouraging. Then fast again; but the second fast is a day shorter than the first, and the second period of feeding

a day longer, until by the fourth period of fasting the patient goes without food only one day and then is given food for four days. This schedule need not be followed exactly, but the general plan has proved most efficacious.

When the 24-hour quantity of urine is sugar-free one can usually give a few grams of carbohydrate to the patient without the appearance of glycosuria. The carbohydrate is generally given in the form of 5 per cent. vegetables, choosing those which are especially bulky. A plateful of lettuce appeals much more to the patient than a small saucer of string beans. When a mixture of 5 per cent. vegetables is given one can be quite sure that the average content of carbohydrate is not more than 3 per cent., or approximately $4\frac{1}{2}$ grams for the 150 grams prescribed, and for convenience sake this is reckoned as one gram of carbohydrate for each 30 grams (one ounce). This small amount of food, of course, has little nutritive value, but is enough to break the fast. Upon succeeding days 5 or 10 grams of carbohydrate are added daily. A patient fasting or on a very low diet often shows an apparent tolerance for carbohydrate far in excess of that which he would have shown if the necessary protein and fat in his diet were simultaneously administered.

Following the trial with 5 per cent. vegetables the addition of carbohydrate can be made according to the desire of the patient until the tolerance is determined.

With children one often makes the mistake of increasing the carbohydrate 5 grams daily, forgetting the fact that 5 grams of carbohydrate to a child weighing 20 kilograms is in the same proportion as 15 grams of carbohydrate to an individual of 60 kilograms.

Patients who have lived for a considerable length of time on a comparatively low tolerance for carbohydrate may upon trial show that the real carbohydrate tolerance is much greater than supposed. The most striking example in my series has been the patient already referred to—No. 610, who fasted for nine days without becoming sugar-free. During the last twelve months she has lived comfortably but the quantity of carbohydrate in the diet has been represented by 60 c.c. of cream (2 grams) for all her vegetables have been thrice washed. Despite this rigid diet sugar kept recurring every few days but she persisted to drive it out by fasting. Recently upon reëtrance to the hospital she became sugar-free overnight, and thereafter the steady addition of 10 grams of carbohydrate a day in the form of vegetables up to 55 grams,

failed to cause glycosuria, to the surprise of us all. At length, as a test, she drank 55 grams of lævulose and even then the urine remained sugar-free. At this time the protein in the diet was represented only by that contained in the vegetables. Thereafter it was gradually increased, and along with it a little fat, so that finally, at the end of ten days following her readmission to the hospital, she was taking 55 grams of carbohydrate, a gram of protein per kilo, and at this writing sufficient fat to be equivalent to about 25 calories per kilogram body weight. Contrast this picture with that of a year ago when it was necessary for her to fast nine days to make the urine sugar-free and when a diet in excess of 2 grams of carbohydrate led to the appearance of sugar in the urine. This very recent experience has given renewed hope to my patients who have been watching its development, and to me. It is a fresh demonstration of the efficacy of energetic treatment.

As a rule when the urine has been sugar-free for two days, 20 grams of protein are added to the diet, and thereafter 15 grams of protein daily until the patient is receiving 1 gram per kilogram body weight. The protein may be given either in the form of eggs, lean meat or fish; an egg of average size contains approximately 8 grams of protein and 30 grams (1 ounce) of lean meat contain approximately 8 grams. By this arrangement a patient weighing 60 kilograms would be taking, within six days from the time he became sugar-free, 1 gram of protein per kilogram body weight. This quantity is quite satisfying to all except children—in fact, it astonishes me to find how few patients care to take as much as a gram and a half of protein per kilo body weight. Children, however, crave and need considerably more, and indeed take with avidity as much as 2 or 3 grams protein per kilogram body weight.

Fish is especially desirable in the early days of protein feeding because it contains so little fat. Cod and haddock, for example, contain less than 1 per cent.

The advantage of giving and increasing protein simultaneously with the determination of the carbohydrate tolerance is that one approaches more nearly normal conditions. What the physician is after is to determine the carbohydrate tolerance while the patient is on a full diet, and not the tolerance for carbohydrate alone, but it is possible that one should defer the addition of protein a few days longer if the carbohydrate can be steadily increased without the appearance of sugar.

There are very few patients who will not bear at the outset as much as 1 gram of protein per kilogram body weight, and I am

very loath to allow the protein to remain permanently below this figure. This can be avoided by still further restricting the carbohydrate, either temporarily or permanently. It is always necessary to bear in mind that one food which the diabetic patient cannot do without is protein, and to it everything else must be subservient.

While testing the protein tolerance, a small quantity of fat is included in the eggs and meat given. It is not at all disadvantageous—in fact, the same rule holds for the testing of the carbohydrate and protein tolerance in the presence of fat as has been said for protein alone. There are two important reasons why fat is not given to the diabetic immediately upon his becoming sugar-free: first, by the omission of fat partial fasting is continued and thereby the patient is gaining a tolerance for carbohydrate, and second, the continued omission of fat is beneficial in counteracting the last vestige of acid poisoning, or preventing the appearance of acid poisoning, which easily might occur in a diabetic patient whose metabolism has not become accustomed to so low a quantity of carbohydrate. But so soon as the patient has received the essential gram protein per kilogram body weight, the fat in the diet should be increased above the 15 to 20 grams which undoubtedly are introduced with the protein ration. If the patient is one in whom acidosis has been an essential factor, or if the patient is obese, the fat should be increased slowly, and for such a patient an increase of 5 to 10 grams a day may be all that he can take without the recurrence of a positive ferric chloride reaction in the urine. On the other hand, attention is called to Case No. 765, who, after persistent periods of intermittent fasting, became sugar and acid-free, and yet the immediate addition of 30 grams fat per day failed to cause the reappearance of acidosis. Cases which have shown little acidosis may easily be allowed an increase of 25 grams fat daily, and for such cases this is desirable, because it rapidly brings the total caloric value of the diet up to a normal figure. Naturally, patients in whose treatment a loss of weight is desired would be given smaller quantities of fat.

The total number of calories which a diabetic requires varies not only with each case, but varies with each case each day. Schematic rules do not hold. One must remember that an individual trained to be quiet and lying down can get along with only 20 calories per kilogram body weight reckoned per twenty-four hours, whereas the average of a large group of normal men and women, not especially trained for the test at the Carnegie Laboratory, consumed 25 calories per kilogram body weight reckoned also

per twenty-four hours. Habits of individuals vary widely. Some are quiet and some are active. All these considerations should be clearly borne in mind by doctors and patients in order not to allow themselves to be held too rigidly by any caloric fetish. Patients coming for treatment with severe acidosis consume from 10 per cent. to 20 per cent. more calories per kilogram body weight than patients after they have become sugar-free and free from acid.

After the diabetic has become sugar and acid-free, he apparently gets along, as Naunyn long ago pointed out, with a smaller amount of food than an ordinary individual. This may be so. From a study of dietary charts in diabetes it appears probable, but I do not believe the question yet settled. Before this can be done, studies should be made upon cases of diabetes of the severest type who have become sugar and acid-free, and remained so for a period of weeks. The caloric values of their diets should then be quantitatively determined. Ordinary calculations, based on dietary tables, will not suffice. Actual analyses of the diets of a group of such patients for a period of several weeks should be made. This is by no means an impracticable matter, and I think the accomplishment of it would be of the greatest help to diabetic patients and would settle many mooted points.

Should the calories be raised above a minimum portion in severe cases of diabetes, glycosuria will return. Therefore great care must be taken to prevent over-eating and undue gain of weight.

The return of sugar demands fasting for twenty-four hours, or until sugar-free. This rule should be inflexibly followed, especially with children. In hospital it simplifies the treatment enormously. So soon as it is understood that the reappearance of sugar means a fast for twenty-four hours thereafter, there is little tendency to break over the diet. Furthermore, most patients are thrifty enough to see the disadvantage of paying their board with no return. The rule must be rigidly enforced with children, because with them disobedience means death. When a patient has been made sugar-free by a preliminary fast, starvation for twenty-four hours will almost invariably be sufficient to free the urine at once if the sugar returns. This will not be the case unless the presence of glucose is promptly detected, and hence the necessity for the patient's examining his twenty-four hour urine daily. Following this accessory fasting day, the previous diet of the patient may at once be resumed except for the elimination of half of the carbohydrate, or the original course of treatment may be followed, except passing through the different stages at a more rapid rate.

The advantage which the older clinician derived from the use of one day's fast in seven in the treatment of his diabetic patients should ever be borne in mind. One striking characteristic of Dr. Allen's helpful suggestions in the treatment of diabetes (and I cannot say more than I already have said elsewhere of my high appreciation of his work) has been that he has apparently sought out every method which anyone has found useful in the treatment of diabetes, tested its worth, and endeavoured to adapt it to modern conditions.

The mild case of diabetes is the case which demands the most energetic treatment, but hitherto has received the least. These cases are analogous to the cases of incipient tuberculosis. As in tuberculosis, a cure may not be effected, but the disease is held in check. Emphasis should be placed on freedom from glycosuria. Naunyn's dictum that many a severe case was originally mild, but neglected, should not be forgotten. It may not be necessary for such patients to practise fasting. In our enthusiasm for new methods it should not be forgotten that even in the past good results were obtained with many diabetics, and that gradual restriction of carbohydrate and the total diet was the means employed. Incidentally, this is good proof that most diabetics are not severe.

It would be wrong to give the impression that the treatment of severe diabetes is simple and free from anxiety. It is true that it is much easier and causes infinitely less worry to the physician than heretofore, but these patients are in most unstable equilibrium and a little upset of trivial character may lead to much danger. The physician who treats severe diabetes successfully must constantly be in close touch with his patient. Forewarned, forearmed! I like to have at least a glance at a severe case of diabetes two, three or four times a day, and the amount of information furnished by the laboratory is never too great.*

* This paper was prepared simultaneously with the text of a book of similar title now being published for the author by Messrs. Lee & Febiger.