THE CANADIAN MEDICAL ASSOCIATION

LE JOURNAL DE

L'ASSOCIATION MÉDICALE CANADIENNE

APRIL 18, 1964 • VOL. 90, NO. 16

Observations on the Etiology and Therapy of "Brittle" Diabetes

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ABSTRACT

Salient aspects of prolonged metabolic studies on seven excessively labile diabetic patients and a review of the literature concerning causation and therapy of brittle diabetes are presented. Brittleness is redefined as "a syndrome of excessive insulin-sensitivity and ketosis-proneness manifested by extreme and unexplainable short-term and long-term fluctuations in the parameters of the disease". Evidence on the causation of hyperlability points to dysfunction of plasma-protein transport and of hepatic and peripheral tissue metabolism of insulin. No objectively demonstrable complete and lasting stabilization was possible by means of any antidiabetic or adjunctive therapeutic measures. However, achievement of quantitative improvement in the accuracy of regulation of diabetes and moderation in deviations from the acceptable range of parameters were feasible. To this end, therapy recommended for everyday use incorporates the following principles found to be most helpful in following the oscillations of the disease on the research ward: flexibility in the plan of therapy; accuracy, especially in timing of therapeutic events; and employment of an insulin program best suited to the patient's needs and comfort.

SOMMAIRE

L'auteur expose les aspects saillants d'une longue étude métabolique portant sur sept malades atteints de diabète labile très prononcé et passe en revue la littérature sur l'étiologie et le traitement de cette forme de diabète. L'instabilité du diabète labile est de nouveau définie comme étant "un syndrome d'hypersensibilité à l'insuline et une tendance excessive à l'acétonémie, se manifestant par des fluctuations, extrêmes et inexplicables, tant à court terme qu'à long terme, des paramètres de la maladie." En ce qui concerne les facteurs étiologiques de cette hyperinstabilité, certains signes tendent à démontrer qu'elle peut relever d'un trouble du transport des protéines plasmatiques et d'un trouble fonctionnel du métabolisme de l'insuline, au niveau du foie et des tissus périphériques. Aucun antidiabétique, ni aucun moyen thérapeutique adjuvant n'a permis d'assurer une stabilisation durable et complète de l'affection, du moins qui soit démontrable objectivement. Toutefois, il a été possible d'améliorer quantitativement et avec précision la régulation du diabète et de maintenir, dans des limites acceptables, les déviations des paramètres. A cette fin, le traitement routinier quotidien devrait se baser sur les principes suivants qui se sont révélés très utiles pour pouvoir suivre les oscillations de la maladie, dans la salle d'observation: souplesse du traitement global, précision et ponctualité des mesures thérapeutiques et recours à l'insulinothérapie qui est la mieux adaptée aux besoins et au bien-être du malade.

METABOLIC instability is not an exclusive characteristic of certain diabetic patients, but in few other chronic illnesses do such wide fluctuations of clinical and biochemical parameters occur as they do in the "brittle" diabetic.

The use of the term "brittleness," coined by Woodyatt,[1] is restricted by my colleagues and myself[2, 3] to denote diabetic hyperlability of such degree in lean, ketosis-prone, insulin-deficient and variably insulin-sensitive persons that parameters of metabolic derangements fluctuate widely, despite attempts at the best possible treatment. This definition excludes lability caused by therapeutic errors

From the Section of Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minnesota, U.S.A.
Presented at the 58th Annual Convention of the Alberta Division, Canadian Medical Association, and the 50th Anniversary of the School of Medicine, University of Alberta, Edmonton, Alta., September 19, 1963.

of the patient or physician, and requires that a rigorous and usually prolonged trial of therapy be undertaken before the term is applied. As we see it, only when regimens of diet, exercise and insulin have been finely adjusted and considerable oscillations between hyperglycemia and hypoglycemia still remain is use of the term "brittle" equitable. The cardinal symptom is the unexpected and unpredictable occurrence of hypoglycemic reactions. However, even when these are held to a minimum, tests of the blood and urine for glucose and other indices of diabetes yield highly variable results.

The definition in each case is difficult. Small wonder that it is hard to estimate the frequency of occurrence of brittleness in diabetes. The incidence of 2 to 10%[4-6] assigned to brittle diabetes in the insulin-using diabetic population may be too high or too low, depending upon the criteria applied. On the one hand, physicians may be too likely to make the diagnosis of "brittle diabetes" in patients who do not follow instructions as a consequence of error or neglect. On the other hand, the diabetes of some patients may appear to be more stable than it really is because regulation of their diabetes is so poor that even the nadirs of their blood-glucose waves are within the hyperglycemic range. Incidentally, probably not too many instances of true hyperlabile diabetes are missed because of faulty regulation and neglect; actually, victims of this form of diabetes are so susceptible to ketoacidosis as to become comatose if insulin deficiency is permitted to become progressively more severe. Overly zealous therapy with excessive doses of insulin can, of course, make inherently stable diabetes appear labile.[7] Thus, the diabetes of such a patient oscillates between extremes of insulin-induced hypoglycemia and endogenously (counter-regulatory factors) and exogenously (therapeutically) produced hyperglycemia. The latter extreme tends to result as body, patient and physician strive to undo the ravages of too much insulin.

As etiologic and therapeutic factors affecting lability in diabetes are presented herein, I believe our definition of brittleness will be clarified, documented and justified.

ETIOLOGIC CONSIDERATIONS

Fundamental to any realistic hope for the rational therapy of brittle diabetes is acquisition of information concerning etiologic factors which make the disease of such patients unstable. Candor compels the admission that very little such information is presently available. A systematic survey of the field is nevertheless enlightening.

It is known that in the normal, non-diabetic state, the release of insulin is intimately associated with the concentration of glucose in pancreatic arterial blood.[8, 9] The supply of insulin is adjusted on a minute-to-minute basis to the body's needs.[10] It may be that the liver, rather than the pancreas, is responsible for minute-to-minute regulation.[11] In any case, in the patient dependent on an exogenous supply of insulin, only crudely gauged by patient or physician, the automatic relationship of insulin supply of blood-glucose concentration is lost. This loss of automaticity might be expected to lead to loss of stability and failure of prompt compensation for either hyperglycemia or hypoglycemia. Logically, therefore, the diabetic person dependent upon exogenous insulin would be expected to have wide fluctuations in values for blood glucose. What is to be wondered at is that so many insulin-taking persons have stable diabetes and that so few have the disease in its highly unstable form. Indeed, the pathophysiologic aspects of whatever factor(s) permits stability in diabetes might be worth investigating.

There is no scientific evidence to justify blaming brittleness on either a total lack of endogenous insulin or the opposite, namely, undesirable and ill-timed addition of spontaneously released endogenous insulin to the supply of exogenous insulin. Both the extremes mentioned, however, remain etiologic possibilities worthy of study.

More to the point in any explanation of an apparently erratic mechanism of insulin activity would be the theory of irregularity in the binding and release; that is, the inactivation and reactivation of insulin by serum or tissue proteins. In all patients who have taken insulin for about three months, such insulin-binding by so-called insulin antibodies is readily demonstrable.[12] It is regrettable that at present methods for the measurement of the magnitude of insulin-binding are too crude to permit assay of the relatively minor changes which could account for the excesses or deficiencies of active insulin which in turn might explain the fluctuations of brittle diabetes.[13]

Studies of the dynamics, meaning the magnitude and rate of association and dissociation between exogenous insulin and insulin antibody in the same patient but at different times, are even more difficult to do and the results thus far are of no help.[13, 14]

In groups of pregnant and of menstruating diabetic women we have serially measured insulin-binding capacities in relation to major and minor changes in apparent insulin needs.[13] Some of our patients had diabetes which was definitely brittle. With the techniques available to us, a remarkable constancy of insulin-binding was demonstrated in each patient from hour to hour, day to day and even year to year.

That insulin is not exclusively bound by serum proteins but also is bound by the tissues has already been mentioned. Specifically, hepatic and peripheral tissue-binding is known to occur.[15, 16] Both these processes may be etiologic factors in lability. Madison and Unger[15] have pointed out the different results obtained from supplying insulin via the natural pathway and the artificial ingress, meaning the portal *versus* the systemic circulations to the liver. They also redemonstrated the profound

influence of insulin on the hepatic output of glucose, an influence which was overlooked until Bearn, Billing and Sherlock[17] described it. Then Butterfield and Holling[18] drew attention—and this consideration takes us back to the problem of lability—to incoordination between the hepatic output of glucose and the peripheral utilization of glucose in the presence of brittle diabetes. Their observations are in plausible agreement with clinical facts, and they direct attention to the role of the liver in an organism supplied with insulin exogenously. No means of augmenting or diminishing the release of insulin from the site of subcutaneous injection is available to such a patient. Indications of a suboptimal or an excessive supply of exogenous insulin are clinically appreciable only after some delay, at a time when symptoms and signs of hyperglycemia or hypoglycemia have appeared.

The fact that the hepatic output of glucose should be spontaneously reduced, and even shut off, by small excess quantities of insulin which simultaneously enhance the uptake of glucose in peripheral muscles and fat explains the genesis of the hypoglycemic reaction, but *not* why this reaction occurs with such ease and rapidity and unpredictability in patients who have brittle diabetes. Pending proof to the contrary, the hepatic metabolism of insulin, and variable serum-protein insulin binding, remains a strong etiologic possibility in the syndrome of hyperlability.

The role of episodes of latent hypoglycemia which aggravate alimentary and spontaneous hyperglycemia and cause temporary refractoriness to insulin[2, 3, 7] again has been re-emphasized and documented in studies on labile diabetic patients with the method of continuous *in vivo* blood-glucose analysis.[19] That overt and latent hypoglycemia is indeed responsible for some of the ensuing hyperglycemic waves seems established. The ketogenic potential of insulin hypoglycemia is likewise clear.[20] What remains unclear is just how much of the fluctuation in a brittle patient's blood glucose is brought about by this mechanism, what relationship such relatively short-term fluctuations bear to more longer-term undulations, and what causes or permits the episodes of hypoglycemia. The latter do not occur in a consistently explainable relationship to insulin therapy. The occurrence of such episodes must remain, for the present, merely a descriptive characteristic of the hyperlabile diabetic state.

Before we leave the subject of the role of insulin in the phenomenon of brittleness, we should give some attention to studies on the absorption of insulin from subcutaneous or intramuscular depots. The use of I^{131}-labelled insulin has demonstrated in several laboratories that irregularities of absorption of insulin from normal or even damaged (lipoatrophic, lipohypertrophic) sites of injection do not account for clinical brittleness.[21, 22]

Although an excess of endogenous glucagon could account for some peaks of hyperglycemia, posthypoglycemia "overshoots" and even some tendency toward ketosis, proof is lacking as to the place of this pancreatic hormone in the lability of diabetes. It seems highly unlikely that exogenous glucagon, a contaminant of clinical insulin supplies, plays any causal part in brittleness.

No pituitary, adrenal, thyroidal or gonadal abnormalities have been demonstrated to exist in other than isolated instances of diabetic hyperlability. Hypophysectomy performed for diabetic retinopathy in patients with brittle diabetes has not been found to alter lability. Adrenal, thyroid or gonadal ablation, whether by surgical or other means, has been without notable effect, so far as brittleness of diabetes is concerned.

To turn to consideration of other than endocrine organs, the potential role of the liver already has been emphasized. A low renal threshold for glucose also has been claimed to exist in some patients as an explanation of brittle diabetes.[23] However, once glycosuria at a normal or low concentration of blood glucose is discovered and appropriate adjustments are made, the unpredictable lability should disappear and the patient should become manageable as a stable person. This is the case in pregnant diabetic patients in whom the threshold for glucose is frequently lowered.[24] By no means do all pregnant diabetic women have the brittle disease. On the other hand, in none of our patients with the most brittle form of the disease did we encounter a persistent lowering of the so-called renal threshold. In advanced stages of diabetic nephropathy some increase in insulin sensitivity and a lowering of insulin needs tend to develop. These are seldom accompanied by much lability.

Abnormalities in electroencephalograms have not appeared in our patients with brittle diabetes, nor have any aberrations in the central, peripheral or vegetative neurologic systems been consistent accompaniments of lability.

Lastly, the emotions must be considered in an enumeration of potential etiologic factors in excessive lability of diabetes. There is no doubt that patients who have brittle diabetes of long standing are likely to be tense, anxious and often depressed. The question is, which comes first: the labile personality or the unstable diabetes? Has the emotional state of the individual seen when brittle diabetes already is at hand resulted from the frightful pressures of uncertainties and outright dangers the patient must cope with as a stable internal milieu eludes him? We have tried to evaluate the emotional and personality status of all our patients by use of a battery of psychological tests and by means of psychiatric interviews. We found that the predominant mood was one of depression, but every other shade of near-normal to abnormal emotional pattern also was represented. We have not seen evidence of the disappearance of brittleness after sedation, tranquillization, psychotherapy or even shock therapy. Hinkle and Wolf[25] have demonstrated the ketogenic nature of

emotional stress. It is no wonder that the already excessively ketosis-prone patient with brittle diabetes is so vulnerable to more ketosis, both metabolically and emotionally. We do not believe that lability is psychogenic, but brittleness certainly can be aggravated as much by emotional oscillations and swings in mood as by all the physical stresses of life. This must be kept in mind as the patient's therapy is planned. Treatment is then logically our next consideration.

THERAPY OF BRITTLE DIABETES

The causation of the hyperlabile state remains obscure. The patient with brittle diabetes must be treated. In this frame of reference we have conducted therapeutic research with the dual aim of evaluating therapeutic modalities as well as testing hypotheses concerning the nature of brittle diabetes.

A typical example of this was our examination of the concept that the condition of the hyperlabile diabetic patient could be better controlled by multiple daily doses of insulin than by a single daily dose of long-acting insulin. Allied to that investigation was the inquiry of a deeper portent: Is brittleness exogenous or endogenous? Can an exogenous regimen be devised which is so nearly perfect that the brittle diabetes of a patient becomes, even temporarily, stable? For if such is the case, erroneous therapy, an exogenous factor, could be shown to have caused the lability.

Figs. 1 and 2 illustrate our method of study. A 31-year-old volunteer, previously proved to have brittle diabetes and to have been diabetic for 23 years, was studied continuously in a metabolic ward. He subsisted on a weighed, balance-study type of diet and ate, slept and exercised by the clock. Specimens of urine were tested and samples of excreta were collected, similarly by the clock. He was one of seven patients thus studied. Urine was tested qualitatively for glucose and ketones before meals and at bedtime. All urine was collected in five-hour fractions of the day and during nine hours of the night. Specimens were quantitatively analyzed for glucose by an autoanalyzer as well as for ketones and nitrogenous constituents in some of the studies.[2, 3]

The first figure[2] illustrates our method of charting the results. Insulin therapy is presented as the daily dose of a single injection of semilente-lente mixture, results of which were later compared with results of three five-hour injections of unmodified (regular) insulin and a fourth daily dose of semilente insulin for the night. The resulting reactions and the urinary excretion of glucose, daily weight and periodic multiple estimations of the glucose content of the blood, carried out daily, complete the chart. Note that the four daily fractions of urine analyzed for glucose are represented both as the hourly excretion of glucose and as 24-hour totals. The two expressions taken together give a good profile of brittleness.

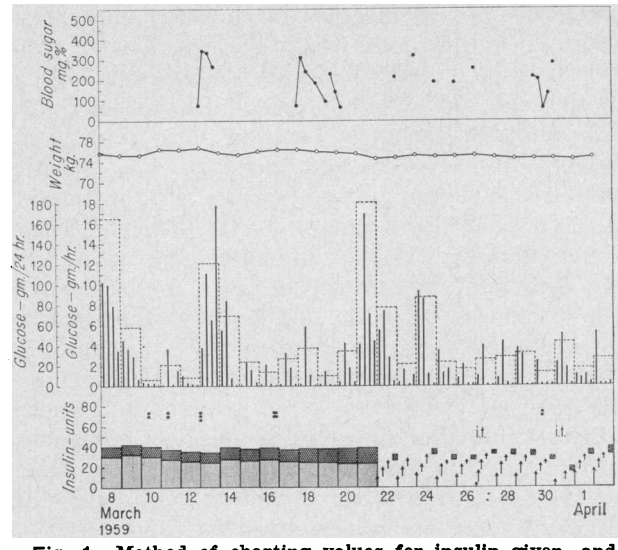

Fig. 1.—Method of charting values for insulin given, and for the urinary excretion of glucose, weight and content of blood sugar in a 31-year-old volunteer with brittle diabetes who had been diabetic for 23 years.
Insulin therapy: dotted area = single daily dose of lente insulin.
Cross-hatched area = single daily dose (mixed with lente) or night dose of semilente insulin.
Arrow = unmodified (regular) insulin.
Daily dose of insulin is indicated cumulatively upward.
i.t. = insulin tolerance test (intravenous).
Symbols = insulin reactions as follows: * = light; ** = mild; *** = moderate; **** = severe.
Solid vertical bars = hourly glucose excretion in four daily fractions; dotted bars = 24-hour total glucose excretion.
Solid circles = blood-glucose values; those connected were obtained within the same day.

The second figure[2] continues where the first concluded. It illustrates that a regimen of four doses a day produces good diabetic control, a state which deteriorates when the one-daily-dose program is resumed.

Our results, analyzed statistically,[2] validate the significance of the advantage of short-term prediction over the long-term extrapolation in the management of labile diabetes. It is evident in the figures that fluctuations and insulin reactions have never completely left the clinical picture.

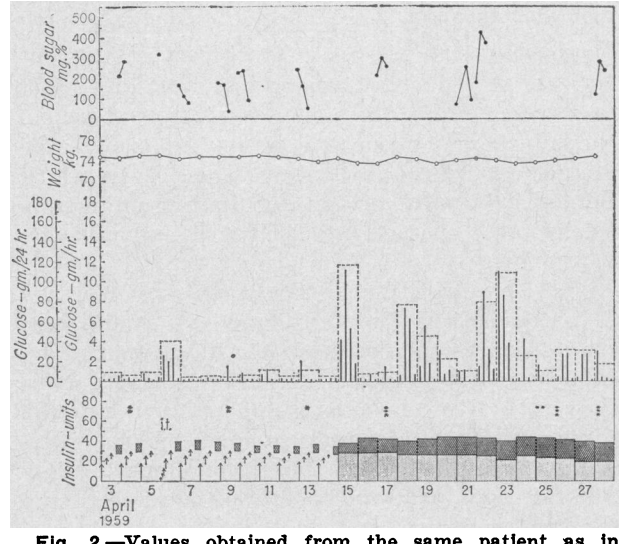

Fig. 2.—Values obtained from the same patient as in Fig. 1: it is seen that good control is maintained by use of a regimen of four doses of insulin a day as opposed to one dose a day.

Since our 5-5-5-9-hourly program of testing, feeding and giving insulin was not identical to the six-hourly regimen, with which virtual abolition of fluctuations has been claimed,[26] we compared our scheme with the each-six-hour equal feedings and doses of unmodified insulin therapy.[3] There was no appreciable difference in either accuracy of diabetic control or degree of lability. The effect of the semilente insulin dose for the nine-hour night period could not be distinguished from the effect of the six-hourly unmodified insulin scheme of therapy. The results[3] strengthen the case for endogenous lability rather than for something which can be blamed on, or totally corrected by, exogenous insulin therapy.

Much as we respect the thesis of Somogyi[7] concerning excesses in exogenous insulin as a cause for brittleness, we have not been able to stabilize the condition of patients in a measurable way, even over periods of years, by simply reducing the dosage of insulin, as he recommends. This is not to deny the dictum that the smallest possible dose of insulin compatible with good control is the best for the diabetic patient. But, in contradistinction, we do not find that simple avoidance of excessive doses of insulin will correct hyperlability.

The idea of stabilizing brittle diabetic patients by reducing the dose of insulin with oral hypoglycemic drugs is attractive but, like so many other logical hypotheses, simply does not stand up under practical application. First of all, brittle diabetes, by definition,[2] does not respond to sulfonylurea therapy. So far as phenformin therapy is concerned, I am unaware of any instance of brittle diabetes which could be managed by means of this drug alone. Reduction of the dose of insulin can often be achieved, but lability is not affected thereby. In the treatment of the patient whose status has been detailed in the previous illustrations, phenformin was added to a single daily dose of semilente-lente insulin mixture. In Fig. 3[2] it is seen that during concurrent therapy it was indeed possible to reduce the dose of insulin to half or less. Unfortunately, this action did not affect lability, and insulin reactions were frequent. Nor did five other patients of ours fare better when similar combined therapy was employed.

Another fact to be faced is that whereas phenformin does not of itself cause hypoglycemia, it is very likely to contribute to the potential of insulin to do so. In our patient (on May 9, 1959) a most severe and subjectively unusual hypoglycemic shock ensued.

Long before effective and safe agents were available for oral hypoglycemic therapy, careful thought was given to the effect of dietary constituents upon diabetic lability. It was recognized that, from the metabolic standpoint, civilized man's dietary habits produce cycles of feast and famine, especially where the brittle diabetic patient's sensitivity to overnight starvation ketosis is concerned. Hence the helpful effects of six-hour equal-feeding

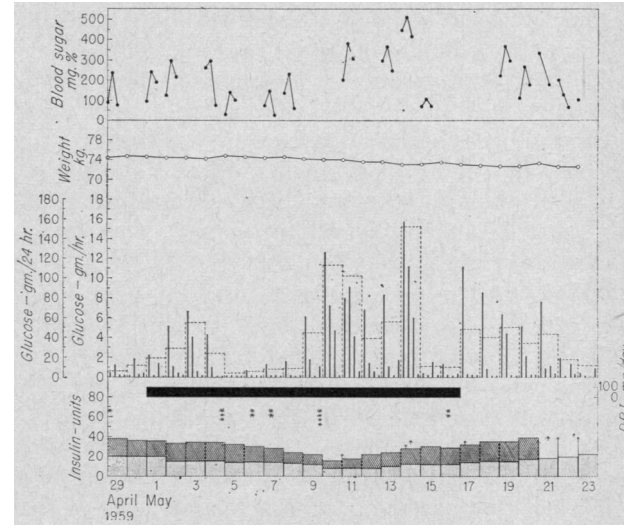

Fig. 3.—Values obtained from the same patient as in Figs. 1 and 2. It was possible, as depicted here, to reduce the dose of insulin to half or less of what it has been by concurrent administration of phenformin (DBI), but this action did not affect lability and insulin reactions became frequent.

schedules and our modification of nearly equally sized meals at 5-5-5-9-hour intervals.

We have also examined the claim that high-fat, low-carbohydrate diet programs exert a beneficial effect on lability.[27] On a sequential rotation between equicaloric high-fat and control diets, neither overall control (measured by the 24-hour urinary excretion of glucose), nor lability (gauged by figures for the hourly excretion of glucose) was dependably or consistently affected.[2]

Diet therapy is and remains of fundamental importance to good diabetic management, but we have not found any dietary factors, singly or in combination, which have exerted appreciable effects on brittleness.[2, 3]

Exercise has a special therapeutic role in this context. Since exercise long has been recognized as a therapeutic adjunct which ameliorates diabetes and lowers the dose of insulin, patients who have brittle diabetes seem to be especially aware of the relationship of exercise to their major complaint—insulin reactions. The paradox of this relationship is that few, if any, such patients would claim insensitivity to the effect of exercise on their diabetic regulation, yet this effect is difficult to demonstrate in hyperlabile patients. This has been the experience of Soskin *et al.*,[28] Errebo-Knudsen[29] and of ourselves.[2, 3] Thus, in acute experiments, values for glucose in arterial and venous blood showed no effect from vigorous standardized exercise which was alternated with matched rest periods, whether insulin was simultaneously administered or not.[2] In another study on hyperlability, standardized, measured exercise was performed for six-day periods and was interspersed with periods of rest in bed. Again, excepting for greater frequency of hypoglycemic reactions during periods of activity, even the major contrast between rest in bed and vigorous exercise has not brought out a consistent effect attributable to exercise on the excretory

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pattern of glucose and ketones or total nitrogen balance. Periodically obtained multiple daily specimens of blood, examined during the same study, showed that values for glucose, ketones, free fatty acids and other blood fats also were *not* consistently affected by six-day periods of exercise.[3] We postulate that the quantitative changes resulting from the patient's inherently labile diabetes may be of greater magnitude than the effects of exercise.[3]

Another factor in antidiabetic therapy is time, or the timing of therapeutic events. It is little wonder that this is important to the total economy of the patient who has brittle diabetes. After all, the all-important automaticity of the regulation of metabolic events is lost, along with the supply of insulin, in juvenile diabetes of long standing. As we approach the matter of the practical aspects of the management of brittle diabetes, emphasis on accurate timing is of great importance. There is no doubt that if all therapeutic factors could be kept exactly the same from day to day, we could come closer than we do to imitating nature's ways of normal processes.

TABLE I.—PRINCIPLES OF THERAPY—PATIENTS WITH HYPERLABILE DIABETES

1. Accurate timing of insulin, meals and exercise.
2. Good dietary program; day-to-day nutrition should follow same pattern.
3. Additional feedings to provide equivalent of four, five or six meals a day (ideal would be a feeding each four to six hours, around the clock, each feeding of identical composition).
4. Less insulin or more food usually needed for increased (more than usual) expenditures of energy. Requirements may be anticipated or adjusted during or after exercise.
5. Emotional factors: philosophical attitude, self-control, tranquillization.

Optimal timing of insulin, diet and exercise therapy is as important as are the quality and quantity of each individual component. Unfortunately, even the best rhythmic periodicity does not achieve stability in brittle diabetes. Nevertheless, the matter of timing heads the list of practical principles and recommendations for the management of hyperlabile diabetic patients (Table I). This regimen (Tables I and II) is the essence of what we recommend to our own patients as well as to physicians who minister to patients with brittle diabetes.

In Table III are outlined some of the currently favoured insulin programs to exemplify and illustrate the principles shown in Table II. Table III includes consideration only of unmodified (crystalline-zinc, regular) and of the lente insulins. This has been done to avoid confusion between the several intermediate and long-acting insulins. Isophane (NPH), globin and protamine-zinc insulin probably can be used equally efficaciously in place of lente (30% semilente and 70% ultralente mixture), semilente and ultralente, respectively.

TABLE II.—INSULIN THERAPY—PRINCIPLES FOR PATIENTS WITH HYPERLABILE DIABETES

1. Give dose when major effect of previous dose is over (this is violated by scheme in which multiple daily doses include ultralente or similarly long-acting insulin).
2. Avoid insulin reactions, especially at night (no scheme should violate this).
3. Avoid excessive dosage; use the "least possible dose for the best possible metabolic regulation".
4. Keep therapy flexible to follow fluctuations in changing needs for insulin.

TABLE III.—INSULIN THERAPY FOR PATIENTS WITH HYPERLABILE DIABETES

1. *Four doses* a day:*
   (a) Unmodified insulin taken every six hours.
   (b) Unmodified insulin taken every five hours during the day; semilente for a nine-hour night period.
2. *Three doses* a day:*
   Unmodified insulin taken before breakfast (± 7 a.m.) and lunch (± 1 p.m.); semilente before supper (± 7 p.m.)
3. *Two doses* a day:*
   Semilente insulin: 2/3 to 4/5 of daily dose before breakfast; 1/3 to 1/5 of daily dose before supper or at bedtime.
4. *One dose* a day:*
   Lente or *ad hoc* semilente-ultralente mixture (with additional unmodified insulin if needed).

*As a general rule, we recommend that the dose be modified on the basis of results of qualitative urinalysis for the glucose content of freshly voided specimens. Usually such a test is most helpful in the 10- to 40-unit dosage range: four or more hours after an injection of unmodified insulin; six to eight hours after an injection of semilente insulin; or 14 to 24 hours after an injection of ultralente insulin. The magnitude of the change in the dose recommended varies according to the degree of glycosuria present and the presence of ketonuria, and, above all, with the previously established dosage-pattern worked out by or for the individual patient by trial and error.

Most of our truly hyperlabile patients cannot be managed satisfactorily on a single injection daily. The 70% ultralente component of the lente mixture often provides excessive insulin action for the night. When an *ad hoc* semilente-ultralente mixture is worked out, it commonly contains half or less in the form of the long-acting insulin. However, when the degree of lability of a patient's diabetes is being evaluated, it seems appropriate to start with one dose a day and to proceed to more complex and cumbersome schemes as shown in Table III, proceeding inversely from point 4 to point 1. It is best to proceed slowly (in terms of months) and to accept the least complex regimen which will permit both a socially and medically acceptable existence for the patient.

SUMMARY

Brittle diabetes mellitus is redefined as a syndrome of extreme and unpredictable metabolic lability not amenable to stabilization by presently used antidiabetic measures. Dysfunction of plasma protein transport and of hepatic and peripheral tissue metabolism of insulin may cause the hyperlability in these excessively insulin-sensitive and ketosis-prone patients. Therapeutic recommendations include flexible, short-term insulin programs designed to follow oscillations of the disease with the most appropriate dietary and exercise regimens, as well as attempts at emotional and social adjustment for the patient.

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Le dosage des séromucoïdes dans la cardite rhumatismale

(Etude de 120 cas)

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Une étude du dosage des séromucoïdes a été faite chez 120 cas de cardite rhumatismale âgés de 5 à 20 ans, dans la phase aiguë, subaiguë ou chronique de la maladie. Les résultats obtenus montrent que: (1) le taux des séromucoïdes est élevé chez nos 32 cas aigus et demeure au-dessus de la normale durant toute la crise rhumatismale; (2) le test n'est pas influencé par le traitement aux stéroïdes; (3) le dosage est plus élevé dans les formes graves de la maladie. C'est donc un test utile pour poser le diagnostic, suivre l'évolution et évaluer la gravité des cas de fièvre rhumatismale.

ABSTRACT

Seromucoid values were determined in 120 patients with rheumatic carditis, aged 5 to 20 years, who were in the acute, subacute or chronic phase of the disease. The following results were obtained: (1) Seromucoid values were elevated in all 32 of the acute cases and remained above normal as long as rheumatic activity was present. (2) Seromucoid values were unaffected by cortisone therapy, unlike the sedimentation rate and the level of C-reactive protein. (3) Greater values for seromucoid were found in severe cases.

This study suggests that seromucoid determination is a useful method for following rheumatic activity and may be of value in assessing the severity of the disease.

LE diagnostic et l'évolution de la fièvre rhumatismale reposent sur l'évaluation des signes inflammatoires.[1] Ces signes sont extra-cardiaques, cardiaques et biologiques. Les réactions biologiques qui traduisent le retentissement humoral de la crise rhumatismale sont mesurables au laboratoire.[2] Les examens d'usage sont le taux de sédimentation des érythrocytes et le dosage de la protéine C-réactive. Ces examens sont influencés par la thérapie aux stéroïdes employée communément dans le traitement de nos cas de cardite rhumatismale. Pour cette raison, nous avons voulu déterminer la valeur du dosage des séromucoïdes, car cette épreuve serait un bon indice d'inflammation et échapperait à l'influence des stéroïdes. Nous avons étudié la contribution de ce test au diagnostic et à l'évolution de la fièvre rhumatismale. Il fut donc utilisé dans toutes les phases de la maladie, aiguë, subaiguë et chronique.

Ce travail a été subventionné par un octroi du Ministère de la Santé de Québec, suivant les ententes fédérales et provinciales: projet No. 604-7-347.

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