Thoughts on the Dietary Treatment of Diabetes Mellitus

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Diet, exercise, and hypoglycemic medication continue to be the fundamental treatments for diabetes mellitus. Of these three treatments, diet is the most difficult. I believe there are two primary reasons for this difficulty. First, there is considerable controversy among health-care professionals regarding dietary recommendations for people with diabetes. Because the strength of most scientific controversies is inversely related to the amount of applicable data, it would seem that we have too little data on which to base our recommendations. Nevertheless, this lack of data has not prevented professional organizations like the American Diabetes Association from making rather comprehensive recommendations. Although well intentioned, such recommendations create public confusion and erode public confidence when scientific data later prove them to be incorrect. A second primary reason that dietary therapy is difficult for people with diabetes is that adherence to any diet is difficult. This is particularly true if the diet is not satisfying or if the diet differs from that of the general population.

What then can we say with confidence about the dietary therapy of diabetes? In my view, only four things. First, for diabetic patients receiving treatment with constant daily dosage of hypoglycemic medication, it is advisable to attempt to achieve consistency in day-to-day carbohydrate and caloric intake so that the hypoglycemic effect of medication will match the hyperglycemic effect of food. Second, diabetic patients who are overweight should reduce energy intake, increase energy expenditure through exercise, or do both in an attempt to lose weight. This is particularly important for obese type II diabetic patients because weight loss will predictably result in improved metabolic status (1,2). Unfortunately, we do not have reliable dietary or medical methods to help our obese diabetic patients achieve and maintain long-term weight loss. Gastric reduction surgery is the most effective means of accomplishing long-term weight loss currently, but the risk-benefit ratio of this procedure for patients with diabetes has not been adequately studied. Third, people with diabetes should attempt to follow a diet that is low in saturated fat. Diabetic patients who reduce their intake of saturated fat are likely to experience a decrease in serum LDL cholesterol (3). Fourth, based on recently acquired data, it appears that diabetic patients with established nephropathy should restrict dietary protein to ~0.6 gm · kg ideal body $wt^{-1} \cdot day^{-1}$ (4,5). Such restriction of protein intake can be expected to retard the progression of nephropathy.

Other dietary recommendations for people with diabetes should, in my opinion, be viewed with skepticism until solid scientific data supporting them become available. For instance, it is not yet certain what is the optimal distribution of macronutrients in the diabetic diet, whether glycemic indexing of foods has usefulness in reducing glycemia, whether there is any rationale for restricting dietary sucrose other than to prevent dental caries, whether the use of fructose as a sweetening agent is advisable, whether dietary fiber has any independent salutary metabolic effects (most studies of dietary fiber have modified macronutrients as well as fiber), or whether reducing protein intake has any merit for diabetic patients without nephropathy.

One of the most important unresolved issues regarding the diabetic diet pertains to the optimal distribution of macronutrients. The American Diabetes Association, in its most recent position statement on nutrition, recommended a diet in which 55–60% of total energy is derived from carbohydrates and <30% of total energy is derived from fats (6). This recommendation is supported by several studies demonstrating that a diet high in carbohydrate and low in fat produces desirable metabolic effects in diabetic subjects (7–10). However, several recent reports have challenged this recommendation, and in this issue of *Diabetes Care* (p. 1560–71) Garg et al. present additional evidence that a high-carbohydrate diet may not be optimal for people with diabetes. In the Garg study, a crossover design was used to compare isocaloric high-carbohydrate and high-fat diets that were fed to 10 type II diabetic men for 28 days. An important feature of the design was that the high-fat diet was low in saturated fat and contained primarily monounsaturated fat. Garg et al. found that the high-fat diet, when compared to the high-carbohydrate diet, produced reductions in plasma total cholesterol, plasma VLDL cholesterol, and plasma triglycerides without signifi-

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TYPE II, NON-INSULIN-DEPENDENT DIABETES MELLITUS; LDL, LOW-DENSITY LIPOPROTEIN; VLDL, VERY-LOW-DENSITY LIPOPROTEIN; HDL, HIGH-DENSITY LIPOPROTEIN.

cant change in plasma LDL cholesterol or plasma HDL cholesterol. These desirable effects on plasma lipids were accomplished without any demonstrable adverse effect on glycemia.

The Garg et al. study is consistent with a previous report by Garg et al. (11) and two reports by Coulston et al. (12,13), demonstrating that high-fat diets, relative to high-carbohydrate diets, have beneficial effects on plasma lipids as long as the saturated fat content of the high-fat diets is kept low. These three reports also demonstrate that high-fat diets, relative to high-carbohydrate diets, decrease daylong (preprandial plus postprandial) plasma glucose levels. Preliminary results from a larger, multicenter trial support the idea that a diet high in total fat but low in saturated fat reduces both plasma lipids and plasma glucose in diabetic subjects (14).

What then might one conclude about the optimal distribution of macronutrients in the diabetic diet? Scientific evidence increasingly suggests that the diabetic diet should derive approximately equal amounts of energy from fat and carbohydrate (40–45% of total energy derived from each). However, the fat in the diet should be primarily monounsaturated and the content of saturated fat should be low (<10% of total energy). It appears that, relative to diets deriving more energy from carbohydrate, such diets will produce reductions in glycemia and plasma triglycerides and, perhaps, increases in plasma HDL cholesterol while maintaining the reductions in plasma total and LDL cholesterol, which can be accomplished with high-carbohydrate diets. A cautionary note, however, may be necessary. It is possible that high-fat diets increase the long-term risk of some types of cancer (15).

Another aspect of the studies by Garg et al. (11, and this issue, p. 1560–71) and Coulston et al. (12,13) deserves further comment. In all four studies, meals were prepared in metabolic kitchens by study personnel. Thus, the investigators had rigorous control of the nutrients provided to subjects. Such control greatly increases my confidence in the conclusions reached. In many nutrition studies, subjects are provided with dietary counseling, meal plans, or nutrient supplements to add to their meals. It is then assumed that the subjects prepare and consume foods as they have been instructed. In such studies, the investigators probably do not have sufficient control of nutrient intake to determine the metabolic effects of the specific nutrients under study. In my opinion, such approaches should be used only to determine whether effects demonstrated in more rigorous studies like those of Garg et al. and Coulston et al. can be translated to the outpatient setting.

Finally, I return to what I cited as the second primary difficulty with the diabetic diet. That is, even if the optimal diet for diabetes can be defined, most patients will have difficulty adhering to it. In our society, food has many purposes in addition to meeting nutritional needs. Food is often at the center of social activities. Moreover, food is frequently used as a reward, as a means of expressing affection, and as a means of helping cope with anxiety and stress. To make this point more clearly, how many of us would be happy to receive from our significant other on Valentine's Day a box of broccoli? We, as health-care professionals, often ignore many important factors when making dietary recommendations and later judging the effectiveness of our patients in implementing them. Our understanding of the difficulties our diabetic patients face with diet would be greatly facilitated if we each designed for ourselves a diabetic diet and attempted to follow it for at least 1 wk. I think we would then gain appreciation of how difficult it is to follow a meal plan when eating in a restaurant, how difficult it is to pass an open box of chocolates at work without eating one, and, when gazing into the refrigerator just before bedtime, how difficult it is to do the right thing.

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Quality Control Measures in Glucose Monitoring

With the increase of on the spot technology in monitoring blood glucose levels, similar advances must follow in introducing quality assurance procedures and training programs for such techniques (1). With this in mind, a workshop for Boehringer Mannheim Reflolux meters (Mannheim, Germany) was instituted, and a potential area for inaccuracy was identified. Glucose control solutions provided by Boehringer Mannheim and other laboratories are colorless and difficult to see on the test pad. Should the pads be inserted into the meter without first being wiped clean, the glucose solution coats the carriage, and the next 3–4 readings are inaccurate.

Boehringer Mannheim recommends that the strip guide be cleaned when each new pack of its BM-Test 1–44 is used, but perhaps it would be prudent to clean the carriage after the use of each clear control solution.

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Acute Onset of Seeming IDDM in an AIDS Patient

The onset of acute symptoms of IDDM in an HIV-positive subject who progressed towards clinical AIDS 2 yr ago might argue against our knowledge of the pathogenesis of IDDM, an autoimmune disease characterized by an increase in activated $CD4^+$ cells (1–3).

We report here of a white man aged 24 yr, who in October 1990 developed classical signs of IDDM. He had no family history of IDDM or NIDDM; his symptoms, blood glucose level of 15 mM, HbA_1 of 9.9%, and ketones in the urine accompanied by a rapid loss of body weight (10 kg in 2 mo), prompted the commencement of insulin therapy. Metabolic control was achieved with 25 IU of a mixture of rapid- and slow-reacting insulins. Basal and glucagon-stimulated C-peptide levels (0.4 and 0.6 mM, respectively) confirmed diagnosis of IDDM.

This patient had been found to be HIV positive in 1985, and in 1988 had started therapy with zidovudin as progression towards AIDS manifested, with $CD4^+$ cells declining and persisting below 200/mmc up to the time of IDDM diagnosis. During the 2 yr that preceded the onset of IDDM, the patient showed generalized lymphadenopathy but otherwise remained relatively healthy. No apparent viral infections were observed before the insurgence of symptoms of IDDM.

Within 3 mo of clinical diagnosis, insulin was reduced gradually and later withdrawn as the patient suffered from repeated hypoglycemia. Subsequently, daily blood glucose profiles and HbA_1 levels were persistently within the normal range, indicating complete clinical remission. In September 1991, basal and glucagon-stimulated C-peptide secretion support a β-cell function restored towards values observed in normal subjects (1.0 and 2.3 mM, respectively). In December 1991, he was still free from insulin. As islet cell antibodies and other autoantibodies were repeatedly negative before and after diagnosis of IDDM, we speculate that an acute damage to β-cells, possibly virally induced (4), may have been the cause for the insurgence of hyperglycemia. However, in the absence of markers indicating an autoimmuno process against β-cells (5), damage to these cells can be reversed, and complete regeneration can take place. Acute damage alone is not sufficient to result in β-cell destruction leading ultimately to the development of IDDM. Moreover, it is possible that the reduction of $CD4^+$ cells could have been the reason for the incomplete process, thereby allowing the β-cells to regenerate.

In conclusion, this case supports the role that $CD4^+$ cells have in the pathogenesis of IDDM, as in their near absence the disease should not develop.

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IDDM, INSULIN-DEPENDENT DIABETES MELLITUS; HIV, HUMAN IMMUNODEFICIENCY VIRUS; AIDS, ACQUIRED IMMUNE DEFICIENCY SYNDROME, NIDDM, NON-INSULIN DEPENDENT DIABETES MELLITUS.

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Intracellular Magnesium Deficiency

The article by Nadler et al. (1), which suggests that patients with type II diabetes have intracellular Mg deficiency, adds to the growing body of literature that confirms the importance of Mg in the metabolic economy of the body and in the diabetic patient especially when the diabetes is poorly controlled (2).

Mg tends to follow K in its distribution (largely intracellular) and excretion. Therefore, it is not surprising to find that hypomagnesemia occurs in situations that are known to cause hypokalemia (e.g., use of diuretics and uncontrolled diabetes) (3). Based on data published over the past 20 yr, we have routinely utilized Mg in the treatment of uncontrolled diabetes mellitus (4,5). Our outcomes in an inner city municipal hospital are comparable with those in tertiary care facilities, and our mortality for the pure hyperosmolar nonacidotic group is only 10% overall and 14% in the age-group >50 yr (5).

We have not seen any cases of tetany complicating the use of phosphate in DKA despite our routine use of phosphate repletion as potassium phosphate in this setting, and suggest that this may be attributable to the routine use of Mg (5). Although thromboembolic events have been implicated as a frequent cause of mortality in uncontrolled diabetes and especially in the hyperosmolar patient, our experience does not confirm this (4); and in retrospect, it is possible that supplemental Mg may have played a role in reducing platelet reactivity (1).

In uncontrolled diabetes, we use a commercially available multielectrolyte solution containing Mg (Plasmalyte, Travenol/Baxter, Deerfield, IL) and additional intramuscular and/or i.v. $MgSO_4$ (once the adequacy of urine output is assured) (5). Additionally, we use this solution as our routine i.v. vehicle in hospitalized patients with diabetes, to the exclusion of saline and saline-containing preparations.

Many theoretical reasons could be given for routinely providing Mg in the i.v. fluids of patients with diabetes. Many studies support the contention that i.v. Mg may reduce mortality in cases of myocardial infarction and may decrease serious arrhythmias (6); Mg depletion may result in refractoriness to K repletion (3) and, as shown by Nadler et al. (1), enhance platelet reactivity. Further, hypomagnesemia may impair insulin-receptor interaction (7) and result in insulin resistance (2).

It now appears reasonable to recommend the replacement of saline by Mg-containing multielectrolyte solutions for hospitalized diabetes patients with adequate renal function who require i.v. fluids. Such solutions are commercially available (e.g., Plasmalyte, Isolyte, and Normosol, Abbott, Chicago). They more closely resemble physiological replacement solutions than the traditional and archaic normal saline. Saline contains excess chloride, which is problematic in DKA and hyperchloremic states. It contains no K, Mg, or bicarbonate precursor, whereas multielectrolyte solutions contain all of these. We have used such solutions successfully for >20 yr and have no regrets about having set aside our saline.

In uncontrolled diabetes, additional Mg as $MgSO_4$, intramuscular or i.v., may be beneficial and (absent renal failure) is safe (5). We believe that K should be repleted as the phosphate and/or acetate rather than as KCl, unless chloride depletion and metabolic alkalosis are present, or unless one is willing to risk the development of hyperchloremia in these patients.

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TYPE II DIABETES, NON-INSULIN-DEPENDENT DIABETES MELLITUS; DKA, DIABETIC KETOACIDOSIS.

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Treatment of Malignant Otitis Externa in a Younger Diabetes Patient

Malignant otitis externa is a severe form of otitis externa caused by *Pseudomonas aeruginosa* that can progress to serious complications, such as local invasion of cartilage, bone, and soft tissues; nerve palsies; deafness; and death (1). It is a rare form of infection that previously has been reported to occur exclusively in elderly diabetic patients (2). It has been suggested that patients with this condition should be hospitalized and treated with i.v. antibiotics (2). We wish to report a case of malignant otitis externa that occurred in a 32-yr-old woman with IDDM, which, under careful review, was successfully treated with oral antibiotics.

The patient had a 22-yr history of poorly controlled IDDM and a 5-wk history of foot infection, which was being treated with Augmentin 500 mg three times a day. She presented with a 4-day history of severe pain in the left ear, accompanied by purulent blood-stained discharge from the ear. The patient had tried to treat herself with hydrogen peroxide washes and the installation of a proprietary antiseptic cream.

On examination, the patient was afebrile, with no soft tissue or bony pain around the ear. Examination of the left ear revealed inflammation of the anterior part of the pinna, marked local tenderness, extensive swelling at the external auditory meatus, and inflammation of the external auditory canal with pus formation. No evidence of otitis media or cranial nerve palsy was found. Examination of the right ear was unremarkable. The white cell count was 8.0 K/uL, and the sedimentation rate was 16 mm/h. A presumptive diagnosis of malignant otitis externa caused by *Pseudomonas aeruginosa* infection was made, and this was confirmed by multiple cultures taken after a 24-h incubation. The patient was treated with Ciprofloxacin 500 mg three times a day and followed closely as an outpatient. After 2 days, we noted marked improvement in her symptoms, with reduction in local inflammation; and after 1 wk of treatment, her infection had resolved.

This case demonstrates that malignant otitis externa caused by *Pseudomonas aeruginosa* can occur in younger diabetic patients, and that the condition can be treated successfully and without complication by using oral antibiotics under careful supervision.

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IDDM, INSULIN-DEPENDENT DIABETES MELLITUS.

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Criteria Critique

Naylor (1) begins with a basic misconception in his criticism of the criteria proposed by O'Sullivan and Mahan (2) and adopted by the National Diabetes Data Group (3) in recommending oral glucose tolerance test diagnostic standards for pregnancy. The premise of his criticism is that the criteria are faulty because they were not based on adverse maternal-fetal outcomes. However, it is unrealistic to expect all adverse perinatal outcomes to result from a single cause, i.e., hyperglycemia, and to derive diagnostic criteria for the glucose tolerance test in pregnancy based on such outcome events.

The destructive effects of diabetes in pregnancy provided the original reason for mandating the detection of gestational hyperglycemia. Therefore, the more logical basis for diagnostic criteria is the level of clinically relevant hyperglycemia that selects the mother at risk for diabetes mellitus (2).

Having altered the goal originally assigned to the criteria, Naylor (1) proceeded to identify what he considered another fundamental flaw, namely, the sample of women used to provide the diagnostic standard, which he considered "unrepresentative" due to its racial and socioeconomic composition. In fact, this sample of 752 unselected, carefully documented pregnant women could have been faulted only if it had been used for deriving criteria based on pregnancy outcome data, which it was not. For criteria based on the risk of later diabetes, the sample's representativeness cannot be validly criticized because no convincing evidence existed to demonstrate racial or economic differences in glucose tolerance test results.

On the other hand, Naylor (1) can be faulted for inappropriately combining samples to provide a false diabetes incidence rate for subjects with negative oral glucose tolerance test results in preg-

nancy. Thus, he fails to support his resulting conclusions concerning the generalizability of the O'Sullivan and Mahan (2) study results. Many of his other criticisms are generic, could be applied to any study in a clinical setting, and need not be addressed specifically at this time.

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Reply to Dr. O'Sullivan

I am grateful for Dr. O'Sullivan's interest and remain impressed by his pioneering work in the 1960s and 1970s. Unfortunately, I do not agree with his counterarguments.

Let us review Dr. O'Sullivan's original chain of inference, repeated in brief by his letter: Overt and established diabetes mellitus in the mother is associated with adverse effects. Some of these women have increased rates of gestational complications before their diabetes mellitus becomes overt. Identification might allow treatment to prevent those complications. Therefore, screening should be oriented toward detecting the level of "clinically relevant hyperglycemia that selects the mother at risk for [later] diabetes mellitus."

This rationalization is convoluted and unconvincing. The O'Sullivan and Mahan criteria have been applied in the context of screening and treating millions of women for the express purpose of preventing maternal–fetal complications related to hyperglycemia in pregnancy. For that reason, the criteria should be recalibrated with reference to the adverse outcomes of interest, and the levels of "clinically relevant hyperglycemia" in pregnancy should be those associated with excessive maternal–fetal complications in that pregnancy, when otherwise similar women are compared. To justify screening and treatment, we should also prove that complications can be prevented by specific interventions directed at that risk factor, with side-effects that are tolerable for our patients. These direct lines of evidence are what must guide practice in the 1990s and not some inferential path based on the mother's later risk of an abnormal oral glucose tolerance test in the nongravid state.

By the same token, Dr. O'Sullivan's second point is moot. He argues that the generalizability of the first sample (or training set) of 752 women could be "faulted only if it had been used for deriving criteria based on pregnancy outcome data, which it was not." I am less sanguine than Dr. O'Sullivan about the generalizability of his training sample with respect to later risk of diabetes mellitus. In any event, because the criteria are used to drive interventions during pregnancy, and those treatments in turn are directed at improving pregnancy outcomes, one thing is clear: We would not use a similarly unrepresentative sample to derive criteria for gestational diabetes today.

Finally, the statement about "inappropriately combining samples" is unclear. If Dr. O'Sullivan believes that it is sufficient to ignore the other criticisms of his criteria as "generic" in nature, perhaps he can forgive me for not addressing his final point more "specifically at this time."

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