but were usually under some form of professional care. Questions of motivation for, or convenience of, clinic attendance, while important enough to merit a separate study, are still subsidiary to the major variable—regular and good preventive supervision.

To me, the weakest part of the study relates to failure to identify the differences between the care received by the patients who came to the clinic and those who did not. Understandably, the latter information would be difficult to come by, but its inclusion would have added greatly to the value of the article. It is unlikely that the difference would be simply an institutional versus a noninstitutional setting, or even specialized versus primary care.

How important was the motivation of the Steno staff and their dedication to the goal of keeping the patient "symptom free and socially well adapted?" Their emphasis on patient education so as "to enable the patient himself/herself to carry out the necessary adjustments in the treatment conditioned by the irregularities of daily life?" This particular orientation—not always present in specialty clinics any more than in general practice—may have been just as important as patient motivation or professional specialization. We would like to know.

It is customary, at least in the United States, for research papers to end by saying that "more research" is needed along the same line. One of the refreshing aspects of the Danish study is the authors' failure to follow this American ritual. Nevertheless, their conclusion does cry out for a sequel: a carefully designed, carefully matched comparison of the care rendered at Steno and that generally available to other Danish patients, e.g. in GP offices, clinics in communities other than Copenhagen, etc. Even though all Steno services were free, it is clear that residential dispersion alone makes it impossible for all Danish diabetic individuals to take advantage of them. It would appear essential, therefore, that efforts be made to replicate the Steno experience in other settings accessible to the entire population.

Such information should be helpful to physicians and other professionals in the United States, as well as in other countries, as we seek to define the contents of good primary care and to encourage less expensive noninstitutional care insofar as appropriate.

If the Deckert article ends by raising more questions than it answers, this is a tribute to the importance of the subject and its unequivocal answer to the questions it does address: the health-effectiveness and cost-effectiveness of a first-rate specialized program of patient education and preventive care for juvenile-onset diabetics.

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The UGDP and Insulin Therapy

In the July 7, 1978, issue of the *Journal of the American Medical Association* there appeared the seventh report of the University Group Diabetes Program (UGDP), this report dealing with "mortality and selected nonfatal events with insulin treatment."[1] The investigators compared outcomes after nine years of follow-up in three groups of subjects: (1) those treated with diet and placebo (placebo group); (2) those treated with diet and a fixed dose of insulin based on the patient's body surface area at time of entry into the study (insulin standard group); and (3) those treated with diet and insulin in a dose adjusted to lower blood glucose to defined levels (insulin variable group). The investigators reported that despite the achievement of significantly lower fasting blood glucose values in the insulin variable group, there was no difference either in mortality or in the frequency of certain nonfatal events relative to the heart, eyes, kidneys, and peripheral vasculature. They therefore concluded that their "findings provide no evidence that insulin or any other drug lowering blood glucose levels will alter the course of vascular complications in the type of diabetes that is most common, adult-onset diabetes." That is a very strong statement, to say the least. It will clearly trigger another "great debate" over the merits of the UGDP study. Therefore, it is worthwhile to examine the evidence reported in this study.

First, it must be noted that the period of observation was only nine years. Even the authors casually acknowledged in their discussion that longer periods of follow-up might yield differences in the rates of occurrence of some of the complications. That this is more than likely is attested to by the fact that the frequency of elevated serum creatinine reported was significantly higher in the placebo group compared with the insulin standard group and nearly statistically significant in comparison with the insulin variable group. Since the frequency of occurrence of both retinopathy and nephropathy is highly correlated with duration of disease[2–4] and usually occurs after 10 years duration, the nine-year follow-up period is probably much too short to draw any meaningful conclusions about these two diabetic complications.

Second, all patients enrolled in the UGDP study had *mild* diabetes. Indeed, mean fasting blood glucose values for each of the three groups at entry was in the range of 136 to 142 mg. per deciliter. More importantly, after nine years of therapy, mean fasting blood glucose in the placebo and insulin standard group had deteriorated only to 167 and 165 mg. per deciliter, respectively. Mean fasting blood glucose in the insulin variable group could be maintained at 122 mg. per deciliter. (These values were calculated by me, based on the scanty information provided by the authors, who did not choose to report the values other than graphically.) Thus, the study really only addresses the ques-

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tion of whether or not a 43 to 45 mg. per deciliter decrement in fasting blood glucose has significant benefit over nine years. (Actually, for a substantial period of the nine years, the graph suggests that differences were even smaller.) The study does not address at all the issue of insulin therapy if the fasting blood sugar is greater than 165 mg. per deciliter. That is indeed a substantial portion of the population with adult-onset diabetes.

A fair conclusion to draw from the data presented might be that the lowering of fasting blood glucose from 167 to 122 mg. per deciliter, not surprisingly, does not affect the frequency of development of some vascular complications during the first nine years after onset of mild adult-onset diabetes mellitus. This alone is an important conclusion because it addresses the question of the *degree* of control desirable in diabetic patients and implies that fasting blood glucose values in the range of 120 to 165 mg. per deciliter may be tolerable for nine years, from the standpoint of clinically *obvious* vascular disease.

Unfortunately, the UGDP investigators did not draw such conclusions. Since their report basically constitutes a study of mild diabetes, observed for only nine years, and studies small differences in blood glucose in the range of 122 to 167 mg. per deciliter (fasting), it is, in my opinion, the height of irresponsibility to conclude that there is "no evidence that insulin or any other drug . . . will alter the course of . . . adult-onset diabetes." It is particularly irresponsible to draw such a conclusion in a "general" medical journal, the audience of which is more diverse than specialists in the field of diabetes. This irresponsibility is aggravated further by the fact that the report really only constituted a preliminary report, since a detailed report (presumably containing sufficient data for meaningful analysis) was noted to be in preparation. The purpose of the publication of a preliminary report, in a general rather than specialty journal, can only be to flame the issue. The widespread public dissemination of the unjustified conclusions of the report—in the lay press and broadcast media—served only to create panic for the diabetic public. Such irresponsibility can only be condemned.

The UGDP study has been embroiled in controversy since the preemptory leak of its first findings eight years ago. Throughout the subsequent years, I have generally chosen to avoid public comment on the controversy because of the respect I have had for many of the investigators who are participants in the study and because of the acknowledged difficulty in mounting any large-scale, controlled clinical trial. The investigators can only be praised for persevering as long as they have, despite tremendous adversity. They have been vindicated, in part, by the blessings of the Biometric Society, who found their statistical methods acceptable.[5] Despite statistical validity, however, many of their findings may be clinically irrelevant, since their study design is not comparable to conventional methods of practice. Unfortunately, too, they have repeatedly reached beyond their data to draw unjustified conclusions. Early, they applied their results relative to tolbutamide to other sulfonylureas not studied. Early, they extrapolated their results obtained with mild, asymptomatic patients to patients with more severe and/or symptomatic diabetes.

The early reports of the UGDP stimulated a careful analysis of treatment practices for diabetes and our approach to dietary therapy. They also stimulated review of the nature of controlled clinical trials and of statistical methods applied to clinical studies. On these grounds, perhaps, the overstatement of their case has been worthwhile and could have been forgiven. Unfortunately, some of the individuals who include both protagonists and antagonists of the UGDP became either enamored with the study or bogged down in emotionalism. One has to suspect that, given the history of emotional responses to the original UGDP study, investigators might be more apt to overstate their case, and that this could account for the most recent conclusions of the UGDP. Even if this is the case, it only explains and does not excuse the UGDP investigators' current irresponsible actions. To make the same mistake once again, i.e. to extrapolate their results unjustifiably, is not only irresponsible but it is to commit an unpardonable sin. I am deeply saddened by the actions of the UGDP investigators.

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