NIDDM patients makes their detection through screening seductive for an organization such as ADA. However, no data, new or old, support this approach. In the absence of effective therapy to decrease morbidity or mortality in the asymptomatic phase, large-scale screening is not justified. Although one may argue that there is no harm in identifying such patients, the expense of such programs drains medical resources that may be better spent. In addition, the impact of labeling an individual as diabetic is not trivial, with regard to both the patient's self-perception of health and employment and insurance issues (11). We encourage ADA to reconsider its position statement in light of the above information.

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Reply

The Committee on Professional Practice (COPP) of the American Diabetes Association (ADA) is the body responsible for the development of all scientific and medical position statements. These documents are usually prepared by a task force comprised of four to six health professionals with an interest in the subject matter. After a statement emerges from the writing group, it is discussed by COPP and then sent to at least a dozen reviewers. The reviewers are chosen on the basis of their expertise and familiarity with the issue, and reviewers are selected who are familiar with any regional variations in clinical practice that may be important. Individuals who have an opinion that may conflict with the thrust of the statement are also chosen.

Nearly two dozen experts served as reviewers for the position statement on screening for diabetes. In addition, the final statement underwent review and approval by COPP and the ADA Executive Committee. The point of view articulately conveyed by Drs. Nathan and Singer was heard, but the majority of the scientific and medical community surveyed disagreed with their opinion. ADA position statements do not convey or portend to convey the unanimous belief of all professionals. Rather, position statements are intended to reflect a consensus medical opinion, one that the vast majority of practitioners espouse.

COPP appreciates the concerns expressed by Schlossbach. We definitely do not want people who assist with fingersticks or draw blood samples to contract an infectious disease. The recent Centers for Disease Control guidelines on the handling of specimens from suspected or known carriers of human immunodeficiency virus or hepatitis should be followed.

The position statement refers to plasma because that is the fluid in which glucose is measured. Indeed, plasma is tested by many strip methods when whole blood is placed on a strip or, of course, when it is intentionally isolated from whole blood.

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Insulin as Risk Factor for Vascular Disease

The consensus statement of the American Diabetes Association on the role of cardiovascular risk factors in the prevention of macrovascular disease in diabetes de-emphasizes the role of insulin as a significant contributory factor in the development of diabetic macrovascular dis-

ease (1). There is no widely used method of insulin delivery that can reproduce the physiological effects of insulin. Circulating insulin concentrations in insulin-treated diabetic patients are generally twice those measured in healthy nondiabetic individuals (2,3). In healthy individuals, insulin is secreted into the hepatic portal circulation, where a major portion is extracted by the liver and never gains entry into systemic circulation (4). This hepatic insulinization cannot be accomplished by current methods of insulin delivery.

In the diabetic patient, large blood vessel disease is most often manifested by coronary heart disease (5). A decade-long study of ~1000 Finnish policemen found that myocardial infarction correlated best with a high insulin response to an oral glucose challenge (6). A strong correlation between coronary heart disease and high fasting insulin levels was found in another study of >7000 male Parisians (7). In fact, there was greater correlation between plasma insulin concentrations, and coronary artery disease than between lipid levels and coronary artery disease. A striking relationship between high insulin concentrations and cardiovascular disease was also found in a study comparing a group of healthy individuals with type II (non-insulin-dependent) diabetic patients. Type II diabetic patients were divided into groups treated with insulin or treated with diet and oral hypoglycemic agents. In the non-insulin-treated groups, there was a significant correlation between the incidence of coronary heart disease and C-peptide levels (8). In the insulin-treated group, C-peptide levels were obviously lower than in the other two groups, but the incidence of cardiovascular disease was the highest. Furthermore, in insulin-treated patients, both dose and plasma insulin concentrations were higher in subjects who developed blood vessel disease over the 5-yr study.

There is firm evidence from animal experiments that insulin is atherogenic. A group of alloxan-induced diabetic rabbits fed a high-cholesterol diet experienced a lower incidence of atherosclerosis than nondiabetic controls (9). In chickens, insulin has been shown to prevent the regression of atheromatous changes when a high-cholesterol diet is changed to a normal diet (10). Insulin infused into one femoral artery of pancreatectomized diabetic dogs produced ipsilateral atherosclerosis, which was not present in the contralateral saline-infused artery (11). This study implicates insulin itself as a direct cause of atherosclerosis. Sato et al. (12) have shown that the administration of insulin to normal rats for 1 yr produces extensive atherosclerotic changes in their aortas but not in the aortas of saline-treated controls.

Although there is no direct evidence implicating high plasma insulin concentrations to diabetic microangiopathy, there is significant circumstantial evidence linking insulin to small blood vessel disease. Studies from the Steno group (13) and other groups (14,15) have clearly shown that the major difference between rigidly controlled (more insulin) and conventionally controlled diabetic patients was the development of accelerated retinopathy that occurred in the rigidly controlled groups. A direct effect of insulin on the proliferation of the endothelium of small blood vessels has also been demonstrated (16).

There are few available methods of treating diabetes that do not result in systemic hyperinsulinemia. An innovative approach would involve the use of pancreatic grafts or islet cell transplants that would drain into the hepatic portal circulation. However, pancreatic grafts are generally not drained into the portal circulation. The Roux-en-Y technique described previously would permit pancreatic endocrine drainage into the portal circulation and would thereby limit systemic hyperinsulinemia (17).

Another more simple approach that would promote hepatic insulinization and limit systemic hyperinsulinemia would be dependent on perfection of techniques to deliver insulin to areas of the gut that drain into the portal circulation. Orally administered insulin, coated with an azoaromatic polymer that releases insulin in the colon, has been given to dogs (18), and we have accomplished the same result using insulin coated with a methacrylic acid copolymer in humans (19).

Until methods that reproduce physiological delivery of insulin are perfected, it is doubtful whether glycemic control alone will prevent, retard, or ameliorate microangiopathy or macrovascular disease in diabetic patients.

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Trends in Treatment Among Unselected Geographically Defined Diabetic Population

It is with great interest that we read the article by Kennedy et al. (1) describing trends in the use of oral hypoglycemic agents (OHAs) in the United States. Furthermore, data of the treatment pattern obtained from a cross-sectional survey performed in France in 1985–1986 were published in this journal (2). Therefore, we would like to add the data of the treatment pattern of an unselected diabetic population of the geographically defined area of Berlin, German Democratic Republic.

OHAs have been used in the treatment of non-insulin-dependent diabetes mellitus (NIDDM) since tolbutamide was approved by the Food and Drug Administration. Therefore, the treatment pattern is comparable in the U.S. and the GDR. In the GDR, a nationwide diabetes register has existed for over a quarter of a century that permits a precise assessment of the epidemiological situation with regard to the total population of the country (3,4). The data of all diabetic patients of the area of Berlin, newly diagnosed and deceased, are registered in a central computer of the department of data processing of the Centre of Diabetes and Metabolic Disorders (5). The age, age at onset of diabetes, sex, treatment, and change of treatment are constantly registered.

As of 31 December 1970, there were 27,431 people known to have overt diabetes in Berlin or 2525/100,000 people. Within the 18-yr follow-up period 1970–1988, the prevalence rose from 2.53 to 3.78% of the total population of Berlin. As of 31 December 1988, there were 3784/100,000 people with overt diabetes according to the World Health Organization criteria. There was a parallel increase in the number of diabetic patients treated by diet alone or combined with OHAs until 1978. In 1980, structured dietary teaching programs were introduced in the management of all newly diagnosed NIDDM patients (6). Since then, the absolute number of diabetic patients who were kept on diet alone has grown, whereas there has been a slight decrease in the number of patients on OHAs. Simultaneously, there has been an increase in the number of insulin-treated patients (503/100,000 people in 1970 and 743/100,000 people in 1988). The prevalence rates of insulin-treated patients were 0.5% in 1970 and 0.74% in 1988. This has come as a result of the emphasis being shifted toward near-normoglycemic control of blood glucose and an increase in the number of NIDDM patients treated with insulin.

In 1970, 39% of all diabetic patients were treated with diet alone and 42% with OHAs (27,431 total diabetic patients). In 1988, the relative proportion of patients on diet increased to 44% and of patients on OHAs decreased to 36%, respectively (48,104 total patients). This is quite different from the data of the survey in France, which showed that 73.5% of all diabetic patients are treated by OHAs (2). However, the bias of the study was discussed by the authors, i.e., that all the health-care expenses were reimbursed only in cases where the diabetic patient was prescribed an antidiabetic drug and not for those who were treated with diet alone (2). We fully agree with the opinion of Kennedy et al. (1) that data on the national use of OHAs, which have previously been lacking in the literature, are very useful.

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