The results of the Diabetes Control and Complications Trial (DCCT), published in this issue of the Journal, demonstrate that intensive insulin therapy can delay the onset and slow the progression of retinopathy, nephropathy, and neuropathy in patients with insulin-dependent diabetes mellitus (IDDM). These findings, which extend those of two other recent studies, should put to rest the longstanding debate over whether attempts to improve glycemic control beyond that required to control the symptoms of diabetes are worthwhile.

But the DCCT raises a new and equally challenging set of questions. The study was limited to a small subgroup of people with diabetes -- highly motivated patients with IDDM between the ages of 13 and 39 years, without hypertension or macrovascular disease and with little or no microvascular disease. Achieving the benefits of intensive therapy in this group entailed substantial risks and costs. It required special skills on the part of both patients and practitioners, services that many insurance policies do not cover, and the delivery of care by patient-centered teams. As the results of the DCCT are translated into practice, we shall need to answer the following questions. Who among the many patients with diabetes is likely to benefit from intensive therapy? How can this intervention be made more affordable and more widely available? And what payment and delivery systems will best support the efficient provision of effective diabetes care?

These issues are important to policy makers, both as they pertain to the current health care system and in the broader context of health care reform. Approximately 12 million Americans have diabetes. Fifty-seven percent of adults with diabetes are covered under government-funded programs (Harris M: personal communication). Changes in diabetes management can therefore have a major impact on federal and state expenditures, and government policies can substantially influence the care that patients with diabetes receive. Since 90 percent of
patients with diabetes have non-insulin-dependent diabetes (NIDDM), the implications for them of the DCCT results are a key concern. Indeed, decisions about the use of intensive therapy in patients with NIDDM will be the most important factor determining the resources needed to support this intervention.

In relating the findings of the DCCT to patients with NIDDM, it is helpful to separate the benefits achieved by lowering blood glucose concentrations toward the normal range from the therapy used to achieve that lowering. For patients with NIDDM, as for those with IDDM, hyperglycemia is correlated with microvascular complications. Consequently, improvements in glycemic control could potentially reduce the substantial burden of blindness, end-stage renal disease, and peripheral vascular disease in patients with NIDDM. Direct evidence to test this hypothesis should be available shortly from the U.K. Prospective Diabetes Study. But extrapolating the benefits of the DCCT to NIDDM does not necessarily mean that patients with NIDDM should receive intensive insulin therapy. On the one hand, the ratio of benefit to risk may be considerably less favorable in patients with NIDDM than in those with IDDM. More important, patients with NIDDM, unlike those with IDDM, can often achieve excellent glycemic control (at least in the early stages of the disease) with much simpler and less costly interventions -- diet and exercise, for example.

One concern about using intensive insulin therapy in NIDDM is that it might exacerbate macrovascular complications, the leading cause of morbidity and mortality in this disease. Hyperinsulinemia and insulin resistance, both very common in patients with NIDDM, are associated with an increased risk of hypertension, coronary artery disease, and stroke, raising the possibility that insulin itself has atherogenic actions. If this is so, the high doses of insulin that are frequently required to achieve euglycemia in patients with NIDDM, and the associated weight gain that enhances insulin resistance, could have deleterious effects that offset any potential benefits of intensive therapy in reducing the risk of microvascular complications.

The risk of hypoglycemia with intensive insulin therapy is also a serious concern for the large proportion of patients with NIDDM who have macrovascular complications. Although insulin resistance in patients with NIDDM may offer some protection from hypoglycemia, the consequences when hypoglycemia occurs -- angina, myocardial infarction, and stroke -- are likely to be more serious than in patients with IDDM. For patients who have symptomatic complications, this risk may not be worth taking, since there is no evidence that therapies aimed at achieving euglycemia can reverse such complications.

A more desirable therapy in patients with NIDDM would be one that improved glycemic control by enhancing insulin sensitivity, involved little or no risk of hypoglycemia, and could be instituted safely before complications developed. Diet and exercise are readily available therapies that satisfy these criteria. Moreover, in many patients with newly diagnosed NIDDM, these therapies can result in glycosylated hemoglobin values similar to those in intensively treated patients with IDDM. The problem with this approach is that regimens centered around diet and exercise are rarely successful in the long term, because of either poor compliance or disease progression. An intriguing question is whether the progression to diet-resistant hyperglycemia, as well as the development of complications, can be delayed by early intervention.

Where does this leave us? Perhaps the most important message of the DCCT is that in patients with IDDM -- and probably in patients with NIDDM -- treatment that lowers blood glucose concentrations well below the concentrations that merely relieve symptoms is beneficial, but the best way to achieve this objective may well be...
different in the two conditions. For most patients with IDDM, the appropriate treatment is intensive insulin therapy, and we now face the considerable task of providing patients and practitioners with the support they need to make this therapy generally available. The importance of the patient-centered team in achieving the results of the DCCT suggests that policies affecting the way care is organized, assessed, and paid for are likely to be as important as those affecting benefits, insurance coverage, and access to care.

For NIDDM, more information -- some of which should be available shortly from the United Kingdom study -- is needed before definitive recommendations can be made. In the meantime, the results of the DCCT provide health care professionals with strong reasons to encourage patients with NIDDM, as well as those at risk for the disease, to adopt healthy dietary and exercise routines. Until more compelling evidence is obtained to support the use of intensive therapy in NIDDM, patients in whom diet and exercise programs fail should be treated with oral hypoglycemic drugs or currently recommended protocols for insulin therapy. In addition, all patients should be screened regularly for early complications and treated appropriately. Recent surveys suggest that the care of patients with NIDDM could be substantially improved if these approaches were incorporated into routine practice2.

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References

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