# Diabetes Care: What Should We Try to Achieve?

Patrick J. O'Connor, MD, MPH
*Hartford, Connecticut*

A common clinical predicament that primary care physicians face is how to care for the patient with non–insulin-dependent diabetes mellitus (NIDDM) when the disease no longer responds to dietary management and maximal doses of an oral hypoglycemic agent. Current standard care would be to discontinue the oral agent (OA) and begin subcutaneous injections of insulin, increasing the dose until satisfactory glycemic control is attained. Some experts suggest that good glycemic control could thus eventually be achieved in almost all diabetic patients, and the risks of associated microvascular complications of diabetes might therefore be reduced.[1]

What is wrong with this picture? Studies of diabetes care in office practice uniformly show that "good" glycemic control is achieved in less than 50% of unselected adults with diabetes (glycosulated hemoglobin level of less than 8% or fasting plasma glucose [FPG] level of less than 7.8 mmol/L [140 mg/dL]).[2] Experts suggest that primary care physicians may use inadequate doses of insulin, while primary care physicians point to patients' nonadherence to diet as the major problem. Complicating the scenario still further are the serious risks of aggressive insulin treatment: hypoglycemic reactions,[3] weight gain,[4] and accelerated atherosclerosis.[5] Furthermore, current concepts of the pathogenesis of NIDDM show that most patients have adequate or elevated endogenous insulin levels in the early years of the disease, and that resistance of peripheral tissues to insulin action is the dominant problem.[6] Thus, there are serious theoretical and practical constraints to the aggressive use of insulin therapy for NIDDM, especially in older, nonadherent, or less motivated patients.

As a practical matter, the goals of diabetes care may differ from patient to patient. For some patients, good glycemic control is a realistic goal and should be aggressively pursued. For other, less motivated patients, the physician must settle for a "middle ground" of fair metabolic control (FPG <11.1 mmol/L [<200 mg/dL]), hoping that microvascular complications may be determined more by genetic factors than by glycemic control.[7] Achieving moderate diabetic control may be of some benefit to the patient, possibly avoiding hypoglycemia and extreme hyperglycemia, lowering risk of infection, improving functional status, and avoiding osmotic diuresis.[8]

For many patients with NIDDM, a decision point occurs when the patient reaches maximal doses of an OA (glypizide 40 mg per day, or glyburide 20 mg per day) and is still in poor glycemic control with an FPG level over 11.1 mmol/L (200 mg/dL).[9] When the duration of diabetes is less than 10 years, and the patient is not losing weight, the problem is usually one of dietary nonadherence rather than insufficient endogenous insulin. In such a patient, achieving euglycemia will likely require high doses of insulin, may have little beneficial effect, and may cause weight gain, hypoglycemia, and increased risk of atherosclerosis. In an article in this issue of the Journal, Kabadi and Kabadi[10] advocate continuation of OA therapy in such patients, along with the introduction of a single morning injection of mixed regular and Ultralente insulin to reduce the amount of insulin needed for good glycemic control. Others have advocated use of bedtime NPH insulin in combination with OA therapy.[11] Are these reasonable strategies?

Controversy about the use of combined insulin and OA therapy originated around 1956.[12] Proponents of monotherapy held sway for the next 30 years, until recently when data emerged that suggest that insulin may accelerate atherosclerosis.[5,13] Some experts have begun to question the use of large doses of exogenous insulin for treatment of a disease characterized by excess mortality from stroke and myocardial infarction.[14] At the same time, glycemic control continues to be viewed as an important goal of diabetes care. There has therefore been a renewed interest in combination therapy that uses less insulin. Prevention of microvascular complications, how-

*From the Department of Family Medicine, University of Connecticut Health Center and St Francis Hospital and Medical Center, Hartford, Connecticut. Requests for reprints should be addressed to Patrick J. O'Connor, MD, Asylum Hill Family Practice Center, 123 Sigourney St, Hartford, CT 06105.*


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ever, requires near normoglycemia,[15] which has rarely been obtained in patients on combination therapy. Furthermore, studies that have evaluated patients on combination therapy have not shown patients' circulating insulin levels to be lower than those in patients on insulin monotherapy, despite lower exogenous insulin doses. This is probably due to the increased endogenous insulin secretion that occurs with the addition of OA.[9] While a few clinical trials[9,10,16] suggest improved short-term glycemic control with combination therapy, several of the potential risks of such therapy, including increased hypoglycemia and accelerated atherosclerosis, have not been resolved.

We are left then with the difficult clinical question of how to treat the patient with NIDDM who has poor glycemic control (FPG > 11.1 mmol/L [>200 mg/dL]) despite maximum doses of an OA. Treatment decisions should be guided by the physician's knowledge of the patient and by careful monitoring of the patient's glucose level, weight, and dietary and medication adherence. If a patient with poor glycemic control on maximal dose of an OA is glycosuric and rapidly losing weight, clinical common sense suggests the need for exogenous insulin. If the patient in poor glycemic control is maintaining or gaining weight, renewed emphasis on dietary adherence and intensified patient education are probably what are needed. For some patients, the physician may have to accept suboptimal glycemic control, especially in cases of dietary nonadherence. Dissatisfaction with this situation tempts the physician to use combination therapy or to administer very large doses of insulin. The potential risks of this course of treatment, however, may outweigh the potential benefits. Primum non nocere.

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*See article on page 349.*