Intensive glucose control halves complications of longstanding type 1 diabetes

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Near-normal control of glucose beginning as soon as possible after diagnosis would greatly improve the long-term prognosis of type 1 diabetes, concludes a study published in the July 27, 2009, issue of the *Archives of Internal Medicine*, which updates information about the clinical course of type 1 diabetes. The study also found that the outlook for people with longstanding type 1 diabetes has greatly improved in the past 20 years due to a better understanding of the importance of intensive glucose control as well as advances in insulin formulations, insulin delivery, glucose monitoring, and the treatment of cardiovascular risk factors.

"The demonstration that near-normal glucose control substantially lowers microvascular and cardiovascular complications has heralded a new era of type 1 diabetes care," says lead author David M. Nathan, M.D., of Massachusetts General Hospital. Nathan is also co-chair of the landmark Diabetes Control and Complications Trial (DCCT) and its follow-up study, the Epidemiology of Diabetes Interventions and Complications (EDIC), both funded by the National Institutes of Health. "The remarkable improvement in long-term outcomes achieved with intensive glucose control should encourage clinicians and patients alike to implement intensive therapy as early in the course of type 1 diabetes as possible."

The DCCT, conducted from 1983 to 1989, found that intensive glucose control was superior to conventional control in delaying or preventing the complications of type 1 diabetes. EDIC continues to follow DCCT

participants to determine the long-term effects of prior intensive versus conventional blood glucose control.

The authors compared overall rates of eye, kidney, and cardiovascular complications in three groups of people diagnosed with type 1 diabetes an average of 30 years earlier. Two groups consisted of DCCT/EDIC participants--those randomly assigned to intensive glucose control or to conventional control. The third group was a subset of patients in the Pittsburgh Epidemiology of Diabetes Complications (EDC) study, who were matched to DCCT/EDIC participants by age, duration of diabetes, and degree of eye damage. The EDC, also funded by NIH, is a population-based study that has been following residents of Allegheny County, Pa., who were diagnosed with type 1 diabetes from 1950 to 1980.

After 30 years of diabetes, DCCT participants randomly assigned to intensive glucose control had about half the rate of eye damage compared to those assigned to conventional glucose control (21 percent vs. 50 percent). They also had lower rates of kidney damage (9 percent vs. 25 percent) and cardiovascular disease events (9 percent vs. 14 percent) compared to those receiving conventional glucose control. Eye damage ranged from significant damage without vision loss to blindness. Kidney damage ranged from mild kidney disease to kidney failure. Cardiovascular events encompassed heart attack, stroke, angina, and obstruction of the coronary arteries.

The intensively treated DCCT group also had lower complication rates than EDC participants, whose rates were similar to DCCT's conventional control group: eye damage (47 percent), kidney damage (17 percent), and cardiovascular disease events (14 percent).

"Better treatment of blood pressure and cholesterol is also helping to reduce complication rates. The similar event rates in the DCCT

conventional control group and the EDC study suggest that the results of the DCCT trial are likely to be generally applicable to those with type 1 diabetes," said Trevor Orchard, M.D., of the University of Pittsburgh, who heads the EDC study.

Not only did intensive glucose control halve the rates of eye and kidney damage, but the rates of vision loss and kidney failure were much lower than had been seen historically. "After 30 years of diabetes, fewer than 1 percent of those receiving intensive glucose control in the DCCT had significantly impaired vision, kidney failure, or needed a limb amputation due to diabetes," noted Saul Genuth, M.D., of Case Western University, who co-chairs the EDIC study. "Tight control is difficult to achieve and maintain, but its benefits have changed the course of diabetes."

The DCCT compared intensive management of blood glucose to conventional control in 1,441 people 13 to 39 years of age with type 1 diabetes. At the time, conventional treatment consisted of one or two insulin injections a day with daily urine or blood glucose testing. Participants randomly assigned to intensive treatment were asked to keep glucose levels as close to normal as possible. That meant trying to keep hemoglobin A1c (A1C) readings at 6 percent or less with at least three insulin injections a day or an insulin pump, guided by frequent self-monitoring of blood glucose. (A1C reflects average blood glucose over the previous two to three months.)

In addition, the rates of eye damage (30 percent) and kidney disease (12 percent) in all DCCT/EDIC participants who had type 1 diabetes for 25 years were also significantly lower than the rates of eye damage (40-53 percent) and kidney disease (35 percent) reported in the medical literature for comparable patients diagnosed in the 1950s to 1970s.

"These data give clinicians a realistic description of the clinical

outcomes they can discuss with their patients. When intensive therapy, now the standard of care, is implemented early in the course of diabetes, most patients with type 1 diabetes should be able to avoid the disastrous long-term complications that were so common in the past," said Nathan.

Major improvements in glucose monitoring and insulin delivery introduced in the past decade are now helping patients control their blood glucose more precisely and conveniently and reduce the risk of hypoglycemia. For example, several continuous glucose monitoring devices approved by the Food and Drug Administration give both trend and real-time information on glucose levels. Insulin pump technology is also improving, and researchers have begun testing a system that combines both technologies in patients with newly diagnosed type 1 diabetes.

In the United States, nearly 24 million people have diabetes. In adults, type 1 diabetes accounts for 5 to 10 percent of all diagnosed cases of diabetes. Formerly called juvenile-onset diabetes or insulin-dependent diabetes, type 1 diabetes develops when the body's immune system destroys pancreatic beta cells, the only cells in the body that make the hormone insulin that regulates blood glucose. This form of diabetes usually arises in children and young adults, but it can occur at any age. Management involves keeping blood glucose levels as close to normal as possible with three or more insulin injections a day or treatment with an insulin pump, careful monitoring of glucose, and close attention to diet and exercise.

Type 2 diabetes, or adult-onset diabetes, accounts for about 90 to 95 percent of all diagnosed cases of diabetes in adults. It usually begins as insulin resistance, a disorder in which the cells do not use insulin properly. As the need for insulin rises, the pancreas gradually loses its ability to produce it. Type 2 diabetes is associated with older age, obesity, family history of diabetes, history of gestational diabetes,

impaired glucose metabolism, physical inactivity, and race/ethnicity. African Americans, Hispanic/Latino Americans, American Indians, and some Asian Americans and Native Hawaiians or other Pacific Islanders are at particularly high risk for type 2 diabetes and its complications.

Source: National Institute of Diabetes and Digestive and Kidney Diseases