CLINICAL CAPSULES

Four Genes Linked to Diabetes Onset

Scientists have identified four genetic codes associated with the onset of type 2 diabetes mellitus, according to data from a case-control study.

Researchers from Imperial College London, McGill University in Montreal, and other institutions wrote that the genetic loci they identified, along with another previously discovered locus, help explain about 70% of diabetes cases (Nature 2007 Feb. 11 [Epub doi: 10.1038/nature05616]).

The association between each of the loci and the onset of diabetes was fairly weak, but establishing the loci provides new pathways to study in diabetes development.

The researchers compared the genetic makeup of about 700 nonobese French patients with diabetes who have at least one first-degree relative with diabetes with that of 700 controls. They examined genotypes for 393,000 single-nucleotide polymorphisms, looking for mutations that might be statistically linked to diabetes. They then tested the genetic makeup of a further 2,600 diabetes patients, no longer restricted on obesity or familial diabetes criteria, and 2,900 controls to confirm the initial findings.

One of the loci identified is known as TCF7L2, a genetic factor in insulin secretion previously linked to diabetes onset. One newly discovered mutation was in SLC30A8, a zinc transporter involved in insulin biosynthesis. Overexpression of the gene in insulinoma cells increases glucose-stimulated insulin secretion, the authors wrote. Patients with the mutation on a single allele are at 15%-65% higher risk of diabetes depending on the mutation.

Repeat BMD Tests Don't Aid Prediction

Repeat bone mineral density testing 8 years after initial measurement does not improve the ability to predict fractures in healthy elderly women, according to Dr. Teresa A. Hillier and her associates.

The Study of Osteoporotic Fractures included 9,704 white women aged 65 years and older who were living in four regions of the United States. Of the women, 4,124 underwent initial BMD measurement in 1989-1990 and then had a repeat BMD measurement a mean of 8 years later, forming the sample for the current study, said Dr. Hillier of Kaiser Permanente Center for Health Research Northwest, Portland, Ore., and her associates (Arch. Intern. Med. 2007;167:155-60).

They were followed for an additional 5 years to track the incidence of fractures. The BMD measurements were taken at the proximal femur, femoral neck, trochanter, intertrochanter, and Ward's triangle.

Both measurements of BMD were significant predictors of hip fracture and nonspinal fracture risks. However, the repeat BMD did not add to the overall predictive value for any type of fracture risk. These results persisted in subgroup analyses of women who used estrogen or bisphosphonate, compared with those who did not.

The findings do not imply that repeat BMD measurement may not be useful for certain individual patients, "particularly if intervening clinical factors are present that would likely accelerate BMD loss greater than average," they asserted. They also noted that the results may not be generalizable to men, nonwhite women, or women younger than 65 years.

Glycemic Control in Young Diabetics

Poorer glycemic control was independently associated with higher serum lipid levels in children with both type 1 and type 2 diabetes in a large, cross-sectional study.

Higher hemoglobin A_{1c} levels (HbA_{1c}) were associated with significantly higher total cholesterol, LDL cholesterol, and triglycerides in a study of 1,963 children aged 10 years and older. The findings were significant even after adjustment for age, gender, diabetes duration, body mass index, and race/ethnicity. Glycemic control did not correlate with HDL cholesterol levels (Arch. Pediatr. Adolesc. Med. 2007;161:159-65).

The data were extracted from the SEARCH for Diabetes in Youth Study, a comprehensive, ethnically diverse study of children with diabetes managed in a variety of settings (J. Pediatr. 2006;149:314-9).

Mean HbA_{1c} concentration was 8.6% in the 1,680 children with type 1 diabetes and 8.3% in the 283 with type 2 diabetes. In those with type 1 diabetes and poor glycemic control, 35% had high concentrations of total cholesterol (200 mg/dL or greater), 27% had high LDL cholesterol (130 mg/dL or greater), and 12% had high triglycerides (200 mg/dL or greater). In type 2 diabetes patients with poor glycemic control, 65% had high total cholesterol levels, 43% had high LDL cholesterol, and 40% had high triglycerides.

For each unit increase in HbA_{1c}, the slope of the increase in total cholesterol was 7.8 mg/dL in the type 1 group and 8.1 mg/dL in the type 2 group.

The authors were not able to establish a cause-and-effect relationship between poor glycemic control and elevated serum lipids because of the cross-sectional design of the study.

—From staff reports