

## Midlife Diabetes Diagnosis Doubles Dementia Risk

BY HEIDI SPLETE

A midlife diagnosis of diabetes increases the risk of developing Alzheimer's disease and vascular dementia, based on results of a twin study including more than 13,000 individuals.

Previous studies have shown that people with diabetes are at increased risk for dementia, but little is known about the mechanism of action, wrote Dr. Weili Xu of the Karolinska Institutet, Stockholm, and the Stockholm Gerontology Research Center. Dr. Xu and colleagues conducted this twin study to examine the effect of diabetes on dementia and assess the possible role of genetics (Diabetes 2009;58:71-7).

Data were taken from a national registry of Swedish twins who were at least 65 years old when they entered the study between 1998 and 2001. Of 13,693 study participants, 13,056 had no dementia, 467 had dementia, and 170 had questionable dementia, based on DSM-IV criteria. Midlife diabetes was defined as the onset of type 2 diabetes before age 65 years.

A total of 1,396 individuals had type 2 diabetes; 643 developed diabetes before age 65 years and 753 developed diabetes at age 65 years or older.

Overall, diabetes was significantly associated with an increased

risk of dementia (increased risk of 63%), and patients whose diabetes was diagnosed at midlife were more than twice as likely to develop dementia as those diagnosed with diabetes later in life (increased risk of 176%), even after controlling for diabetes duration and twin factors.

In addition, data from co-twin matched case-control analyses showed that the effect of midlife diabetes on dementia remained significant while the effect of later-life diabetes diagnosis on dementia did not.

These data suggest that adult lifestyle traits such as diet, exercise, smoking, and diabetes control may have a substantial impact on the link between midlife diabetes and dementia. But "unmeasured familial factors" including genetic factors and environmental influences in early life might contribute to the association between late-life diabetes diagnosis and dementia, the researchers noted.

The study's limitations include the prevalence of dementia cases, the use of self-reports, and the lack of information about genes and environmental factors.

The study was supported in part by research grants from sources including the National Institute on Aging and the American Alzheimer's Association. The researchers disclosed no financial conflicts of interest. ■

## Return to Normal Glucose Tolerance Reaps CV Benefits

BY MIRIAM E. TUCKER

Patients who revert from impaired to normal glucose tolerance, especially those who do so via intensive lifestyle modification, can significantly reduce their cardiovascular risk factors, according to an analysis of data from the Diabetes Prevention Program.

The Diabetes Prevention Program (DPP) was a landmark study that showed that intervention with intensive lifestyle (ILS) modification and, to a lesser degree, metformin could reduce or delay the progression to diabetes over a mean 3.2 years follow-up in patients who had impaired glucose tolerance (IGT) at baseline (N. Engl. J. Med. 2002;346:393-403).

The new analysis in those 3,234 DPP patients also showed a lesser improvement with metformin (Diabetes Care 2009 Jan. 26; doi:10.2337/dc08-0494). "Importantly, improvement of glucose tolerance is associated with a more favorable risk factor profile, with intensive lifestyle accompanied by larger improvements than metformin," said DPP writing group chair Dr. Ronald B. Goldberg, of the University of Miami, and his associates.

Overall, deterioration of glucose tolerance was associated with a worsening of risk factor levels, whereas improvement in status was associated with a beneficial risk factor change. The relationship between changes from normal glucose tolerance (NGT) to IGT to diabetes and changes in risk factors for

cardiovascular disease (CVD) were significant for all risk factors except LDL peak particle density (LDL-PPD) in the intensive lifestyle group and for HDL cholesterol in the placebo group, they reported.

The biggest changes in CVD risk factor profile occurred among the patients in the intensive lifestyle group who transitioned from IGT to NGT. Their systolic blood pressure and triglyceride levels fell by about 25% over the study period, whereas HDL cholesterol and LDL-PPD increased by about 8% and 17%, respectively, from baseline.

**'Improvement of glucose tolerance is associated with a more favorable [CV] risk factor profile.'**

DR. GOLDBERG

Among those whose glucose tolerance status didn't change throughout the study, risk factors also didn't change among those with IGT. For those who achieved NGT during the study, risk factor profiles improved slightly in the intensive lifestyle group: Systolic blood pressure fell by 7%, diastolic blood pressure by 9%, and triglycerides by 7% from baseline, while HDL cholesterol and LDL-PPD increased by 5% and 6%, respectively.

Among the patients who progressed from IGT to diabetes, there were small—but mostly insignificant—deteriorations in their cardiovascular risk factor profiles. In the ILS group, progression from IGT to diabetes was not associated with any significant change in risk factors.

"There is no unique effect of conversion to diabetes but rather a linear relationship between glycemic measures and risk factor levels," the researchers said. ■



## U.S. Prevalence of Diabetes and Prediabetes Reaches New High

BY HEIDI SPLETE

More than 40% of American adults aged 20 years and older have hyperglycemic conditions, according to review of data from the 2005-2006 National Health and Nutrition Examination Survey.

In this study, Catherine Cowie, Ph.D., of the National Institutes of Health and her colleagues compared NHANES data for 1988-1994 with data for 2005-2006 (Diabetes Care 2009;32:287-94). The total crude prevalence of diabetes, including diagnosed and undiagnosed cases based on fasting plasma glucose or 2-hour glucose tests, was 13% in individuals aged 20 years and older. The total diabetes prevalence peaked at approximately 30% among all age groups older than 60 years, and the prevalence of diabetes was approximately the same in both men and women.

After the researchers controlled for age and sex, the total diabetes prevalence was 70% higher in non-Hispanic blacks and 80% higher in Mexican Americans, compared with non-Hispanic whites.

The total crude prevalence of prediabetes, in-

cluding both diagnosed and undiagnosed cases based on impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) tests was 30%, and this prevalence was highest among individuals aged 75 years and older, where it reached 47%.

The total prevalence of diabetes and prediabetes, both diagnosed and undiagnosed, was significantly higher in men, compared with women (48% vs. 34%), but most of this difference was because of the greater prevalence of prediabetes among men. And the prevalence of any hyperglycemic condition was significantly higher in non-Hispanic blacks, compared with whites (44% vs. 39%), and in Mexican Americans vs. non-Hispanic whites (52% vs. 39%).

When the researchers compared the 2005-2006 data with the data for 1988-1994, they found that the crude prevalence of diagnosed diabetes rose significantly, from 5% to 8%.

"The sheer magnitude of prevalence of hyperglycemic conditions found in 2005-2006 portends all the consequences of diabetes, including its myriad of complications and costs both to individuals and to society," the researchers wrote.

The researchers had no financial conflicts to disclose. ■

## Physical Activity Can Affect Genetic Tendency to Obesity

Individuals who are genetically predisposed to obesity can prevent weight gain by being physically active, according to findings from a Finnish study of young adult twins.

The investigation involved more than 4,000 monozygotic and dizygotic twins, aged 22-27 years (average age 25), who were enrolled in a population-based longitudinal twin study.

Dr. Linda Mustelin of the University of Helsinki and her associates evaluated the impact of physical activity on the degree to which genetics influences body mass index and waist circumference, using quantitative genetic analyses of data from the twins and their families.

A high level of physical activity significantly modified the heritability of BMI and waist circumference, which they said was a new finding. Specifically,

the analysis showed an inverse relationship between physical activity and waist circumference in males ( $r = -0.12$ ) and females ( $r = -0.18$ ), and between physical activity and BMI in females ( $r = -0.12$ ).

The findings are consistent with previous studies suggesting that physical activity helps prevent obesity, but "most importantly, this study demonstrates that a physically active lifestyle is able to counteract genetic predisposition to obesity," they concluded (Int. J. Obes. 2009; 33:29-36).

Only a few studies have looked specifically at individuals with a genetic predisposition to obesity and the impact of physical activity on their weight.

They cited changes in expression patterns of genes regulating weight and adiposity as a possible mechanism.

—Elizabeth Mechatie