In This Issue of *Diabetes Care*

Edited by Helaine E. Resnick, PhD, MPH

A Measurable but Modest Association Between Diabetes and Alzheimer Disease

Given current trends, there is growing concern about the public health burden associated with the increasing prevalence of both obesity- and aging-related conditions. In recent years, there has been some evidence to suggest an association between diabetes, a common obesity-related condition, and Alzheimer disease (AD), a degenerative neurologic condition commonly associated with advancing age. If a link between diabetes and AD exists and this link is causal, it follows that well-publicized increases in diabetes prevalence may soon be followed by increases in AD. New data in this issue of *Diabetes Care* (**p. 2015**) suggest that there may be a temporal relationship between diabetes and AD, although the magnitude of the observed association was modest. Using data from the Finnish National Prescription Register and the Special Reimbursement Register, investigators identified all community-dwelling individuals with a verified AD diagnosis on 31 December 2005. In a particularly large sample, 28,093 AD cases were identified in this manner, and these individuals were matched to a non-AD control matched for age, sex, and region. Historical data on these matched pairs were examined from 1972 onward. The investigators report that diabetes was present in 11.4% of the overall sample, in 10.7% of control subjects, and in 12.0% of AD subjects. The crude odds ratio for diabetes was 1.14 (95% CI 1.08–1.20), but this association increased to 1.33 (95% CI 1.22–1.41) when cardiovascular disease was taken into account. Despite these intriguing findings, the authors cautioned that key confounding factors such as obesity, smoking, and education were not available in the Finnish registries, precluding adjustment for these factors. In addition, only clinically verified diabetes was ascertained in this study, and among these cases, diabetes was analyzed in a homogenous fashion because variables describing glucose control, such as A_{1c}, were not available. Despite these limitations, the large sample size and long follow-up period are key strengths of the new study, which suggests that there may be a modest association between clinically verified diabetes and AD. — *Helaine E. Resnick, PhD, MPH*

Tolppanen et al. History of medically treated diabetes and risk of Alzheimer disease in a nationwide case-control study. Diabetes Care 2013;36:2015–2019

Discouraging Results for Real-Time Continuous Glucose Monitoring in Pregnancy

The offspring of women with pregestational diabetes are at increased risk of unfavorable outcomes including macrosomia and preterm delivery. These outcomes are associated in large part with maternal hyperglycemia, suggesting that effective approaches to improving maternal glycemic control would be beneficial. Continuous glucose monitoring (CGM) measures interstitial glucose in real time, thereby offering an opportunity to identify episodes of both hyper- and hypoglycemia in pregnant women with diabetes. The idea that this technology could improve glycemic control is supported by evidence in nonpregnant women showing that CGM improved HbA_{1c}. Building on these findings, a new study from Secher et al. in this issue of *Diabetes Care* (**p. 1877**) randomized 123 women with type 1 and type 2 diabetes to one of two groups: intermittent CGM plus routine care or routine care only. The objective of the study was to determine if CGM resulted in improved neonatal outcomes among women with pregestational diabetes. On top of routine pregnancy care, women in the intervention group were instructed to use CGM for 6 days at weeks 8, 12, 21, 27, and 33. The primary outcome was the percent of births that were large for gestational age. Despite its promise, results of this trial were disappointing. There were no differences in glycemic control throughout the trial, no differences in episodes of hypoglycemia, and no differences in the proportion of infants that were large for gestational age. It should be noted that compliance with CGM was low: only 64% of women in the intervention group used the technology according to protocol. Overall, the investigators' attempt to improve routine pregnancy care with intermittent CGM was not successful. The lack of positive findings could be attributable to factors such as low compliance with CGM use in the intervention group, or that intermittent (vs. continuous) use of CGM does not add measureable benefit beyond routine pregnancy care. Although data in the current study do not support use of intermittent CGM, the obesity epidemic will undoubtedly result in increasing numbers of women with pregestational diabetes who will benefit from new approaches to improving glycemic control during pregnancy. — *Helaine E. Resnick, PhD, MPH*

Secher et al. The effect of real-time continuous glucose monitoring in pregnant women with diabetes: a randomized controlled trial. Diabetes Care 2013;36:1877–1883

The *Diabetes Care* Symposium: Continued Excellence in 2013

This issue of *Diabetes Care* features five outstanding articles that were presented at the *Diabetes Care* Symposium, held at the 73rd Scientific Sessions of the American Diabetes Association in Chicago. These articles, selected from more than 150 submissions, cover diverse topics and highlight state-of-the-art findings relevant to the care of people with diabetes. One report (**p. 1859**) indicates a role for FGF19–*CYP7A1*–BA pathway in the etiology and remission of type 2 diabetes following Roux-en-Y gastric bypass surgery, and another study (**p. 1851**) demonstrated proof of concept for a wearable artificial pancreas system that capitalized on smart phone technology. A third report (**p. 1842**) showed results from the SEARCH for Diabetes in Youth study suggesting that certain nutritional factors are associated with preservation of β-cell function in type 1 diabetes. A fourth report (**p. 1834**) highlighted data indicating that multidetector computed tomography coronary angiography provides clinically relevant prognostic information among diabetic patients and assists with risk stratification, even among patients without atherosclerosis. The final report (**p. 1827**) in this year's *Diabetes Care* Symposium showed that serum osteoprotegerin predicted cardiovascular events as well as peripheral vascular events and amputation over 10 years of follow-up. These studies underscore the continued progress that is being made in clinical diabetes care, screening, risk stratification, and prevention. The *Diabetes Care* Symposium provides an important platform to disseminate cutting-edge findings, and it will continue to provide diabetes care professionals with state-of-the-art knowledge at future Scientific Sessions. — *Helaine E. Resnick, PhD, MPH*

Gerhard et al. A role for fibroblast growth factor 19 and bile acids in diabetes remission after Roux-en-Y gastric bypass. Diabetes Care 2013;36:1859–1864

Kovatchev et al. Feasibility of outpatient fully integrated closed-loop control: first studies of wearable artificial pancreas. Diabetes Care 2013;36:1851–1858

Mayer-Davis et al. Nutritional factors and preservation of C-peptide in youth with recently diagnosed type 1 diabetes: SEARCH Nutrition Ancillary Study. Diabetes Care 2013;36:1842–1850

Andreini et al. Prognostic value of multidetector computed tomography coronary angiography in diabetes: excellent long-term prognosis in patients with normal coronary arteries. Diabetes Care 2013;36:1834–1841

Gordin et al. Osteoprotegerin is an independent predictor of vascular events in Finnish adults with type 1 diabetes. Diabetes Care 2013;36:1827–1833

Continuing Debate on Risks and Benefits of GLP-1–Based Therapies

Although the glucose-lowering effects of incretin-based therapies are unequivocal, there has been growing concern on the part of some investigators and clinicians about the long-term effects of these therapies. In particular, several recent studies have raised questions about the effects of this class of drugs on acute pancreatitis as well as their potential ability to promote chronic changes in the pancreas that may lead to precancerous lesions and, perhaps, pancreatic cancer. In this issue of *Diabetes Care*, point-counterpoint narratives dive into these hotly debated issues. In the point narrative (**p. 2118**), Butler et al. suggest that extreme caution is in order with regard to GLP-1 therapies because of the lack of data suggesting long-term benefit and because of an accumulation of data suggesting harm. In support of this view, Butler et al. point to data from animal studies, adverse events reported to the U.S. Food and Drug Administration (FDA), as well as histological changes in the exocrine pancreas with GLP-1 treatment. Butler et al. note that the principle of "innocent until proven guilty" does not apply in the area of drug safety and that we should not accept the idea that "absence of evidence is evidence of absence" with regard to these therapies. Dr. Nauck defends incretin-based therapies in his counterpoint (**p. 2126**). He raises the issue of whether animal studies suggesting that GLP-1 induces pancreatitis can be extrapolated to acute or chronic pancreatitis in humans. He also raises a basic question of causality in studies suggesting GLP-1–induced pancreatitis in both humans and animals. Summarizing the findings of numerous studies, Dr. Nauck contrasts the clinical benefits of these therapies in relation to their risks and argues that these benefits far outweigh the risks. He also compiles odds ratio data from a number of studies examining diagnosis of and hospitalization for acute pancreatitis and concludes that there is no suggestion of increased risk associated with GLP-1 therapy. Finally, Dr. Nauck points out that no cases of clinically evident chronic pancreatitis have been reported after incretin-based treatment, nor has there been a case report of pancreatic cancer following exposure to GLP-1–based therapies. Given that these therapies were introduced relatively recently, continued accumulation of data related to their long-term use will shed light on these important questions. In the meantime, the debate on risks and benefits of GLP-1 therapy is likely to remain in the spotlight. — *Helaine E. Resnick, PhD, MPH*

Butler et al. A critical analysis of the clinical use of incretin-based therapies: are the GLP-1 therapies safe? Diabetes Care 2013;36:2118–2125

Nauck. A critical analysis of the clinical use of incretin-based therapies: the benefits by far outweigh the potential risks. Diabetes Care 2013;36:2126–2132

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