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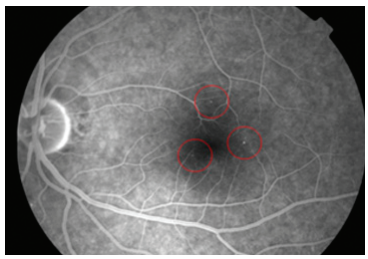
In This Issue of *Diabetes*

Edited by Helaine E. Resnick, PhD, MPH

Early Neuronal Damage in Diabetic Retinopathy

Data from Reis et al. (**p. 3926**) in this issue of *Diabetes* suggest that among patients with type 1 diabetes, retinal neuronal damage can be measured not only before vascular damage occurs, but also before there is evidence of disruptions in the blood-retinal barrier (BRB). These findings may offer a new strategy for early identification of retinal changes among patients with diabetes. The report is based on cross-sectional data from three groups of patients with type 1 diabetes. The first group included patients with normal ocular fundus and no breakdown of the BRB, the second group was comprised of patients with normal fundus or initial diabetic retinopathy and disrupted BRB, and the third group included normal control subjects. The investigators measured a number of psychophysical and neurophysiological outcomes including measures of contrast sensitivity and multifocal electroretinography. The data revealed significant decrements in these functional outcomes between both clinical groups and the control subjects, indicating that even when changes in the BRB and vascular damage are absent in patients with type 1 diabetes, retinal neuronal changes can still be detected. These findings may have implications for neuroprotective treatment strategies that target these early retinal changes. — *Helaine E. Resnick, PhD, MPH*

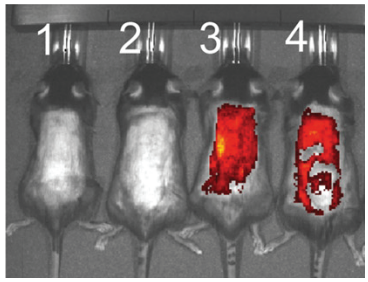


The left eye of a patient with initial diabetic retinopathy and three identified microaneurisms (red circles).

Reis et al. Neuroretinal dysfunction with intact blood-retinal barrier and absent vasculopathy in type 1 diabetes. Diabetes 2014;63:3926–3937

Sunshine Versus Vitamin D Supplementation in Suppressing Metabolic Changes

Intriguing results from a new report by Geldenhuys et al. (**p. 3759**) in this issue of *Diabetes* suggest that sunlight exposure inhibits the unfavorable metabolic changes associated with obesity, and that these benefits occur via mechanisms that are independent of vitamin D. There has been a great deal of interest in the well-described association between poor metabolic profiles and lower levels of vitamin D. However, reduced vitamin D levels could be explained by decreased sunlight exposure among overweight, sedentary individuals coupled with increased concerns about skin cancer risk among light-skinned populations. Moreover, demonstration of a causal link between vitamin D deficiency and risk of obesity and metabolic dysfunction has been a challenge. Nevertheless, there is ongoing interest in vitamin D supplementation for the prevention of obesity and metabolic syndrome despite disappointing results in previous trials of vitamin D supplementation for weight loss and prevention of both type 2 diabetes and cardiovascular disease. The newly published data involve a series of experiments in mice that aimed to distinguish the impact of ultraviolet radiation (UVR) and vitamin D supplementation on the development of obesity and diabetes. In these experiments, four diets were studied. Two groups were on a high-fat diet (HFD), one of which also received vitamin D supplementation. Similarly, the other two groups were on a low-fat diet (LFD), and one of these was supplemented with vitamin D. Within each of the four diet groups, one group received no UVR, a second received suberythemal UVR (1 kJ/m^2 twice a week), and the third received erythemal UVR (4 kJ/m^2 once every two weeks). The data showed that vitamin D supplementation did not inhibit weight gain. In contrast, both the suberythemal and erythemal UVR exposure groups suppressed weight gain in the HFD group, and erythemal UVR exposure also inhibited weight gain in the LFD group. Similarly, vitamin D supplementation did not suppress the development of glucose intolerance or insulin resistance in the HFD mice, while these outcomes were suppressed in mice in both the suberythemal and erythemal UVR groups. These data support the idea that sunlight exposure may be an effective strategy to inhibit weight gain, and that the beneficial effects of this exposure work through mechanisms that are independent of vitamin D. — *Helaine E. Resnick, PhD, MPH*



Representative skin fluorescence in 4-week-old mice fed an LFD for 4 weeks.

Geldenhuys et al. Ultraviolet radiation suppresses obesity and symptoms of metabolic syndrome independently of vitamin D in mice fed a high-fat diet. Diabetes 2014;63:3759–3769

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New Insight on Insulin Resistance in Type 1 Diabetes

Data in this issue of *Diabetes* by Jelenik et al. (**p. 3856**) support the idea that insulin resistance in both liver and muscle may be present during the development of type 1 diabetes. In the newly published research, female NOD mice were studied at two points in time: Data from one group were collected 3 days after the onset of diabetes (acute diabetes) and from a second group at 8 weeks after diabetes onset (chronic diabetes). These two groups were compared to nondiabetic NOD mice that were matched for age and body weight. The investigators first observed that both nondiabetic NOD mice and their acute diabetic counterparts were insulin resistant. In addition, both groups exhibited tissue-specific differences in insulin sensitivity. Mice with acute diabetes as well as those without diabetes displayed lower insulin-mediated suppression of endogenous glucose production than did wild-type mice, an observation suggesting hepatic insulin resistance in the acute and nondiabetic NOD groups. By contrast, suppression of fatty acids in acute diabetic mice was similar to that observed in the nondiabetic group. In the fed state, both diabetic and nondiabetic NOD mice showed lower fasting muscle mitochondrial oxidation, but increased lipid peroxidation. These interesting experiments, which were conducted prior to and at the point of type 1 diabetes onset, show that insulin resistance is present in type 1 diabetes in both muscle and liver, and that these changes are accompanied by oxidative stress. Improved understanding of the mechanisms that underpin insulin resistance in type 1 diabetes may offer novel opportunities to develop prevention and treatment strategies. — *Helaine E. Resnick, PhD, MPH*

Jelenik et al. Tissue-specific differences in the development of insulin resistance in a mouse model for type 1 diabetes. Diabetes 2014;63:3856–3867

Utility of Retina Calibers as a Tool for Risk Stratification

Long-term follow-up of patients with type 1 diabetes by Broe et al. (**p. 3906**) shows that changes in retinal vascular caliber—wider venular caliber and narrow arteriolar caliber—predicted the onset of diabetic peripheral neuropathy (DPN), nephropathy (DN), and retinopathy (DR). These intriguing findings are based on data from a cohort of children with type 1 diabetes that was first examined from 1987–1989. At that time, the average age of patients in the study was 21 years, and they had an average diabetes duration of 13.5 years. In 1995, color retinal photographs were collected from the patients, and these images were used to determine central retinal artery and vein equivalents (CRAEs and CRVEs). These measures are based on the diameters of the six largest arterioles and the six largest venules into the central artery and vein. In prospective analyses covering 16 years of follow-up, CRAEs and CRVEs were examined in relation to the incidence of DPN, DN, and DR. Results showed that wider CRVEs and narrower CRAEs predicted the onset of all three of the major diabetic microvascular complications. An obvious application of these results is the idea that the measurement of retinal calibers may be a useful tool for early, noninvasive risk assessment and stratification among patients with diabetes. With the added information that is offered by this tool, it may be possible to intervene even earlier in the course of diabetic microvascular disease. — *Helaine E. Resnick, PhD, MPH*

Broe el al. Retinal vessel calibers predict long-term microvascular complications in type 1 diabetes: The Danish Cohort of Pediatric Diabetes 1987 (DCPD1987). Diabetes 2014;63:3906–3914

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