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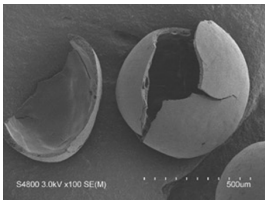
Diabetes Care®

In This Issue of *Diabetes Care*

By Max Bingham, PhD

Niacin Targeted to the Ileum/Colon May Improve Insulin Sensitivity: Prediabetes Implications?

Microencapsulated niacin targeted to the ileocolonic region of the gut appears to result in improved measures of insulin sensitivity, according to Fangmann et al. (**p. 398**). As a result, they suggest the approach might represent a potential therapy for prediabetes—a claim that will need substantiation in future trials. According to the authors, obese individuals without type 2 diabetes had a lower dietary intake of niacin than nonobese individuals. At the same time, based on DNA sequencing of stool samples, they found that obesity was also associated with reduced gut microbiota α-diversity and *Bacteroidetes* abundance. Reportedly, a correlation between niacin intake and the bacterial measures did exist. Together with previous evidence, this led them to hypothesize that niacin delivered directly to the ileocolonic region might result in improved metabolic outcomes and that they were somehow mediated by the bacterial phylum *Bacteroidetes*. Using delayed-release microcapsules with varying doses of either nicotinic acid or nicotinamide, the authors go on to show in a small study of 10 healthy humans that nicotinic acid but not nicotinamide resulted in significant decreases in myostatin, fetuin-A, and osteopontin, which they say are markers for skeletal muscle, liver insulin resistance, and metabolic inflammation, respectively. Concurrently, *Bacteroidetes* abundance in stool samples reportedly also increased over a 6-week period. Commenting more widely on the research, author Matthias Laudes told *Diabetes Care*: "We feel that this type of intervention will be a promising approach for the prevention of the progression of prediabetes into type 2 diabetes. The reason is that despite prediabetes prevalence increasing worldwide, and the conversion rate into type 2 diabetes is 5–10%, in most countries it is not considered as a disease on its own. Therefore, a pharmacotherapy, such as metformin or GLP-1 analogues, might not be accepted by the general population as an adequate treatment. In contrast, a 'functional food–based' approach targeting the microbiome is more likely to be accepted in such a preventive setting."



Scanning electron microscope photograph of whole opened nicotinamide microcapsules

Fangmann et al. Targeted microbiome intervention by microencapsulated delayed-release niacin beneficially affects insulin sensitivity in humans. Diabetes Care 2018;41:398–405

Kidney Disease Is "Virtually Universal" in Long-standing Type 1 Diabetes

A majority of patients with long-standing type 1 diabetes are likely to experience some form of kidney disease, according to Costacou and Orchard (**p. 426**). In particular the authors state that given that the life expectancy of patients with type 1 diabetes is increasing, we should expect a parallel increase in the numbers with advanced kidney disease, which they say will have "dire implications for the patient as well as for the health care system." As a result, they call for an immediate focus on prevention and approaches that go beyond glycemic control, including intensive lipid and hypertension management. The study examines 50-year cumulative kidney risk in a cohort of type 1 diabetes patients diagnosed in childhood at some point between 1950 and 1980. Of the 932 individuals identified, 144 participants died prior to baseline (1986–1988), 130 had only periodic survey data, and the rest had biennial surveys and/or clinical examinations for up to 25 years. The authors report that by 50 years, end-stage renal disease (ESRD) affected 60% of the cohort, while macro- and microalbuminuria affected 72 and 88%, respectively. There was also little evidence for any declines in cumulative incidence of macro- and microalbuminuria. Incidence of ESRD, however, did appear to decrease by 45% in more recently diagnosed cases. Author Tina Costacou said: "The hope that improvements in diabetes management and the availability of renoprotective medications would lead to lower diabetic kidney disease rates has not materialized and the vast majority of the U.S. type 1 diabetes population continues to develop some form of kidney disease. This suggests that our current management methods, which largely focus on glycemic control, do not prevent kidney disease, although they may delay its progression to kidney failure. It is therefore critical that additional risk factors, including genetic, which accelerate kidney complication development, are identified and targeted in an effort to reduce its incidence."

Costacou and Orchard. Cumulative kidney complication risk by 50 years of type 1 diabetes: the effects of sex, age, and calendar year at onset. Diabetes Care 2018;41:426–433

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Moving More May Match Exercise Sessions for Improved Heart Health in Prediabetes

Physical activity and conversely sedentary time are likely associated with a variety of cardiometabolic risk markers in prediabetes, according to Swindell et al. (**p. 562**). Specifically, the researchers say that total physical activity accumulated over the day may be as important as moderate-to-vigorous exercise to improve a range of heart health markers in prediabetes. As a result, they suggest that replacing sedentary time with light physical activity might be a practical approach to improve cardiometabolic health in individuals with prediabetes who do not regularly engage in exercise sessions. The study focuses on 2,326 individuals with prediabetes who were tracked with accelerometers for 7 days to objectively assess their physical activity. Laboratory blood analyses and a 2-h oral glucose tolerance test were then used to assess a variety of cardiometabolic risk factors at baseline. According to the authors, moderate-to-vigorous exercise was negatively associated with insulin resistance, waist circumference, fasting insulin levels, glucose levels, triglycerides, and C-reactive protein levels. Total daily physical activity was reportedly comparable or better at reducing many of the same cardiovascular health measures. Conversely, sedentary time was positively associated with the same measures suggesting increased risk for poorer cardiovascular health. While underlining the apparent strength of using accelerometers to objectively measure physical activity, Swindell et al. do point out that they do not capture all movement data. They also highlight that the cross-sectional design means direction of causality between activity levels and the heart health markers cannot be assessed. According to author Nils Swindell: "Accumulating movement over the course of the day may be more attainable than achieving the intensity of moderate-to-vigorous exercise, particularly for individuals who have previously been inactive. I am hopeful that this study will lead to further research in this population, looking at total physical activity and exploring the substitution of sedentary time with a combination of activity intensities that are most appropriate for adults with prediabetes."

Swindell et al. Objectively measured physical activity and sedentary time are associated with cardiometabolic risk factors in adults with prediabetes: the PREVIEW study. Diabetes Care 2018;41:562–569

Low Rates of ESRD in Patients With Type 1 Diabetes in Norway

The incidence of end-stage renal disease (ESRD) among patients with childhood-onset type 1 diabetes in Norway is low in comparison to other countries, according to Gagnum et al. (**p. 420**). Moreover, they suggest that receiving a diagnosis prepuberty seems to imply a lower risk, or at least a delay, in the development of ESRD. The authors suggest that the reasons for the low rates are likely multifaceted but they highlight the near universal health care availability in the country, plus national guidelines that focus on intensive insulin treatment and the widespread use of ACE inhibitors as likely contributing factors. The study used the nationwide population-based Norwegian Childhood Diabetes Registry and included newly diagnosed type 1 diabetes patients (aged <15 years) in the periods 1973–1982 and 1989–2012. The researchers then tracked the patients until development of ESRD, death, emigration, or a cutoff date of 30 November 2015. To estimate the rates of ESRD, Gagnum et al. linked the diabetes records to the Norwegian Renal Registry via national registration numbers. They report that among 7,871 patients diagnosed with type 1 diabetes, 103 developed ESRD at some point over the maximum 43 years of follow-up. That equates to an average rate of 1.3%. At 20 years of diabetes duration the rate was 0.7%, at 30 years it was 2.9%, and at 40 years it was 5.3%. Additionally, the study showed that the risk for ESRD was lower in women than in men overall and the risk was higher in individuals diagnosed with type 1 diabetes aged 10–14 years versus <10 years. Puberty and it's changes in hormones seemed to be key in explaining the different outcomes.

Gagnum et al. Low incidence of end-stage renal disease in childhood-onset type 1 diabetes followed for up to 42 years. Diabetes Care 2018;41:420–425

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