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Diabetes Care®

In This Issue of *Diabetes Care*

Edited by Helaine E. Resnick, PhD, MPH

High Geographic Variability in Gut Microbiota of High-Risk Children

Preliminary data in this issue of *Diabetes Care* (**p. 329**) shed light on the potential contribution of the gut microbiome to geographic differences in the prevalence of type 1 diabetes. More than 1,100 stool samples from 90 high-risk children enrolled in the TEDDY study were examined to understand the association between the infants' gut colonization patterns and where they lived. The 90 children in the new report were from six clinical centers in Europe and the U.S.: Finland, Sweden, Germany, Colorado, Washington, and Georgia/Florida. Stool samples from these children were collected at multiple points in time between about 150 and 540 days after birth. High-throughput rRNA sequencing was used to quantify the abundance of various bacteria, and the Shannon diversity index (SDI) was used to describe the bacterial diversity in the samples. The abundance of several bacteria, including *Bifidobacterium*, *Veillonella*, *Faecalibacterium*, *Streptococcus*, and *Akkermansia*, differed by site, even when adjusted for clinical and dietary characteristics. There were notable differences in SDI across the sites, as well as variability in which bacteria were dominant at a given point in time. In particular, Colorado and Finland had less bacterial diversity than the other sites, whereas the gut microbiome in Georgia/Florida and Germany was more diverse and *Bifidobacterium* was dominant in children in Sweden and Washington until 8 and 10 months of age. Although these preliminary data suggest that colonization patterns in high-risk children differ by where they live and over time, it is not clear if these patterns explain the observed geographic differences in prevalence of type 1 diabetes or if they are simply markers of enhanced risk. Nonetheless, these data provide an intriguing backdrop for further studies of environmental determinants of diabetes risk. — *Helaine E. Resnick, PhD, MPH*

Kemppainen et al. Early childhood gut microbiomes show strong geographic differences among subjects at high risk for type 1 diabetes. Diabetes Care 2015;38:329–332

Eighty Percent of Patients With Type 1 Diabetes Have Detectable Insulin Secretion

The vast majority of a large population-based sample of people with type 1 diabetes has detectable endogenous insulin production. The new findings, reported in this issue of *Diabetes Care* (**p. 323**), are from a study of more than 900 patients who had type 1 diabetes for at least 5 years at the point when C-peptide was assessed. The results are notable because they are derived from a large, representative sample that provides a reliable estimate of the extent to which β-cell function is preserved among patients with long-standing type 1 diabetes. Using postmeal urine C-peptide–to–creatinine ratio (UCPCR), the investigators explored the proportion of patients who had any detectable C-peptide (UCPCR >0.001 nmol/mmol), as well the proportion of patients whose C-peptide exceeded two specific thresholds. The first threshold corresponded to C-peptide of 30 pmol/L, which was a common detection limit in the past. The second corresponded to C-peptide of 200 pmol/L, which is associated with reduced microvascular complications and risk of hypoglycemia. The results of this interesting study showed that even after having type 1 diabetes for a minimum of 5 years, 80% of the patients had detectable levels of C-peptide, although most were microsecretors. Nonetheless, 20% of the sample had C-peptide levels between 30 and 200 pmol/L and 8% exceeded 200 pmol/L. Other data showed that as duration of diabetes increased, C-peptide decreased, but the inverse association was observed for patient age at diagnosis. These results, which reflect the experience of a community-based sample of patients with type 1 diabetes, confirm the notion that β-cell loss is not complete in most patients, even many years after the diagnosis. This important observation offers insight for future treatments if the mechanisms that either regenerate these β-cells or protect them from immune attack are better understood. — *Helaine E. Resnick, PhD, MPH*

Oram et al. Most people with long-duration type 1 diabetes in a large population-based study are insulin microsecretors. Diabetes Care 2015;38:323–328

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Variant Hemoglobin Does Not Impact Utility of A1C in Africans

Data in this issue of *Diabetes Care* (**p. 213**) have important public health implications for diabetes screening in the developing world. Based on data from 216 African immigrants in the U.S., the new report provides an important methodological foundation for informed approaches to identification of diabetes in sub-Saharan Africa. The authors point out that sub-Saharan Africa is predicted to see a 109% increase in diabetes by 2035, a larger increase than anyplace else in the world. Against this backdrop, the importance of identifying the most effective screening strategies to identify diabetes in this part of the world is obvious. However, it is unclear whether the recent adoption of HbA_{1c} as a means to identify normal glucose tolerance in the U.S. and elsewhere is a viable strategy in sub-Saharan Africa and other areas where heterozygous variant hemoglobin conditions such as sickle cell are common. The new research addressed this issue by collecting fasting and postchallenge glucose measures as well as A1C in a sample of African immigrants. Using 2-h glucose of ≥7.8 mmol/L as the gold standard, the investigators examined the ability of fasting glucose, A1C, and fasting glucose + A1C to correctly identify diabetes and whether the sensitivity of these screening strategies differed by whether the participants had variant hemoglobin. Of the 216 people in the study, 33% had abnormal oral glucose tolerance test results and 21% had variant hemoglobin. The sensitivity of fasting glucose for diagnosing diabetes was 32%, A1C was 53%, and when A1C and fasting glucose were used together, the sensitivity increased to 64%. Importantly, the sensitivity of A1C in identifying diabetes did not differ by whether participants had variant hemoglobin. Although these results suggest that variant hemoglobin will not hinder the utility of A1C as a diagnostic tool if it were widely used in areas where variant hemoglobin is present, they also show the added value of combining it with fasting glucose to optimize screening efforts. — *Helaine E. Resnick, PhD, MPH*

Sumner et al. Detection of abnormal glucose tolerance in Africans is improved by combining A1C with fasting glucose: the Africans in America Study. Diabetes Care 2015;38:213–219

Novel T1D Diagnostic Strategy Shows Promise

Results from two studies of people at high risk for type 1 diabetes support the utility of a novel diagnostic strategy. The newly published report (**p. 271**) is based on data from 2,350 antibody-positive relatives of people with type 1 diabetes from two cohorts—the Diabetes Prevention Trial–Type 1 (DPT-1) and the TrialNet Natural History Study (TNNHS). Researchers studied the screening properties of a new metabolic index—the T1D Diagnostic Index60 (Index60)—and showed that it improved the ability to identify diabetes in both cohorts. The Index60 is based on data from a 2-h oral glucose tolerance test and uses information from log fasting C-peptide, 60-min C-peptide, and 60-min glucose. A key question in the new report was how a threshold of ≥2.00 on the Index60 performed relative to 2-h glucose ≥200 mg/dL. The 2.00 threshold was of interest because it corresponds to a value of 8.02 on the Diabetes Prevention Trial Risk Score (DPTRS), another risk assessment tool. A DPTRS of 9.0 or above is an exceptionally strong predictor of diabetes, but this measure also includes age, BMI, and a more complex use of C-peptide data. The results showed that among the autoantibody-positive relatives of people with type 1 diabetes in both cohorts, an Index60 threshold of ≥2.00 offered considerably more accuracy in identifying diabetes in ROC analyses than 2-h glucose. In addition, the sensitivity of Index60 was also higher in both cohorts, and the positive and negative predictive values were more favorable. These results suggest that Index60 might be a valuable addition to the available toolkit for diagnosing type 1 diabetes. — *Helaine E. Resnick, PhD, MPH*

Sosenko et al. A new approach for diagnosing type 1 diabetes in autoantibody-positive individuals based on prediction and natural history. Diabetes Care 2015;38:271–276

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