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# In This Issue of *Diabetes Care*

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Edited by Helaine E. Resnick, PhD, MPH

## Preliminary Trial of Intranasal GLP-1 Yields Positive Findings

A study in this issue of *Diabetes Care* (p. 2024) highlights preliminary data on a new GLP-1 formulation that is administered intranasally, and the early results suggest that this new delivery strategy may offer a viable option for patients who have difficulty with the injectable form of the drug. Although the GLP-1 analogs are known to be effective in lowering glucose levels, they are administered by subcutaneous injection and are sometimes associated with side effects such as vomiting and nausea. These issues can be challenging for both patients and providers as they seek to identify effective and acceptable therapeutic regimens. The new report presents findings from 26 patients with type 2 diabetes who received the new compound immediately prior to a test meal. Of these patients, 18 received the intranasal powder formulation containing 1.2 mg GLP-1, and the remaining 8 patients received a similar powder without GLP-1. The investigators found that plasma GLP-1 peaked at 47.2 pmol/L, and the maximum concentration was reached at about 8 min after administration. Participants receiving active drug experienced both suppression of glucagon and recovery of early-phase insulin secretion. Nausea occurred in three of the intervention patients, but no vomiting was reported. Although ~99% of the drug was successfully administered using the nasal device, the bioavailability of this formulation is lower than the injectable form—a consideration that may have implications for cost. Further, the intranasal route would need to be used with each meal instead of a once-daily injection. This raises questions about whether the added burden would impact adherence. In the short term, however, these preliminary results suggest that intranasal GLP-1 administration is ripe for further investigation. — *Helaine E. Resnick, PhD, MPH*

Ueno et al. Exploratory trial of intranasal administration of glucagon-like peptide-1 in Japanese patients with type 2 diabetes. *Diabetes Care* 2014;37:2024–2027

## Promising Results for Reducing Nocturnal Hypoglycemia

Among people with type 1 diabetes, pursuit of tight nocturnal glucose control is often balanced against risks associated with hypoglycemia, including the risk of seizures. Responding to the need for novel approaches to attain tight nocturnal control without increasing hypoglycemia risk, a report in this issue of *Diabetes Care* (p. 1885) summarizes results from a randomized trial of a continuous glucose monitoring system and insulin pump. The system is connected to a bedside laptop computer that uses an algorithm to predict and respond to hypoglycemia risk through the night. Using the algorithm, the system can be suspended and restart insulin while the patient sleeps. The newly published trial is based on data from 45 people with type 1 diabetes who were trained to use the device and then were randomly assigned to intervention nights (when the device was in use) and control nights. These patients were unaware whether a given night was intervention or control. Although the main outcome of the trial was the percent of nights when a patient had glucose values  $\leq 60$  mg/dL, safety outcomes including morning glucose and ketone levels were also of central interest. Participants used the device until at least 42 nights included  $\geq 4$  h of continuous glucose monitoring data. The primary analysis was based on 1,912 nights of data of which 942 and 970 were intervention and control nights, respectively. Hypoglycemia was recorded in 21% of the intervention nights and 33% of the control nights, and these proportions translated into an odds ratio of 0.52 ( $P < 0.001$ ), indicating a significant reduction in hypoglycemia during intervention nights. Although median morning glucose was significantly higher during intervention nights relative to control nights (144 vs. 129 mg/dL), morning ketone levels were low and did not differ between the groups, nor did HbA<sub>1c</sub> levels change in either group between baseline and study end. These findings not only suggest that the system can reduce nocturnal hypoglycemia without a meaningful rise in hyperglycemia, but they also have implications for reducing patients' fear of hypoglycemia and helping them achieve better overall glucose control. — *Helaine E. Resnick, PhD, MPH*

Maahs et al. A randomized trial of a home system to reduce nocturnal hypoglycemia in type 1 diabetes. *Diabetes Care* 2014;37:1885–1891

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## Unfavorable Association Between Organic Pollutants and Both Glucose and Body Composition

In recent years, questions have been raised about whether environmental factors have played a role in the dramatic increases that have been observed in both obesity and diabetes. In particular, the potential role played by persistent organic pollutants (POPs)—man-made chemicals that biodegrade very slowly—has been the focus of increasing attention in relation to diabetes risk. Research in this issue of *Diabetes Care* (p. 1951) adds to a growing body of literature linking POPs to certain aspects of glucose metabolism and body composition. In a sample of 151 obese and 44 nonobese participants, data were collected on glucose tolerance, body composition by CT scan, and fat mass using bioimpedance. A number of POPs—mostly polychlorinated biphenyls (PCBs)—were measured in participants' serum, and the POPs were also measured in adipose tissue samples from 53 of the obese participants. One pesticide and three PCBs were found to be the dominant POPs in the biological samples, and these were the focus of the new report. The authors examined the impact of pesticide levels and levels of each PCB, as well as the sum of PCB levels in relation to the metabolic and body composition data. They found that total body levels of all POPs were higher in the obese participants and that all the serum measures were correlated with the ratio of visceral to subcutaneous fat measured by CT. Further, total body POP levels were associated with both waist circumference and CT visceral fat. Two of the three PCBs as well as the sum of PCB levels were associated with higher fasting glucose levels, and postchallenge glucose levels were associated with all the POPs. These intriguing data shed light on the potential importance that environmental factors may play in determining diabetes risk. If these associations are proven to be causal, future research may focus on the impact of interventions aimed at limiting exposure to environmentally based diabetogenic risk factors. — Helaine E. Resnick, PhD, MPH

Dirinck et al. Exposure to persistent organic pollutants: relationship with abnormal glucose metabolism and visceral adiposity. *Diabetes Care* 2014;37:1951–1958

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