

# Glucose Abnormalities Seen After Gastric Bypass

BY BRUCE JANCIN

GRAPEVINE, TEX. — Gastric bypass surgery's status as the gold-standard weight-loss procedure has come under question by new evidence that many recipients develop late, often-unrecognized glucose abnormalities contributing to significant weight regain.

"The gastric bypass has been the procedure of choice, especially for sweet eaters. I think it's time to reconsider. I actually believe that vertical sleeve gastrectomy and duodenal switches that are not severely malabsorptive will be the best operations in the future," Dr. Mitchell S. Roslin asserted at the annual meeting of the American Society for Metabolic and Bariatric Surgery.

His hypothesis is that after weight loss induced by gastric bypass, patients have an enhanced insulin response. A substantial subgroup of these patients develop rapid emptying of their surgically created pouch, with resultant reactive hypoglycemia that contributes to grazing and other maladaptive eating behaviors.

"The combination of an empty pouch and low blood sugar equals hunger," noted Dr. Roslin of Lenox Hill Hospital, New York.

This hypothesis arose from conversations with large numbers of post-gastric bypass patients contemplating revisional bariatric surgery because of troubling weight regain.

"They were essentially saying that 1 or 2 hours after eating they were ravenously hungry. Many complained of being light-headed. The symptoms sounded to me a lot like hypoglycemia," he recalled. "What really struck me wasn't the weight regain, it was how ravenous the patients were. They almost felt out of control. And that's really sad, because they thought in gastric bypass they were choosing something more definitive."

To test his hypothesis, he gave a 100-g oral glucose tolerance test to 63 patients coming to the obesity surgery clinic for routine follow-up a mean of 4 years after Roux-en-Y gastric bypass. Their mean age was 48.5 years, 81% were women, and one-third of the patients had dia-

betes preoperatively. Their mean preoperative weight was 138 kg. They had a maximum 55% excess weight loss, but had regained an average of 12 kg.

Fully 49 of the 63 patients (78%) had an abnormal glucose tolerance test. Six had hyperglycemia as defined by any post-challenge blood glucose value greater than 200 mg/dL with none below 80 mg/dL. Significantly, all but one of these six patients had normal fasting blood glucose. "That means we need to be very careful what we call surgical cure or control of diabetes," he observed.

Another 35 patients had reactive hypoglycemia, defined as a blood glucose value below 60 mg/dL or a decrease of at least 100 mg/dL between hours 1 and 2, with no value greater than 200 mg/dL. Another eight patients had both reactive hypoglycemia and hyperglycemia. Thus, more than two-thirds of the study group had evidence of hypoglycemia. These patients displayed a rapid postchallenge upsurge in blood glucose correlating with a rising insulin level, then a rapid decline in glucose in the second hour of the test.

A normal maximum-to-minimum glucose ratio on the 100-g test is 1.5-2:1. However, 22 patients in this study had ratios greater than 3:1, and 7 had ratios greater than 4:1. "We see higher peaks and more profound drops in the patients who have both hyper- and hypoglycemia," Dr. Roslin noted.

Another way of avoiding problems due to rapid pouch emptying, besides doing a vertical sleeve gastrectomy or duodenal switch procedure instead of gastric bypass, might be to incorporate a valve in the gastric bypass procedure.

"I favor the pyloric valve, which controls the passage of food," he continued.

Indeed, recognizing that his 63-patient oral glucose tolerance test series is merely an observational study, Dr. Roslin is now planning a prospective clinical trial comparing gastric bypass to a pyloric valve-preserving operation.

Dr. Roslin disclosed that he has potential conflicts of interest resulting from commercial relationships with Covidien AG, C.R. Bard Inc., ValenTx Inc., Scientific Intake Ltd., and VentralFix Inc. ■

## Exenatide May Aid Weight Loss in Nondiabetic Patients

BY JOYCE FRIEDEN

WASHINGTON — Exenatide helps increase weight loss in obese nondiabetic patients who also are following a diet and exercise program, recent study results suggest.

Dr. Michael Trautmann, a researcher at Eli Lilly & Co., and his colleagues conducted a double-blind, placebo-controlled study of 152 patients with a mean body mass index of 39.6 kg/m<sup>2</sup>. The patients' average age was 46 years, and 82% were women. The average hemoglobin A<sub>1c</sub> was 5.5%. One-quarter of the patients had impaired glucose tolerance, and average blood pressure was 120/76 mm Hg.

As is typical with obesity studies, 35% of patients enrolled did not complete the study, Dr. Trautmann said.

Patients were randomized to receive placebo or 10 mcg exenatide twice daily. Lifestyle modification—consisting of a balanced, calorie-restricted diet; moderate increase in physical activity, with a target of 150 minutes per week; and counseling sessions at 4-week intervals—was prescribed for all participants, Dr. Trautmann said at the annual meeting of the Endocrine Society.

The study's primary end point was change in body weight. Secondary end points included changes in glucose tolerance, physical activity, and dietary behavior.

After 24 weeks, a significantly higher percentage of exenatide-treated patients had lost at least 5% of their body weight, compared with patients on placebo (31% vs. 17%), Dr. Trautmann

said. All of the patients who had lost 10% or more of their body weight were in the exenatide group.

Average weight loss in the placebo group was 1.6 kg. In the exenatide group, the average loss was 5.1 kg, "a highly significant difference," he said.

In subgroup analysis, "due to the small sample size, one cannot conclude



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too much from these results, but the trend indicates that in patients with mild obesity—with a BMI of less than 35 kg/m<sup>2</sup>—there's no big difference between lifestyle intervention alone and exenatide treatment, while there is a very pronounced difference between the two treatment groups ... in the 35-40 BMI [range], and a smaller difference in ultraobese patients with a BMI greater than 40," he said.

Among patients with impaired glucose tolerance at baseline, three-quarters who were on exenatide normalized their glucose levels, compared with slightly more than half of the patients on placebo, he said. "Clearly, weight loss is known to improve glucose tolerance."

The study was sponsored by Eli Lilly and Amylin Pharmaceuticals. ■

## CDC Recommends Community Intervention to Combat Obesity

BY HEIDI SPLETE

WASHINGTON — Curbing the obesity epidemic in America requires community intervention, Dr. Thomas R. Frieden, director of the Centers for Disease Control and Prevention, said at the CDC's Weight of the Nation conference.

"The only way on a societal basis to reduce the prevalence of obesity is through community action, not through individual clinical interventions," Dr. Frieden said in a press conference.

"We got to this stage in the [obesity] epidemic because of a change in our environment," he said. "Only a change in our environment again will allow us to get back to a healthier place."

To help communities respond to the obesity epidemic, the CDC launched Common Community Measures for Obesity Prevention. As part of this project, the CDC convened a panel of experts in a variety of areas including nutrition, urban planning, and physical activity, as well as obesity prevention (MMWR 2009;58 [RR-7]:1-26).

"We can't wait for the best possible evidence, we have to act on the best available evidence," said Dr. William Dietz, director of the CDC's Division of Nutrition, Physical Activity, and Obesity. Dr. Dietz presented the CDC's recommendations at a press conference.

The panel agreed on 24 strategies, which fall into six categories:

- ▶ To promote the availability of affordable healthy foods and beverages (example: adding grocery stores in underserved areas).
- ▶ To support healthy food and beverage

choices (example: limiting ads for unhealthy food and beverages).

- ▶ To encourage breast-feeding (example: encouraging workplaces to support breastfeeding moms).

- ▶ To encourage physical activity or limit sedentary activity in children and adolescents (example: requiring physical education in schools).



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- ▶ To create safe communities that support physical activity (example: enhancing infrastructure to support walking and biking).

- ▶ To encourage communities to organize for change (example: participating in coalitions and partnerships to address obesity).

The panel chose strategies that are likely to have a broad reach and a long-term, meaningful impact on health, according to the full report. And the panel deemed the strategies reasonable for a community to implement.

"I think there is a responsibility to physicians and the medical profession generally to be active in their communities promoting prevention," said Dr. Frieden. It is often physicians who encourage community actions and influence policy makers, he emphasized. ■