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Weight loss surgery is usually the most effective treatment of obesity. Roux-en-Y gastric bypass (RYGB) surgery may also be one of the most effective treatments for type 2 diabetes (DM). Laparoscopic gastric banding (LAGB) is another weight loss procedure that results in a lesser degree of weight loss and improvement in glycemic control. In LAGB, the return to euglycemia in T2DM patients is predominantly due to the magnitude of weight loss. In contrast, we have shown that RYGB is associated with changes in gut hormone secretion that may promote decreased appetite, increased satiety, insulin sensitivity and secretion. More recently another bariatric procedure, sleeve gastrectomy (SG), has come into favor as a single procedure, when prior it was the first stage preceding malabsorptive operations. Much less is known about SG, but some data suggest that weight loss and metabolic outcomes, including gut hormone changes, are surprisingly similar to RYGB. Thus, it is likely that neurohormonal mechanisms contribute to greater weight loss and improvement in glucose control after RYGB and SG compared with LAGB and dietary caloric restriction. The main objectives of this proposal are to further delineate the metabolic and endocrine changes that occur after different weight loss modalities. In *AIM ONE* subjects with DM placed on an in-patient very low calorie diet will be compared with individuals undergoing RYGB and SG before and after equivalent weight loss (7-10% of body weight) achieved over the same time period (3 wks) in order to determine surgery specific effects on insulin sensitivity and secretion. Subjects will also be followed at 1 year. In *AIM TWO*, glucagon suppression and maximal islet cell function will be measured by a graded glucose infusion and arginine stimulation before and after RYGB or SG and compared with lean controls. The purpose of this study is to determine if there is evidence of islet cell hyperplasia after RYGB that may occur as a result of chronic exposure to increased concentrations of glucagon-like peptide 1. The main objectives of *AIM THREE* are to continue characterization of gut hormone and apolipoprotein A-IV secretion after LAGB and RYGB and the relationship to weight loss and appetitive sensations with prospective long-term follow-up. We will also begin characterization after SG. The effect of these procedures on acyl- and des-acyl ghrelin using a specific two-site sandwich assay will be analyzed in collaboration with Dr. Thorner. The objective of *AIM FOUR* is to investigate alterations in ~200 metabolites, including amino acids, lipid species and glucose intermediates before and after VLCD, LAGB, RYGB, and SG in subjects with and without DM using liquid and gas chromatography and mass spectrometry in collaboration with Dr. Burant and the U of Michigan Metabolomics Core. The ultimate goal is to understand the mechanisms that promote weight loss/maintenance and glucose homeostasis after different weight loss modalities. This information would aid both the patient and physician in the selection of appropriate therapy and guide the development of more effective non-surgical treatments for obesity and DM.