The Control of Diabetes Mellitus (NIDDM) in the Morbidly Obese with the Greenville Gastric Bypass

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Since February 1, 1980, the identical standardized Greenville Gastric Bypass has been performed in 397 morbidly obese patients with an operative mortality rate of 0.8%. The operation effectively controlled weight and maintained satisfactory weight loss even after 6 years (mean weights and ranges: Preoperative: 290 lbs (196–535); 18 months: 175 lbs (110–300); 72 months: 205 lbs (140–320). The gastric bypass favorably affected non–insulin-dependent diabetes (NIDDM), hypertension, physical and role functioning, and several measures of mental health. Rigorous follow-up (97.5% over 6 years) revealed that health problems were common in postoperative patients; there were nine late deaths. Abnormal glucose metabolism was present in 141 (36%) of 397 patients before surgery: NIDDM was present in 88 patients (22%) and 53 patients (14%) were glucose impaired. Of these, all but two became euglycemic within 4 months after surgery without any diabetic medication or special diets. The most recent 42 morbidly obese patients with NIDDM were studied intensively. In that cohort, fasting blood glucose, fasting insulin, and glycosylated hemoglobin returned to normal after surgery; insulin release, insulin resistance, and utilization of glucose improved sharply. The normalization of glucose metabolism after gastric bypass may not be related solely to weight loss and restriction of caloric intake, but may also be due to the bypass of the antrum and duodenum.

DIABETES MELLITUS is a frequent complication of morbid obesity. At least 25% of the morbidly obese have non–insulin-dependent diabetes mellitus (NIDDM) and an additional 10% demonstrate impaired glucose metabolism. This unusually high prevalence of diabetes may account for the high mortality of the morbidly obese from heart disease, atherosclerosis, and stroke.

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We have operated on 397 morbidly obese patients since February 1, 1980, and of these patients, 88 (22%) were afflicted with diabetes mellitus, whereas 53 (13%) demonstrated impaired glucose metabolism. A standardized gastric bypass operation was performed on all patients. Although we anticipated the diabetes mellitus of these morbidly obese patients would improve with their surgically induced weight loss, we were surprised by the rapidity of the improvement of glucose metabolism and the return to euglycemia even though the patients were still clearly morbidly obese and were still within 10–20 lbs of their preoperative weights. This report details our observations of the effect of the gastric bypass on diabetes mellitus. We also describe the effectiveness of the operation in controlling morbid obesity, reversing hypertension, and restoring functional effectiveness.

Methodology

From February 1, 1980 to February 1, 1987, we performed the identical standardized Greenville Gastric Bypass in 397 morbidly obese patients. The group included 343 women (86.4%) and 54 men (13.6%) of which 326 (82.1%) were white and 71 (17.9%) were black. The mean age was 37.6 years (range: 16–65).

Each patient was evaluated with a thorough medical assessment, an interview with a psychiatrist, and several instruments to measure mental health, physical and role functioning, economic status, and educational levels. Additional evaluations, including treadmill tests, cardiac catheterizations, endoscopies, and radiocontrast studies were done in some patients when indicated by the initial evaluation.

Every morbidly obese patient without known diabetes mellitus had a 75-g oral glucose tolerance test (OGTT), as recommended by the National Diabetes Data Group[1] to determine whether they were truly nondiabetics. The 42 morbidly obese patients with diabetes who were recently operated on also had a 25-g intravenous glucose tolerance test to determine the rate of glucose disappearance (kg rate) and insulin concentrations before surgery. Of these 42 patients, 32 had the same tests 1 year after the gastric bypass surgery. Plasma glucose was measured by the Beckman-developed oxygen rate method.[2] Insulin was measured with the double-antibody method.[3] In addition, glycosylated hemoglobin was measured in these patients before and 1 year after surgery by affinity chromatography.[4,5]

All patients, whether referred by other providers or self-referred, were considered for initial evaluation. A patient was considered eligible for the surgery if: (1) he or she exceeded ideal body weight (as defined by the 1983 median weight of the Metropolitan Life Insurance Tables) by at least 100 lbs or if of short stature by 100%, (2) if the patient was an acceptable surgical risk, (3) if the patient was considered capable of understanding the operation and the postoperative consequences, and (4) if the patient gave informed consent.

Patients were usually admitted to the hospital on the day before surgery except for those in cardiorespiratory failure or those with other significant medical problems. Patients with such complications were often admitted several days before surgery to improve their surgical risk. Recently we have admitted a limited number of low-risk patients on the day of surgery, and these individuals have done well.

The Greenville Gastric Bypass, a modification of the procedure devised by Mason,[6] has previously been described[7] in detail; a diagram of the procedure is shown in Figure 1. A Gomez retractor is useful. The abdomen is entered through a midline incision. If the exploration does not demonstrate contraindications to the procedure, specimens of blood, fat, liver, and muscle are taken for our basic science studies. Dissection around the upper portion of the stomach is begun by inserting the index finger gently into the angle at the cardia to the left of the esophagus. At this point there is a weak, thin area of the posterior peritoneum that is easily entered by the dissecting finger. The dissection is gently continued behind the esophagus and cardia and the finger brought out, not at the right side of the esophagus but between the ascending branches of the left gastric artery 2.5–3.0 cm below the esophagogastric junction. A large Malecot catheter (Division of Bard, Inc., Bard Urological Division, Murray Hill, NJ), from which the bulbous end has been cut, is used to pull a double-headed TA 90 Auto Suture stapling instrument (US Surgical Corp., Norwalk, CT) through the passage. A proximal pouch measuring 4 cm in width and 1.5 cm in height is then prepared by firing the staples. A figure-of-eight suture is placed at each end of the staple line to close the ends securely and to serve as guy sutures. The jejunum is divided at its apex, about 30–40 cm from the ligament of Treitz with the GIA stapling instrument and the distal end is then sutured to the gastric pouch. The anastomosis is sewn to fit snugly around a 0.8-cm Salem Sump tube (Sherwood Medical, St. Louis, MO) in two layers with continuous Prolene. The Roux-en-Y enteroenterostomy is then completed by joining the proximal jejunum end-to-side to the distal jejunum with GIA and TA 55 (US Surgical Corp.) stapling instrument. It is important to fasten the Roux loop to the mesocolon to prevent an internal hernia and to oversew any bleeders in the enteroenterostomy before closing it. The abdomen is closed with a running double-stranded 0 PDS absorbable suture. The skin is stapled. The operation can usually be performed in 60–75 minutes; blood loss rarely exceeds 300 mL.

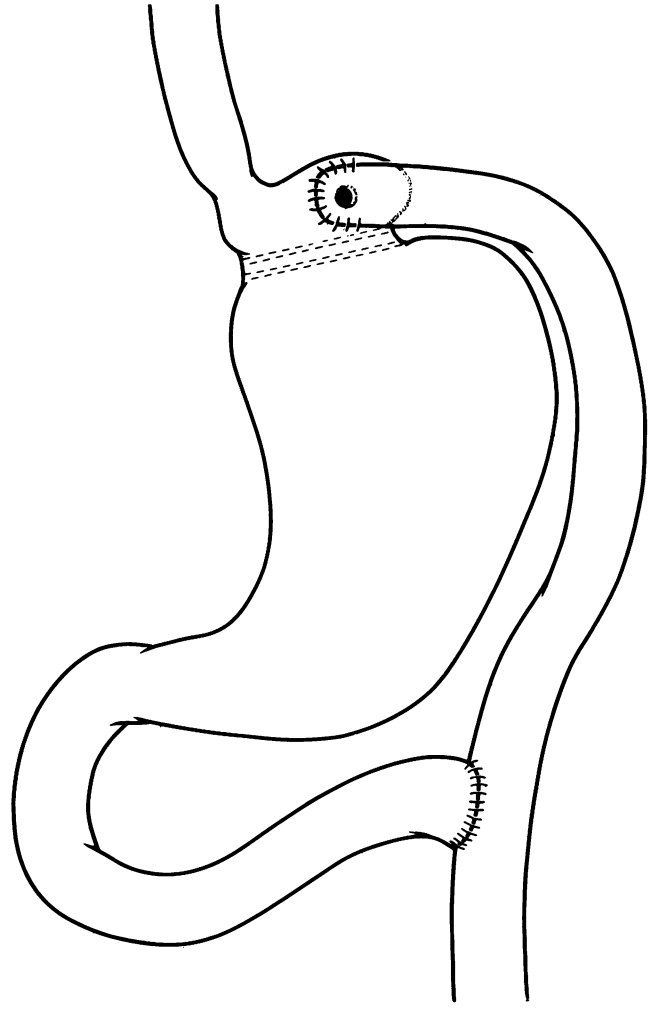

FIG. 1. The Greenville modification of the gastric bypass consists of 30-mL proximal gastric pouch joined to a 40-cm Roux-en-Y jejunal loop with a 0.8-mm gastroenterostomy.

TABLE 1. *Weight Loss after Gastric Bypass for the RY22 Cohort*

Time	N*	Mean Weight (lbs)	Mean % of Original Weight	Mean % of Ideal Body Weight
Before operation	397	290 (186–535)		212 (140–377)
1 month	251	261 (180–480)	90 (80–100)	191 (131–332)
6 months	323	207 (100–418)	72 (42–93)	152 (73–282)
12 months	240	184 (107–397)	63 (32–88)	134 (85–268)
18 months	172	175 (110–300)	61 (40–88)	120 (88–205)
24 months	160	176 (105–367)	61 (37–84)	130 (90–248)
36 months	120	187 (119–359)	64 (43–91)	138 (91–243)
48 months	99	188 (114–360)	65 (41–95)	139 (87–243)
60 months	57	195 (107–308)	69 (45–96)	144 (86–222)
72 months	26	205 (140–320)	72 (56–92)	149 (73–332)

* As of February 1, 1987.

Effect of the Gastric Bypass on RAND Mental Health Measures and Physical and Role Functioning

The effects of morbid obesity and the gastric bypass on mental health, physical and role functioning, *i.e.*, functional effectiveness were measured with the RAND instrument, the Obesity Awareness Scale (OAS), Eating Restraint Questionnaire (ERQ), Multidimensional Health Locus of Control (MHLC), the Zung Self-rated Depression Scale or SDS, and the Family Inventory of Resources for management (FIRM) before operation and during the course of follow-up in the most recent 120 patients.

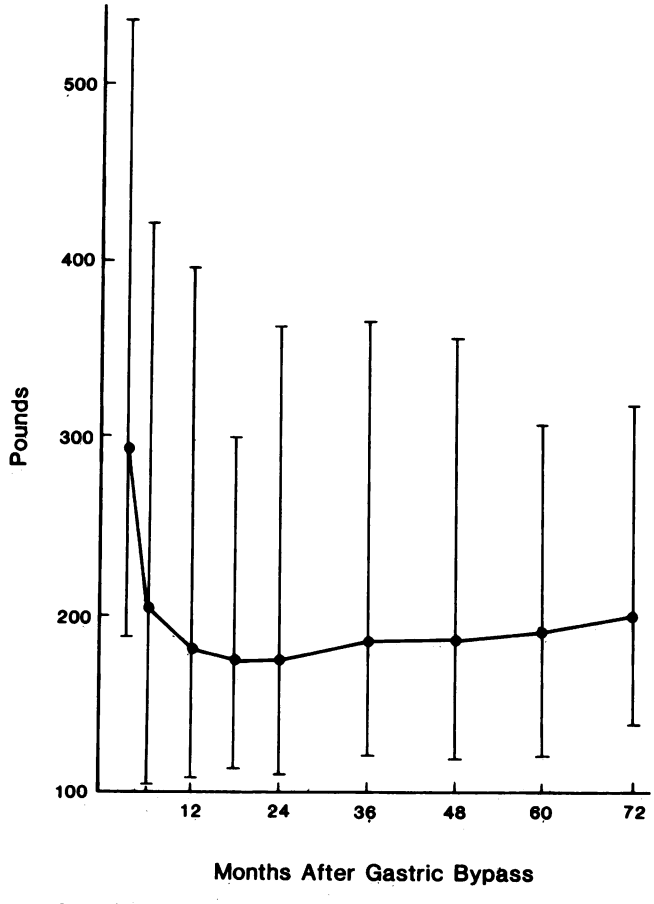

FIG. 2. Weight loss in pounds after gastric bypass in 397 morbidly obese patients.

Results

Follow-up

Follow-up has been rigorous. Of the 397 patients, only 10 did not keep long-term clinic appointments. Fortunately we have maintained contact with eight families of these 10 patients (97.5% follow-up).

Control of Weight

Weight reduction in these patients has been dramatic and well maintained over the 72 months of follow-up. Table 1 and Figure 2 present the weight loss of all 397 patients who have had the gastric bypass during the time intervals after surgery, in terms of mean weight in pounds, mean percentage of original weight, and mean percentage of ideal body weight. (Ideal body weight is determined from the midpoint of the "medium" standard of the Metropolitan Life Insurance Tables of 1983.)

If morbid obesity is defined as 100 lbs over ideal weight, 94% of the patients are "cured" within 2 years. There is, however, some weight gain between 24 and 72 months (176–205 lbs; 14%), reflecting a minority of individuals who learned to "outeat" their pouch and their dumping response by almost continuous snacking. These patients, *i.e.*, those who began to regain their weight, were the only ones given dietary limitations. Although we have had a few dietary failures, most patients will respond to the "Ensure Diet" (Ross Laboratories, Columbus, OH) (taking two cans of this supplement as the only caloric intake two or three times a week) or to formal dietary instruction by a trained dietician.

TABLE 2. *Effect of the Gastric Bypass on Diabetes*

	Before Operation	After Operation
Glucose Impaired	53	—
Diabetes Mellitus (NIDDM)	88	2
Receiving insulin	20	2
Receiving oral agents	13	1*

* One patient receives both insulin and an oral agent from her physician.

The Reversal of Diabetes Mellitus by the Gastric Bypass

The effect of the gastric bypass on adult onset diabetes mellitus (NIDDM) is the most significant finding of this study (Tables 2 and 3). Diabetes Mellitus (NIDDM) was present in 88 (22%) and impaired glucose tolerance was present in 53 (13%) of the 397 patients according to the criteria of the American Diabetes Association. All but two patients (99%) became and have remained euglycemic since surgery.

This normalization of glucose metabolism occurs with surprising speed. Frequently, patients became euglycemic within 10 days, even if they required over 100 units of insulin before surgery. The effect does not appear to be related solely to weight loss or decreased caloric intake, but may also be due to the bypass of the neuroendocrine axis of the antrum and duodenum.

The most recent 42 patients with diabetes were studied intensively. Of these, 12 had been receiving insulin, nine were receiving sulfonylureas, and another two were receiving both medications before the gastric bypass. Of these 42 patients, none now receive insulin and only one requires sulfonylureas. In all, fasting blood glucose, fasting insulin, and glycosylated hemoglobin were restored to normal levels. Insulin release, insulin resistance, and utilization of glucose were sharply improved. Although the maximum insulin release *per se* is not significantly different, these data should be considered in view of the preoperative and postoperative fasting insulin levels, *i.e.*, the basal values of 53 and 14 μU/mL. Thus the preoperative insulin release above basal was 23 μU/mL, whereas the postoperative response of the pancreas to the glucose load was 48 μU/mL, a significant improvement.

TABLE 3. *Effect of the Gastric Bypass on Measures of Glucose Metabolism*

	Before Operation (N = 42)	Year After Operation (N = 32)
Fasting blood glucose (mg%)	213 ± 15	117 ± 8
Fasting insulin (μU/mL)	53 ± 7	14 ± 1
Glycosylated hemoglobin (%)	12.3 ± 1.1	6.6 ± 0.6
Maximum insulin release (μU/mL)	76 ± 11	62 ± 15
Kg rate (%/min glucose disappearance)	0.65 ± 0.08	0.88 ± 0.07

TABLE 4. *Effect of the Gastric Bypass on Hypertension (N = 397)*

	Before Operation		After Operation	
	N	%	N	%
No. of hypertensive patients	225	56.7	73	18.4
Total no. receiving medication	144	36.3	53	13.3
Beta blocker	33	8.3	11	2.8
Diuretic	98	24.7	34	8.6
Vasodilator	11	2.8	6	1.5
Calcium blocker	2	0.5	2	0.5

The Control of Hypertension

Table 4 shows that of the 225 patients who were hypertensive (>140/90 mmHg) before surgery, only 73 remained so after the gastric bypass, a 68% decrease in the number of hypertensive patients. Similarly, the number of hypertensive patients requiring medication decreased from 144 to 53, a drop of 63%.

Effect of the Gastric Bypass on RAND Mental Health Measures and Physical and Role Functioning

The effects of morbid obesity and the gastric bypass on functional effectiveness were measured in our last 120 patients with the instruments listed under Methodology. These data will be reported separately, but in essence demonstrate that the operation sharply improves physical and role functioning, but that the mental health improvements noted during the first year may not be maintained.

Perioperative and Late Complications

The perioperative and late complications associated with this series of gastric bypass operations are summarized in Table 5.

TABLE 5. *Complications Associated With Gastric Bypass (N = 397)**

	N	%
Deaths		
Perioperative (2 Sepsis, 1 MI)	3	0.8
Late		
2 sepsis		
1 cancer of the larynx		
2 automobile accidents		
3 suicides		
1 cirrhosis	9	2.3
Complications		
All complications (major and minor)	390	98.2
Serious enough to delay discharge	45	11.3
Infections	70	17.6
Readmissions	124	31.2

* Mean length of stay = 8.7 days (range: 5–34 days).
MI = myocardial infarction.

TABLE 6. *Perioperative Complications, Within 30 Days after Gastric Bypass (N = 397)**

	N	%
Infections		
Minor wound infection	46	12.0
Severe wound infection	17	4.4
Subphrenic abscess	9	2.3
Intraperitoneal abscess	1	0.3
Postoperative temperature >103 F	16	4.2
Sepsis, unexplained	1	0.3
Peritonitis, otherwise unexplained	2	0.5
Technical problems		
Laceration of spleen	10	2.6
Laceration of liver	6	1.6
Staple misfire	5	1.3
Staple line bleed	2	0.5
Wound hematoma	4	1.0
Wound dehiscence	3	0.8
Wound seroma	28	7.3
Seroma with necrotic fat	12	3.1
Foreign body retained	1	0.3
Small bowel tear	1	0.3
Dehiscence with evisceration	1	0.3
Secondary wound closure needed	1	0.3
Enteric fistula	1	0.3
Systemic Problems		
Pneumonia	7	1.8
Pleural effusion	2	0.5
Arrhythmias	7	1.8
Congestive heart failure	1	0.3
Upper gastrointestinal bleed	2	0.5
Lower gastrointestinal bleed	1	0.3
Liver disease	2	0.5
Diabetic ketoacidosis	2	0.5
Summary		
Patients with complications	226	58.9
Deaths related to surgery	3	0.8
Reoperated	8	2.1
Readmitted	29	7.6

* As of February 1, 1987.

The perioperative mortality rate of 0.8% is low (3/397) for this group of high-risk patients with such complicating preoperative factors as Pickwickian syndrome, inadequately managed diabetes, cardiopulmonary failure, asthma, and disabling arthritis. The 30-day mortality rate (the usual way of defining perioperative mortality) is 0.5%, but since the third patient died on the 35th day of complications resulting from her operation, we have included her as a perioperative death in the summary Table 5. All of the perioperative complications occurring within the first 30 days after surgery are listed in Table 6.

Of the 397 patients who had surgery, 11% had a complication serious enough to prolong their hospital stay; 31.2% required readmission during the 6 years of follow-up for a problem directly or indirectly related to the obesity or the gastric bypass.

Patients who have gastric bypass operations require considerable postoperative medical support. During our 72 months of rigorous follow-up, 98% returned with a large variety of health problems; these are listed in Table 7. Although a number of these concerns were not directly related to the gastric bypass, many were. Problems such as depression, vitamin deficiencies, and dumping may be minor in terms of surgical statistics but are certainly major concerns for the patient and for those who bear the costs for the readmissions and extra office visits. Further, these complications may not become apparent for years, underscoring the great need for long-term follow-up of this and of other operations for morbid obesity.

TABLE 7. *Late Complications and Other Complaints Recorded During the Follow-up of Gastric Bypass Patients More Than 30 Days after Surgery (N = 397)**

	N	%
Infections		
Wound infections/stitch granuloma	8	2.1
Wound necrotic fat	7	1.9
Severe wound infection	4	1.1
Technical problems		
Loose suture in anastomosis	8	2.1
Anastomotic failure by endoscopy (dilated)	9	2.4
Incisional hernia	56	15.0
Dilted proximal pouch	13	3.5
Gastritis by endoscopy	47	12.6
Marginal ulcer	8	2.1
Stenosis of anastomosis; Rx: dilatation	6	1.6
Small bowel obstruction	19	5.1
Systemic problems		
Skin lesions	22	5.9
Musculoskeletal complaints	34	9.1
Headache, neurovisual symptoms	147	39.3
Chest pain	31	8.3
Renal stones	8	2.1
Constipation	151	40.4
Temporary hair loss	124	33.2
Hemorrhoids/fissure	15	4.0
Arthritis	12	3.2
Vitamin B12 deficiency	101	27.0
Other vitamin deficiencies	40	10.7
Dairy food intolerance	178	47.6
Bile reflux/esophagitis	14	3.7
Genitourinary complaints	11	2.9
Hypoglycemia	13	3.5
Psychiatric problems/stress	27	7.2
Depression/Rx: medication	5	1.3
Depression/Rx: psychotherapy	68	18.2
Depression/Rx: hospital	6	1.6
Pedal edema	22	5.9
Colitis	4	1.1
Arrhythmias	48	12.8
Urinary tract infection	33	8.8
Cholelithiasis	27	7.2
Dumping	265	70.9
Nausea/vomiting	58	15.5
Diarrhea	57	15.2
Anemia	55	14.7
Dehydration/malnutrition	15	4.0
Peripheral neuropathy	7	1.9
Abdominal pain	63	16.8
Summary		
Deaths related to surgery	1	0.3
Late deaths unrelated to surgery	8	2.0
Patients with late complications	364	97.3
Readmissions	93	24.9

* As of February 1, 1987.

Most disturbing are the nine late deaths, a late mortality rate of 2.3% (9/397). Although no deaths seem to be directly related to the surgery, they raise concerns. The two deaths from automobile accidents, the three suicides, and the one death from cirrhosis suggest that the gastric bypass does not alleviate the depression commonly seen in the morbidly obese; in fact, the dramatic change in body image and forced modification of eating behavior may exacerbate it in a few patients. Similarly, the two deaths from sepsis and the death from cancer of the larynx raise questions about the effect of the induced malnutrition on immunocompetence in these patients. A tenth late death is expected soon: a woman dying of AIDS, probably acquired from a blood transfusion given during a plastic surgical procedure over a year after her gastric bypass. This mortality will raise the late death rate to 2.5% Unfortunately, we do not have reliable comparison figures for the illness or mortality rate of morbidly obese individuals who did not have surgery.

Discussion

NIDDM or Type II diabetes mellitus represents approximately 85% of all patients with diabetes. It is a heterogeneous disorder characterized by defects in insulin action and insulin secretion.[8–12]

When NIDDM is associated with obesity, insulin resistance significantly worsens. Over 75% of patients with NIDDM are obese and those who are morbidly obese (defined as at least 100 lbs or more than 100% over their ideal body weight) are most frequently refractory to insulin or sulfonylurea therapy, dietary counseling, or physical therapy.

Weight reduction clearly improves NIDDM and dietary control remains the hallmark of treatment for this disease. Consequently, dieting has always been a mainstay in the clinical management of NIDDM. Although the amelioration of NIDDM after jejunoileal bypass had been recognized for a long time, Ackerman[13] was apparently the first to note the rapidity (in days) with which objective improvements in carbohydrate metabolism occurred. Previously the improvement associated with intestinal bypass was considered to be a direct result of massive weight loss, but Ackerman speculated that the early return to glucose tolerance, even during the period of perioperative stress, must have a more complex explanation. He considered such possibilities as decreased carbohydrate ingestion, glucose malabsorption, and the diminution in measured gastric inhibitory polypeptide (GIP) and its insulinotropic effect after intestinal bypass. Halverson et al.[14] have reported similar findings after gastric bypass. They described alterations in glucose tolerance, insulin response, and insulin sensitivity 20 months after surgery. Excess weight loss was accompanied by improvements in insulin receptor number, basal hyperinsulinemia, and glucose tolerance. They also described an unexpected rise in GIP and insulin after the ingestion of oral rather than intravenous glucose in patients after operation, perhaps accounting for the episodic hypoglycemia sometimes seen in these individuals after gastric bypass. Herbst et al.[15] confirmed similar findings in morbidly obese diabetics who had gastric restriction operations and credited the improvement to increased insulin receptors. Schrumpf et al.[16] also reported the positive effect of the gastric bypass on glucose tolerance in obesity and credited this change to lowered basal insulin secretion and increased hepatic extraction of insulin.

Our population of morbidly obese patients with NIDDM has the same characteristics as other similar populations previously described.[14,15,17–19] These patients have fasting hyperinsulinemia, fasting hyperglycemia, and a decreased glucose disappearance rate currently attributed to overall insulin resistance, increased glucose production by the liver, and reduced peripheral glucose utilization. The increment of insulin secretion by the pancreas during the first 10 minutes after the administration of 25 g of glucose intravenously is severely decreased, characteristic of the abnormal first phase of insulin release seen in patients with NIDDM. Furthermore, the glycosylated hemoglobin is increased, indicative of long-term hyperglycemia.

The mechanism of insulin resistance in these severely obese patients with NIDDM currently is unknown. We have developed methodologies to study the three major target organs of insulin action in humans: the liver, muscle, and adipose tissue.[20–23] We have found that the insulin receptor kinase is greatly decreased, compared with controls, in liver and adipose tissue, but not in skeletal muscle. Since the insulin receptor kinase might be involved in the intracellular message of insulin action, our studies so far have provided the first demonstration of a functional abnormality of the insulin receptor in NIDDM. In the muscle, the defect in insulin action might be distal to the insulin receptor kinase.

After gastric bypass surgery there is a dramatic improvement in overall carbohydrate metabolism, insulin action, and insulin secretion in the absence of pharmacologic therapy. From the clinical point of view, the most important observation is that the patients can maintain normal glycosylated hemoglobin. However, it should be recognized that if they are challenged with 25 g of glucose intravenously, it is clear that the ability of the pancreas to secrete insulin and the peripheral tissues to utilize glucose, although greatly improved, is not normal. However, under physiologic conditions, rarely, if ever, do these patients encounter a 25-g glucose load in blood within 1 minute.

The mechanism of improvement of NIDDM after gastric bypass is, no doubt, complex and due to a num-

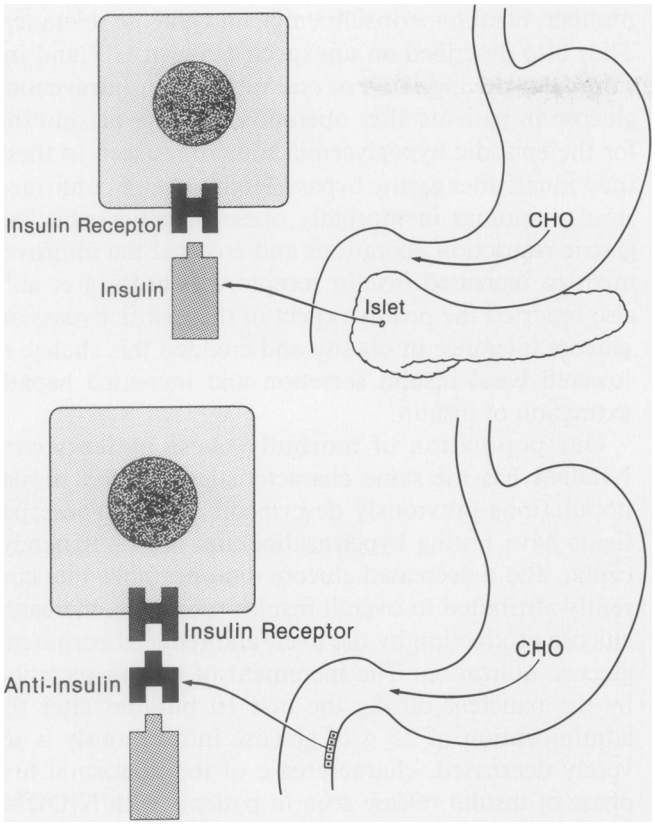

FIG. 3. A hypothesis for the effect of the gastric bypass on insulin action. Carbohydrate or insulin within the lumen of the antrum or duodenum stimulate the release of an anti-insulin blockade to increase insulin resistance. The gastric bypass detours this mechanism.

ber of factors. Decreased caloric intake is known to lead to normalization of blood glucose levels and induced weight loss is one of the factors in reducing insulin resistance. It is also possible (Fig. 3) that the bypass of the antrum and duodenum decreases the stimulation of endocrine cells to produce an anti-insulin blocking agent that influences the action of GIP. Most biologic systems have "stop and go" controlling systems; it is reasonable to expect that there is also an anti-insulin mechanism that responds either to high levels of glucose or insulin within the upper gut. We plan to explore this thesis with a prospective randomized comparison between the effect of the gastric bypass (which bypasses the antrum and duodenum) and the vertical banded gastroplasty (which does not) in a series of morbidly obese patients with NIDDM.

In summary, our series demonstrates that the Greenville version of the gastric bypass is an effective therapy for morbid obesity. The operation produces predictable control of weight, controls NIDDM in almost all patients, ameliorates most cases of hypertension, and sharply improves the functional effectiveness and quality of life in the morbidly obese. The operation is generally well tolerated and can be performed with a low mortality, but the patients must be followed closely for years because malnutrition, late complications of surgery, and psychiatric problems are not uncommon.

Acknowledgments

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Discussion

DR. EDWARD E. MASON (Iowa City, Iowa): Thank you, Dr. Pories for calling attention to this effect general surgeons have on the ratio of benefit to risk in treating extreme obesity with stomach reduction surgery.

The effect is not peculiar to gastric bypass. (Slide) Vertical banded gastroplasty produces the same severe reduction in insulin requirement with the cost savings as much as $4000 in 5 years by elimination of the need for 100 units of insulin per day.

(Slide) What is happening? Vertical banded gastroplasty does not rearrange the gastrointestinal tract, which means that there is no deleterious effect on the absorption of iron, calcium, and certain vitamins, and probably no change in the release of digestive tract hormones.

(Slide) The benefit of all gastric reduction operations is dependent on careful measurement of pouch volume and the outlet, and over the long term of doing something to reinforce the outlet (Slide) to make sure it will not dilate.

(Slide) Vertical banded gastroplasty causes the same severe reduction in weight and usually the elimination of need for insulin, and in this and other ways is as effective as less physiologic operations that rearrange the digestive tract.

(Slide) Why does the insulin requirement drop from 100 to zero so rapidly? Before the patient is released from the hospital, the preoperative insulin level decreases from as high as 100 or 120, often to zero. This occurs probably because of the very severe reduction in glucose intake.

We know, however, according to Dr. Pories' presentation, that there was a doubling in the rate of glucose utilization. When does this occur? Does it occur in the first few days when the requirement for insulin drops? And, in those occasional patients who disrupt the operation or learn to overeat the restriction and regain weight, how long does it take for the cells to lose their insulin receptors?

We have an opportunity here to learn more about the mechanisms of the benefits we produce, and I look forward to hearing more about the mechanisms involved.

DR. EDWARD R. WOODWARD (Gainesville, Florida): We also have observed excellent weight loss after Roux-en-Y gastric bypass and early reversal of diabetes mellitus in nearly all cases. We have operated on 412 patients since 1982 using this procedure. A 2-year follow-up of 238 patients has revealed an average loss of excess weight of 66%. Three-year follow-up of 150 patients has revealed an average loss of excess weight of 64%. We have been particularly pleased with the 4-year follow-up in 67 patients where the average loss of excess weight has been 76%.

We have observed a higher incidence of marginal ulceration than that noted in this report. This diagnosis has been established in 30 of our patients, an incidence of 7%. Eighteen of these were refractory to medical therapy and required reoperation. It is interesting that in 17 of the 30 patients, a defect in the staple line had developed and most of the medically intractable patients were in this group. It appears the staple line defect permitted reflux of acid gastric juice from the main stomach.

In the last 2 years we have had considerable experience using a vertically stapled gastric partition with a Silastic® band controlling the pouch outlet. This is the method described by Dr. Henry Laws of Birmingham (Am J Surg 1981; 141:393–394.). We have noted the same early reversal of diabetes mellitus in these patients, indicating the likelihood that drastically reduced calorie intake is a major factor.

DR. BERNARD M. JAFFE (Brooklyn, New York): I, too, was privileged to review the manuscript. Dr. Pories asked if I would spend a moment speculating as to the possible mechanisms that resulted in improvement of insulin function.

One of the possibilities must be related to dietary changes. However, the documentation that glucose tolerance tests and euglycemic and hyperglycemic clamps resolve so rapidly after operation suggests that it is simply not a matter of dietary glucose or dietary carbohydrate.

Another possible mechanism includes an abnormality in gastrointestinal hormones, and in response to Dr. Pories' request, I have thought about some possible humoral mechanisms that could be involved.

Pancreatic polypeptide is known to be involved in the control of insulin release, and levels of PP are profoundly suppressed in obesity. On the other hand, despite these two pertinent observations, PP is unlikely to be the mediator of this phenomenon. Reversal of the abnormality in PP requires restoration of normal weight, *i.e.*, a much slower effect than that observed in these clinical experiments. Therefore, PP is not the agent.

Somatostatin is another possibility, and obviously bypassing of the antrum would result in lessening of the release of somatostatin. To date, nobody has been able to successfully document changes in physiologic circulating somatostatin levels. The best evidence that makes it unlikely that somatostatin participates in the response is the fact that both the banded gastroplasty and the Roux-Y gastric bypass provide exactly the same alteration, the rapid resolution of the diabetic phenomenon. Since somatostatin is abnormally released in one circumstance and not in the other, antral exclusion certainly does not yield the mechanism.

I believe the phenomenon is probably a matter of resolution of the abnormal insulin resistance. As a result of the correction of insulin resistance, which has been shown to occur rapidly, basal levels of insulin return to normal, and insulin no longer participates in vicious negative feedback inhibition. As a result of these changes, insulin responsiveness returns to normal.

I believe the key phenomenon is the change in insulin resistance, and when we understand why this occurs, I believe we will understand more about this phenomenon.

DR. LEON MORGENSTERN (Los Angeles, California): Dr. Pories, I would like to ask if there were any accidental splenectomies in this large series, and if so, was there any relation to early or late sepsis?

DR. WALTER J. PORIES (Closing discussion): First I would like to thank each of the discussants and, obviously, thank Dr. Mason for having the idea in the first place.

We agree that a comparison between the gastric bypass and the vertical banded gastroplasty offers the elegant experiment to test the effect of the antral and duodenal hormones on glucose metabolism, especially if insulin function and resistance are measured with the rigorous methodology of the insulin clamp. Accordingly, we plan to perform this prospective comparison in the near future and will begin as soon as we have the approval from our institutional review board.

Dr. Woodward, I cannot explain why your number of marginal ulcers is higher than ours (8/397; 2.1%). The use of cimetidine has made it possible to manage these without surgery; we believe that this is a major breakthrough.

I stand in awe of Dr. Jaffe and I have for some time. His speculations are exciting and I hope that he will share his ideas with us during the planning of our next studies.

As Dr. Morgenstern guessed, we have had splenic injuries. There have been 10 (2.6%) in this series and most of these occurred during the first 2 years. Increased experience has helped to diminish this complication.