***THESE* PEOPLE NEED WEIGHT LOSS SURGERY?**
They aren't obese // They don't have high BMIs // They look healthy // But they don't have freedom // From insulin // From the possibility of dialysis // From the risk of organ failure.

Bypassing Diabetes

BY CHARLES SLACK // PHOTOGRAPHS BY ALESSANDRA PETLIN

Gastric bypass surgery can be a lifesaver. For the morbidly obese who can't keep weight off with diet or exercise, having the stomach surgically downsized typically results in a dramatic, permanent drop in pounds and a 50% reduction in mortality compared with people of similar girth who do not have the surgery. Laparoscopic techniques, meanwhile, have decreased discomfort and recovery times, helping to fuel a nearly 1,500% rise in the number of procedures, from fewer than 14,000 in 1998 to 200,000 in 2006.

Philip Schauer, a surgeon at the Cleveland Clinic, performs hundreds of these procedures, also known as bariatric surgery, each year. But the case of one 37-year-old patient in September 2007 was different from most. Though the woman was about 30 pounds overweight, with a body mass index (BMI) of 33, she wasn't clinically obese and would not normally have been a candidate for weight-loss surgery. But for nearly a decade, she'd had another problem—type 2 diabetes, an increasingly prevalent condition in which the body responds improperly to insulin, a hormone that regulates blood sugar. She hadn't been able to control the disease with medication, so now she was going under the knife. The results were striking. Within days, the woman's blood sugar levels had stabilized, and after a

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few weeks, she no longer needed medication for her diabetes.

For nearly two decades, physicians have known that gastric bypass surgery has a profound effect on type 2 diabetes. As in this case, symptoms virtually disappear, and they don't usually return. It's apparently not just the weight loss, either. Schauer and others think there is something more complex going on, some kind of surgically induced metabolic change that spurs the production of insulin and makes "cure" seem a reasonable assessment of what proponents have begun to refer to as diabetes surgery.

But the success of this procedure raises important questions, and none may be more crucial than who should undergo it. While surgeons in the United States and Europe continue to debate just where on the BMI scale to draw the line, Brazilian doctors have taken a stunning step. In a recent study, surgeons in São Paulo performed gastric bypass procedures on 39 patients (16 women and 23 men) who had an average BMI of 30.1—someone who is 5 ft. 6 in. and weighs about 187 pounds. What's more, the thinnest patient had a BMI of 23.4, which translates into a six-footer, for example, who weighs less than 175 pounds. In their report, the Brazilian doctors noted that all of these patients had had chronic diabetes for at least three years. And in almost 90% of the cases, the surgery stabilized blood sugar levels, essentially stopping diabetes in its tracks.

The Brazilian study, among other developments, prompted 150 surgeons, endocrinologists, weight loss experts and other medical professionals to convene in Rome last year for the first Diabetes Surgery Summit. In a follow-up report published in 2008, Schauer and three other conference leaders were optimistic about what surgery could accomplish, writing that "whereas diabetes is traditionally viewed as a chronic, relentless disease in which delay of end-organ complications is the major treatment goal, GI [gastrointestinal bypass surgery offers a novel endpoint: the concept of complete disease remission." Yet the physicians were also decidedly wary about rushing the procedure into common use without clinical trials that might explain its mysterious effect.

The World Health Organization estimates that more than 230 million people suffer from type 2 diabetes, up from 30 million in 1985. That number could grow to 350 million by 2028, according to WHO, and the current 3.5 million annual deaths from type 2 diabetes rival the global yearly toll for AIDS. Though there may be other factors contributing to the surge, much of the blame must be shared with the rise in obesity, diets full of processed foods laden with sugar and fat, and increasingly sedentary lifestyles.

All those millions of diabetics are plagued by an insufficient supply of insulin, which carries glucose, the body's primary fuel, from the blood to individual cells. Without enough insulin, produced in the pancreas by beta cells, the concentration of glucose in the blood rises, potentially leading to heart disease, blindness, nerve and kidney damage, and limb loss from vascular disease. Type 1 diabetes, which usually strikes during childhood, involves a total failure of the pancreas to make insulin, leaving patients reliant on daily doses of the hormone. In people with type 2 diabetes, however, which accounts for more than 90% of cases, the pancreas still produces at least some insulin.

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When type 2 diabetes is mild or in its early stages, an improved diet or additional exercise may be enough to control symptoms. For more serious cases, there's medication. Glucotrol and Diabeta stimulate the pancreas to produce insulin, whereas Glucophage lowers blood sugar levels by decreasing the liver's production of glucose. Other drugs aim to improve insulin's efficiency in delivering glucose to muscles or prevent the intestines from breaking down starches into glucose.

For many patients, though, neither drugs nor lifestyle changes are enough to control the disease, and physicians have long considered type 2 diabetes incurable. Now the notion of diabetes surgery could change that conventional wisdom.

In the most prevalent form of laparoscopic gastric bypass, known as Roux-en-Y, a surgeon uses a flexible, lightweight camera and small, flexible tools to close off most of the stomach, leaving a small pouch able to contain only about two ounces of food. The surgeon then snips the small bowel, called the jejunum, and pulls up the lower portion to connect it to the newly fashioned pouch. The dangling upper portion is then sewn further down on the lower portion to form a Y shape, ensuring a pathway for digestive juices still produced by the stomach to reach food traveling from the pouch. A patient who undergoes the surgery will afterward be interested only in eating small amounts of food.

On one level, it may not seem surprising that such a procedure would have an impact on type 2 diabetes. Obesity is a primary contributor to the disease, and losing weight might logically lead to improved health. Indeed, studies have shown that shedding even a few pounds can have a marked effect. But surprisingly, improvement after surgery comes well before patients have had a chance to slim down. Blood sugar levels tend to get better within a week, says Lee Kaplan, director of the Weight Center at the Massachusetts General Hospital and a leader of the Diabetes Surgery Summit, while weight loss comes much more slowly, over weeks and months, as the smaller stomach changes the patient's eating habits.

Is it possible, then, that the immediate change in diet, rather than losing weight, accounts for the sudden normalization of insulin levels after bypass surgery? In the hospital, patients have to eat what they're given, from a carefully controlled menu, and that might affect their insulin production. Yet as Kaplan and others note, even when bypass patients go home and begin eating regular food again (though in much smaller portions), their insulin levels tend to remain normal. "Something special is going on," Kaplan says.

That idea is what most excites Kaplan, Schauer and others. Though there's much they still don't understand, these advocates of diabetes surgery think the procedure produces complex, wide-ranging effects. Often mistakenly thought to be a mechanical fix, gastric bypass does not in fact prevent patients from eating large amounts (though they may be more likely to get sick from overeating than are people who haven't had the procedure). The strange thing is that after surgery, cravings for fried chicken, hot fudge sundaes and other "pack on the pounds" treats are largely gone. "In many cases, instead of wanting fatty foods, suddenly patients find themselves preferring a salad," says Kaplan, who thinks the change indicates a physiological, hormonal change in the way the body's organs and regulatory systems communicate with one another. Something about gastric bypass surgery apparently instructs the body to change its desires.

"It's an oversimplification to say they want to eat but can't," Schauer says. "They're eating less because they want to eat less. We're just beginning to explore this, to try to understand how the body regulates such things. It involves the gut, the brain and multiple neurochemical pathways. Somehow we trick the body into thinking less food is satisfactory."

Part of the answer may involve a hormone, GLP-1, that is secreted by what are known as L cells in the lining of the intestines. GLP-1

Counting Down to Surgery //

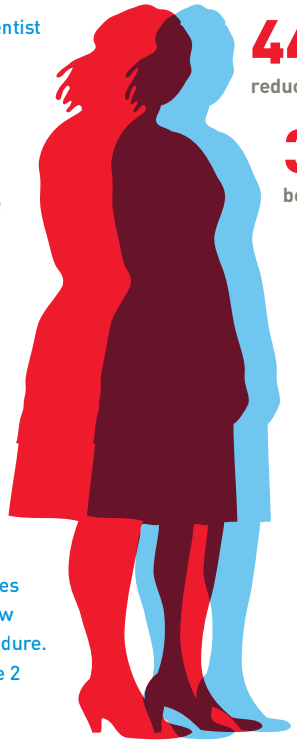
For a diabetic to qualify for gastric bypass, just how high does her body mass index need to be?

The body mass index, developed by the Belgian scientist Lambert Adolphe Jacques Quetelet in the 1830s, is still the gold-standard weight index for medical organizations around the world. One of its chief advantages is simplicity: Anyone with a handheld calculator—or access to any number of online calculators—can learn her BMI within seconds. The formula is weight in pounds, divided by height in inches squared, with the result multiplied by 703.

As a measure of obesity, BMI is not without flaws. For example, the index does not consider what portion a person's weight is muscle or fat. Because muscle weighs more, many athletes have BMIs that would classify them as overweight. Also, BMIs don't consider waist size or body shape, which clinicians increasingly deem important health indicators.

Still, the BMI remains the determinant of candidates for gastric bypass surgery. As benefits of the surgery in helping patients with type 2 diabetes have become clear, surgeons are rethinking just how high a patient's BMI must be to qualify for the procedure.

Consider Sarah, who is 5 ft. 3 in. tall and has type 2 diabetes, and her options at various BMIs...



44 Sarah weighs 250 pounds and is seriously obese, a natural candidate for gastric bypass surgery. The twin goals of reducing weight and helping her diabetes go hand in hand.

35 Sarah weighs 195 pounds, still well into the obese range. Yet this is the lowest weight at which the surgery might be considered necessary both for weight loss and diabetes.

30 Sarah weighs 170 pounds and still needs to lose at least 30 pounds to enter the range considered healthy by the National Institutes of Health. But she is far too slender to be considered for gastric bypass for weight alone. Still, advocates of diabetes surgery think her chronic diabetes could be helped by the procedure.

23 At 130 pounds, Sarah is well within normal range; surgery to lose weight would be unthinkable. Yet Brazilian surgeons operated on such a patient, with a BMI of 23.4 and type 2 diabetes. The patient, like the 38 others in the study, saw dramatic improvement in what had been a chronic condition.

? As surgical techniques become less invasive and the diabetes benefits even clearer, some clinicians suggest that preventive surgery may one day be viable for those of any BMI who are at especially high risk for the disease.

(glucagon-like peptide-1) degrades within a few minutes of being secreted, but during that short time it performs several vital functions related to insulin and blood sugar. For one, it instructs the pancreas to increase insulin production while decreasing the secretion of glucagon, a pancreatic hormone that stimulates the creation of glucose. GLP-1 also helps increase the mass of pancreatic beta cells—the cells that create insulin.

For reasons not yet known, gastric bypass surgery spurs production of GLP-1. As researchers learn more, Kaplan says, surgeons may be able to devise less invasive procedures for slender diabetic patients that would trigger GLP-1 production without radically reducing the size of the stomach. Or there might be a pill to take, eliminating the need for surgery altogether. A new class of medication, DPP-4 inhibitors, works by extending the length of time that GLP-1 operates before being degraded. So eventually, the effects of diabetes surgery could be achieved in other ways.

For now, though, the debate about using gastric bypass to treat diabetes centers on who, if anyone, should undergo it. "There are neither guidelines for these practices nor sufficient plans for clinical trials to evaluate the risks and benefits of such 'diabetes surgery,'" said the Surgery Summit's report, which called for controlled clinical studies to determine whether it makes sense to perform the procedure on diabetes patients with BMIs below 35. (A 5 ft. 11 in. man weighing 250 pounds, or a 5 ft. 6 in. woman at 205 pounds, each has a BMI of 35.)

That doctors are already doing this surgery for diabetes, in advance of most research, is largely the result of how routine and relatively low-risk gastric bypass has become as a treatment for obesity. George Blackburn, a surgeon and nutrition expert at Beth Israel Deaconess Medical Center in Boston, calls bariatric surgery today "amongst the safest abdominal operations by minimally invasive surgery." (According to a study released in early 2008, deaths in the hospital following gastric bypass surgery declined from 0.23% in 2004 to 0.07% in 2007—or, fewer than one death per 1,000 patients. In comparison, the 1.9% mortality rate for coronary triple bypass surgery in 2005 was 25 times greater.) Yet even if the risk of death is low, gastric bypass is a serious procedure, and many diabetes specialists worry about a possible rush to surgery by patients who don't fully appreciate its risks and implications.

"Bariatric surgery is a major, life-altering intervention," says John B. Buse, a University of North Carolina endocrinologist who treats about a thousand patients suffering from type 2 diabetes. Buse also serves as president of the American Diabetes

CHRIS MALEC

Association, which, in a January 2007 position statement, "Nutrition Recommendations and Intervention for Diabetes," devoted just two paragraphs to the subject of surgery. The paper noted the "marked improvement" that patients may experience, but added that surgery should be considered only for patients with a BMI of 35 or higher. "This surgery is a big, big deal, and people have to be willing to die for it," Buse says. "The people I offer surgery to often aren't that interested in it."

Yet surgery advocates note that continuing to live with diabetes carries its own serious risk of complications, including death. "Even with modern medications, we have not altered the natural history of diabetes," Schauer says. "People still die prematurely, and they suffer from retinopathy and other problems. We really haven't reduced those complications that much. What's exciting about surgery is not only the remission, but the fact that it's durable, four or five years later."

Such results have advocates suggesting the possibility that bariatric surgery could become fairly routine for nonobese patients with type 2 diabetes. But that shouldn't happen, they say, until additional research provides a clear picture of how this procedure controls diabetes. Some of the clinical studies recommended by the Diabetes Surgery Summit report are now being planned, and if the results are positive, such surgery might even be considered as a preventive measure for people who have multiple risk factors but have not yet shown signs of the disease. Blackburn, for one, doesn't see that as a stretch. By the time type 2 diabetes can be diagnosed, he notes, insulin production has already been severely compromised, increasing the chance of complications from blindness to heart disease. Early surgery could forestall such potentially devastating consequences, he suggests. For those already suffering from type 2 diabetes, gastric surgery may be less about dropping pounds than finding relief from a condition they had come to think of as incurable. ■

DOSSIER

1. **"Laparoscopic Treatment of Type 2 Diabetes Mellitus for Patients With a Body Mass Index Less Than 35," by A. L. DePaula et al., *Surgical Endoscopy*, Aug. 18, 2007.** Brazilian surgeons describe their gastric bypass procedures on 39 patients, most of whom were not obese but all of whom had chronic type 2 diabetes. A stunning 86.9% of patients had normal blood sugar levels after surgery.
2. **"Betsy Lehman Center for Patient Safety and Medical Error Reduction Expert Panel on Weight Loss Surgery Executive Report," by George L. Blackburn et al., Betsy Lehman Center for Patient Safety and Medical Error Reduction, December 2007.** This comprehensive study examines the rising prevalence of bariatric surgery, improvements in safety, and challenges to be met.