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## **Is There a Surgical Cure for Diabetes?**

**A controversial doctor says yes; his critics say 'bull----.'**

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Diabetes is one of the oldest known diseases of the western world--diagnosed by Hippocrates, and named 300 years before the fall of Rome--but its cause was unknown for centuries until a surgeon stumbled upon it in 1889 with the help of a few unlucky dogs. Oskar Minkowski was curious about the pancreas; neither he nor anyone else knew what its function was. So he removed the organ from several dogs, who promptly after developed diabetes and died. By accident, Minkowski had discovered one of the functions of the organ: regulating insulin levels.

In the decades since, doctors have learned a great deal more about diabetes and its most common form, type 2 diabetes; what it is (the body not producing enough insulin or the cells ignoring the insulin produced) and how to control it (with drugs, up to a point). But there's still a lot they don't understand. So it's a little startling to listen to **Francesco Rubino, a surgeon at Weill Cornell Medical College**, talk about the disease. He thinks he's found one of the root causes and, he says, it isn't necessarily in the pancreas. He also thinks he's found a cure, which happens to be his specialty: gastric bypass surgery. Is he crazy? An opportunist perhaps, seeking to boost his business? Or is he Minkowski's heir, a surgeon whose unexpected findings could forever change the way we think about this common illness?

The exact cause of type 2 diabetes is still unknown. Many doctors subscribe to the "lipocentric hypothesis," which pins the blame on extra pounds. Even if the body makes lots of insulin to process or store blood sugars, the theory goes, the extra weight overwhelms it. "The fat in your belly is very insulin-resistant," says George Fielding, a bariatric surgeon at New York University. "So as that fat increases, the insulin in the body just isn't strong enough to work against it, and the person gets diabetes." That explanation, however, doesn't work for everyone, because it fails to account for the 20 percent of type 2 diabetes patients who aren't overweight. "They're very active, and they eat properly," says Paul Robertson, a prominent diabetes researcher in Seattle. As for what could be causing the illness in those cases, says Robertson, "we're left scratching our heads."

**Rubino** started pondering this problem in 1999, when he was a young surgeon doing gastric bypass for patients who needed it solely for the purpose of weight loss. He was aware of the operation's secondary effects: "It had the most powerful anti-diabetic effect

I'd ever seen," he says. But something didn't make sense. His diabetic patients were being cured of diabetes in the first few weeks after their gastric-bypass operations, before the surgery could lead to substantial weight loss. They were still carrying around their insulin-resistant fat even as their insulin began to work.

**Rubino** recalled a series of stomach and intestine operations from the 1940s that had cured rats of ulcers and gastric cancers, and, as a side benefit, of diabetes, too. He also knew that the gastrointestinal tract produces, among other things, at least two hormones called "incretins" involved in diabetes. So **Rubino** wondered whether some part of the digestive system might be malfunctioning and causing diabetes, and whether he could cure the disease simply by removing that part. First, he tried out his theory in hundreds of rats. In one experiment, he rerouted the upper part of the small intestine of animals that were diabetic (but not obese) so that food did not enter that part of the gut. Sure enough, those rats were cured of diabetes. Next, he compared gastric bypass in obese rats with a "draconian diet" to see whether the operation's effect on diabetes was solely linked to the animals' weight loss. "The operation was more powerful than the diet," he says. Finally, he did a similar comparison between surgery and insulin-boosting meds. Again, the operation won out. He published his results in 2004, and shortly thereafter, doctors around the world took the idea and ran with it. They started a number of human clinical trials in thin patients; trials that are ongoing today. **Rubino**, for his part, kept operating on his overweight patients with traditional bypass surgery, and in the process, curing them of diabetes.

**Rubino's** theory and operation are controversial, to put it mildly. "When I first started this research [nine years ago]," he says, "a colleague told me someone was going to want to kill me." Most doctors remain convinced that the cause of diabetes is not in the gut but in the fat that surrounds it. "Getting rid of that excess fat" is and has always been the key to treating diabetes, says Roger Unger, a leading diabetes expert at UT Southwestern Medical Center.

Fielding also is part of the opposition, arguing that **Rubino's** idea boils down to one impolite word used to refer to the excrement of steers. "When people with gastric bypass regain their weight, and some of them do, their diabetes comes right back," he says. "If **Rubino** were right, that wouldn't happen." There's a reason the disease recedes in gastric-bypass patients so quickly after surgery, he adds: The patients have to switch to a liquid diet for two weeks before the operation. That regimen alone causes them to shed about 20 pounds, he says, which is enough of a change that the body soon goes back to properly processing its insulin.

**Rubino** says he can answer both those objections. First, he says, diabetes recurrence after gastric bypass is quite rare. (Actual data on recurrence are difficult to come by. One study found that gastric bypass surgery resolves 80 percent of diabetes cases.) Second, liquid diets don't cause significant weight loss in rats, and besides, his human patients don't go on them prior to surgery. Still, Fielding has yet another complaint. He points to a recent study in the Journal of the American Medical Association showing that adjustable gastric banding, a different type of weight-loss operation--one he happens to perform--treats

diabetes just as well as bypass surgery does, even though it doesn't remove or bypass any part of the gut.

Undaunted, **Rubino** continues to operate on obese patients, and he's even exploring the idea of treating those 20 percent of patients with diabetes who aren't overweight (and thus would otherwise never need gastric bypass surgery). Roughly a hundred have already enrolled in small clinical trials run by other surgeons in Brazil, Mexico, India and elsewhere, and **Rubino** sometimes acts as a consultant. Those trials are yielding "encouraging results," he says. He hopes to soon start two small U.S. trials of his own in patients who either are "moderately obese" or "might be overweight but aren't obese." They're just trials, he hastens to add, and insists, "this is still not ready for prime time." But if **Rubino's** theories turn out to be right, he may need to get ready for prime time himself.