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Hoping to Avoid the Knife
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In November, the prestigious Cleveland Clinic hailed a "scar-less" weight-loss surgery as one of the top 10 medical innovations expected this year.

Developed by a company aptly called Satiety Inc., the procedure shrinks the stomach by using a stapler inserted through the mouth, rather than by cutting open a person's belly.

But when the results of a clinical trial came in, the procedure resulted in the shedding of far fewer pounds for patients than the company had hoped. Venture capitalists who had invested $86 million in Satiety over a decade shut the company down.

The failure of the procedure, called transoral gastroplasty, pushes back the availability of any incision-less procedure to millions of obese Americans for several years, a disappointment to companies trying to find the next best thing to major surgery. The setback also further restricts options for those who are overweight, because it is occurring on top of federal rejections of a new generation of diet pills.

These defeats are not for lack of effort. Entrepreneurs are developing all manner of odd and ingenious ideas aimed at replacing bariatric surgery. These include a pill taken before meals that would swell up in the stomach, pacemakers that deliver jolts of electricity to the stomach wall, and tubes that line the inside of the small intestine, letting food slide through without being absorbed.

Device makers hope that by going in through the mouth using an endoscope, they can eliminate the infection risk from incisions, and possibly the need for general anesthesia, thereby lowering the current $12,000 to $30,000 cost for bariatric surgery. If weight loss could be made less forbidding and less expensive, many more people might undergo such procedures, including people who are less than severely obese. Even though more than 20 million

Americans are heavy enough to qualify for bariatric surgery, only about 200,000 have the operation each year.

"There's definitely a need for something for the other 99 percent," said Hugh Narciso, chief executive of Baronova, whose experimental device slows the movement of food out of the stomach.

But bringing a device to market can be difficult. The digestive tract, with all its acids and movements, is an inhospitable place for a medical device. Bariatric surgery, meanwhile, has become safer because it is now done through tiny incisions. Just recently, the Food and Drug Administration lowered the weight requirement for Allergan's Lap-Band, making more than 26 million additional people eligible to have it implanted.

Other companies besides Satiety have had problems. Leptos Biomedical went out of business last year. Industry executives say that ReShape Medical has cut many workers; company executives and directors did not return calls. Gastric pacemakers from EnteroMedics and Transneuronix failed in clinical trials. The Transneuronix failure occurred only months after the company was acquired by the device giant Medtronic for $269 million.

"Right now, it doesn't look like anything is on the horizon that will replace surgery," said Dr. Ninh Nguyen, chief of gastrointestinal surgery at the University of California, Irvine.

There are two main types of surgery. The gastric bypass, which restricts the stomach and bypasses part of the small intestine, can cause people to lose as much as 80 percent of their excess weight. In many cases it can also quickly resolve diabetes, a frequent companion disease to obesity.

Gastric banding, like the Lap-Band, involves putting an inflatable ring around the stomach to restrict food intake. It is less complicated than bypass, with a fatality rate during surgery of about one in 1,000, or about one-third that of bypass. But banding does not result in weight loss as significant as that of bypass, and carries potential complications after surgery.

A third approach, sleeve gastrectomy, is starting to gain popularity. The procedure involves stapling the stomach into a narrow tube so that less food can be ingested. The excess part of the stomach is then cut out.

A potential improvement on sleeve gastrectomy is gastric imbrication or plication. The stomach is narrowed by folding and sewing it in place, much like the pleating used to narrow a pair of pants. Those tucks eliminate the need to remove the excess stomach.

Still, entrepreneurs hope that devices through the mouth will be safer and cheaper.

Perhaps the simplest idea is a balloon inserted through the mouth and inflated in the stomach, creating a sense of fullness. Allergan and some other companies sell balloons in Europe, where rules for device approval are easier.

But balloons lose their effectiveness over time, because the stomach expands to accommodate them. And there are risks. A balloon used in the 1980s in the United States caused complications, including potentially fatal blockages, when it accidentally deflated and traveled into the small intestine.

Spatz FGIA of Jericho, N.Y., is developing an adjustable balloon that can be inflated further after the stomach has expanded, providing another jolt of weight loss. It also has an anchor to keep the balloon in the stomach should it deflate.

Gelesis, a start-up in Boston, is testing a capsule that would be swallowed before meals. The capsule contains particles that swell to hundreds of times their size in the stomach by absorbing water, then eventually shrink and are excreted.

In a demonstration, a spoonful of the particles was put into a glass of water. A few minutes later, the glass was filled with a heavy slush.

One big challenge for this idea is that someone anticipating a delicious feast might simply skip the pill.

HourGlass Technologies of Redwood City, Calif. is trying to mimic banding from within. Instead of clamping a ring around the outside of the stomach, it inserts a device through the mouth that sucks in the stomach and clamps it in place.

GI Dynamics of Lexington, Mass., has approval in Europe for the EndoBarrier, which mimics part of bypass surgery. It is a tube, inserted through the mouth, that lines the inside of the small intestine. Food going through the intestine cannot pass through the intestinal wall.

One drawback for devices embedded in the digestive tract is that they should be removed after six months or a year to prevent health problems from developing. Some surgeons question the value of these devices compared with permanent surgery.

"You remove it and there's nothing to prevent the person from going back to the way they were," said Dr. Gregg Kai Nishi, a weight loss surgeon in Beverly Hills, Calif.

Some manufacturers, however, argue that the devices can spur people to change their lifestyles. "It's like nicotine patches," said James McKinley, chief executive of Endosphere, an obesity device developer.

Not all the new devices circumvent incisions. Vibrynt, of Redwood City, Calif., is developing a device shaped like the stomach that is implanted next to the real stomach and compresses it.

Gastric pacemakers are implanted under the skin in the abdomen, with wires leading to the stomach wall. The electric pulses are believed to somehow dampen appetite. IntraPace, of Mountain View, Calif., recently won approval of its pacemaker in Europe.

Even the devices approved in Europe are several years from the market in the United States. Many of the companies have not yet reached agreement with the F.D.A. on the clinical trials needed to win approval.

"There is no clear path to an approval in the U.S.," said Mr. Narciso of Baronova. "The investment community is getting very nervous about obesity right now."

A spokeswoman for the F.D.A. said the agency wanted devices to result in weight loss that was 15 to 25 percentage points greater than a control group's weight loss. In addition, the F.D.A. wants to measure this weight loss six months after the device is taken out, because of the potential for regaining weight.

Some executives say they have been told they need a difference of 25 percentage points, which could be tough. If the control group loses 15 percent of its excess weight, the treated group would need to lose 40 percent. That is more than the median weight loss of 32 percent median achieved by the Lap-Band when it was approved, in a trial without a control group.

Some device makers say they should not be held to the same standards as procedures that involve incisions. "Because this is a less invasive and less risky approach, something with a

lower weight loss may be very helpful and accepted by patients," said Darin Buxbaum, chief executive of HourGlass.

Satiety's procedure resulted in nearly 40 percent loss of excess weight in an early trial without a control group. But in the main trial, it was compared with the results from patients who underwent a simulated procedure, in which a device was briefly inserted down the throat but no stapling was done.

Executives would not provide specific results but the weight loss was far less than in the earlier studies. Satiety executives speculated that patients, not knowing if they had really had the procedure, did not change their diets accordingly.

The failure has "thrown some cold water on the field," said Dr. Richard Rothstein, chief of gastroenterology at Dartmouth Medical School. He is helping to organize a meeting later this year in which industry executives, doctors and the F.D.A. will discuss standards for trial design and approval of obesity devices.

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