The LATEST WORD on WEIGHT LOSS

Scientists are scrambling to develop new treatments for obesity. Here are nine that show promise.

By Beth Howard

Photographs by Ann Cutting
Gastric balloons used to be inserted via a procedure that required sedation. A new system can be swallowed in a capsule.
More than one-third of American adults are now obese, defined as having a body mass index of 30 or higher. Excess weight can be accompanied by serious health risks, including diabetes, heart disease, cancer, and joint problems. To cope with this public health crisis, scientists are racing to develop new treatments to help patients achieve permanent weight loss. Some are newly available; more are on the way. Here are nine up-and-coming medical approaches to watch for.

**AN ABDOMINAL PACEMAKER**
The Maestro Rechargeable System is an implantable device that works by emitting electrical pulses that block hunger signals from the stomach to the brain. The result: Patients feel fuller longer and eat less. In a recent study, device users lost an average of 10% of their body weight over 9 months—about 3 percentage points more than people in the control group who received a sham treatment.

The device is surgically implanted near the connection between the esophagus and the stomach. “Some patients report feeling mild heartburn when the device is on, but the settings can be adjusted to minimize any discomfort,” says Dan Gladney, CEO of EnteroMedics, the device’s maker. There are also some significant side effects associated with the device’s use, including pain in the abdomen or elsewhere that might require hospitalization.

**AVAILABILITY:** Now.

**A WAY TO TAME A HUNGER GENE**
People with certain rare genetic obesity disorders may feel ravenous all the time. In these disorders, the brain processes that regulate appetite stop working, leading to weight gain that can be life-threatening. Now there’s hope, thanks to an experimental drug called setmelanotide, which controls a key brain pathway that influences appetite and energy expenditure. “We now know exactly what causes this form of genetic obesity, and the drug is designed to solve that problem,” says Keith Gottesdiener, CEO of Rhythm, the drug’s manufacturer.

**AVAILABILITY:** Early study results were so impressive that the FDA granted the drug breakthrough therapy designation, meaning it’s being fast-tracked through the approval process.
REPORT

BLAME-FREE THERAPY

People with obesity often face social disapproval, which can contribute to a negative self-image that hinders weight loss efforts. A new approach called acceptance-based behavioral treatment has been helping people lose more weight and keep it off longer than people who receive standard cognitive-behavioral therapy.

Both types of therapy focus on psychological counseling to encourage weight loss. But unlike most therapy, ABT emphasizes acceptance of the facts that weight loss is hard; that hunger, cravings, and feelings of deprivation are normal for people who are struggling with their weight; and that shedding excess pounds requires sacrifice, says Evan M. Forman, a professor of psychology and director of the Center for Weight, Eating, and Lifestyle Science at Drexel University, where he leads the ABT program.

Recent research showed that patients receiving ABT lost 13% of their initial weight after 1 year, compared with 9.8% among participants who received standard treatment.

AVAILABILITY: Now, in limited markets. Drexel is developing a training program for clinicians, so the therapy should be more widely available nationwide within the next 2 years.

A BALLOON YOU SWALLOW

Implanting balloons in the stomach to create a sense of fullness is a method that's been around since the 1980s. But previously, the balloons were filled with saline and were linked to minor side effects, like cramping and nausea, and much more serious side effects, including death.

The Obalon Balloon System, recently approved only for adults with a BMI of 30 to 40, uses a different method: Patients swallow one capsule, which contains a single small balloon, in a doctor's office once a month for up to 3 months. After the capsule is in the stomach, a doctor uses a small catheter to inflate the balloon with gas. Each balloon floats at the top of the stomach and stays in place for 6 months. During that time, patients receive professional diet and exercise support to help them make the lifestyle changes that can lead to lasting weight loss.

After 6 months, the balloons must be removed. In trials, patients lost twice as much weight with the Obalon system as with diet and exercise alone. Potentially serious side effects include bowel obstruction if a balloon bursts.

AVAILABILITY: In doctors' offices now.
New obesity research aims to help people lose weight—and keep it off permanently.
AN ANTI OBE SITY HORMONE

Scientists have discovered that oxytocin—the “love hormone” released by the pituitary gland when people hug, kiss, or otherwise connect socially—may also be used to promote weight loss.

In one small clinical trial of 25 men, a single dose of a synthetic version of oxytocin, delivered through a nasal spray, reduced overall calorie intake, especially of fatty foods. “We think oxytocin may work in part by improving one’s ability to resist the impulse to eat,” says study researcher Elizabeth A. Lawson, an associate professor of medicine at Harvard Medical School and a neuroendocrinologist at Massachusetts General Hospital. “It may also make food seem less rewarding.”

In addition to reducing calorie intake, oxytocin improved subjects’ insulin sensitivity and ability to clear sugar from the bloodstream. The spray showed no strong side effects, but further research will test its effects on women and make sure it’s safe for long-term use.

AVAILABILITY: The trial will take 4 years, and an application for FDA approval will likely follow if results are positive.

A DRUG TO HARNES S IMMUNE CELLS

Provocative research from the University of California, San Francisco, and the University of Washington Medical Center suggests that obesity might be controlled through an unexpected pathway: the brain’s immune cells, called microglia. When people eat high-fat diets, these cells, which usually fight infection, trigger inflammation in the brain.

In a study of mice fed a fat-rich diet, those given a drug that reduces microglia gained 20% less weight than untreated mice did. “This could lead to an expansion of drugs using an entirely new pathway to target obesity,” says Suneil Koliwad, an assistant professor of medicine at the UCSF Diabetes Center.

AVAILABILITY: Human studies are the next step. Even if the results are positive, it will be at least several years before this drug is available.

A GUT BUG-OBESITY CONNECTION

The microbiome—a population of bacteria that lives in the body—has been linked to many diseases and
A NO-CAL MEAL IN A PILL

The Gene Expression Laboratory of the Salk Institute in La Jolla, CA, has developed a fat-burning compound called fexaramine that tricks the body into reacting as if it has consumed food and needs to burn fuel. "It mimics many effects of eating a meal but doesn't provide any calories," says Ronald M. Evans, the lab's director. When mice were given fexaramine daily for 5 weeks, they not only dropped weight but also lost fat and had lower blood sugar and cholesterol levels than untreated rodents did. Since fexaramine is designed to act only in the intestines, researchers hope it will have few side effects.

**AVAILABILITY:** Evans predicts that fexaramine will be FDA approved in less than 5 years.

AN INJECTABLE WORKOUT

Researchers at St. Louis University have developed a drug that appears to mimic the effects of exercise. In an animal trial, the muscles of obese mice injected with the compound showed signs of greater conditioning even though they were no more active than untreated mice. "Treatment led to weight loss and insulin sensitization," says lead researcher Tom Burris. While limited to animal studies so far, the research suggests that the drug could one day be used in humans to help control both obesity and diabetes.

**AVAILABILITY:** "We are probably 2 to 3 years from clinical trials and 5 to 6 years from the market, if things proceed well," Burris says. 

conditions, including obesity. Now Cleveland Clinic researchers have identified one biological connection between body weight and the microbiome: a chemical called trimethylamine N-oxide (TMAO) that’s produced after gut bacteria digest nutrients in red meat and other animal products.

When researchers gave mice a chemical that blocked the production of TMAO, the rodents didn’t gain weight even when they ate a high-fat, high-calorie diet. Research is under way to develop a drug that would block TMAO, helping to change the microbiome and promote weight loss.

**AVAILABILITY:** Researcher Mark Brown says that a TMAO-blocking drug could be available in 5 to 7 years.