



ONCE CONSIDERED A FAILURE OF WILLPOWER, OBESITY IS NOW RECOGNIZED AS A CHRONIC DISEASE WITH COMPLEX CAUSES. NEW RESEARCH AND CLINICAL ADVANCES REVEAL SOME SURPRISING STRATEGIES FOR LOSING WEIGHT AND ENHANCING HEALTH.

TREATING OBESITY NOW

BY CAROL KRUCOFF

On the beaches, flesh bulges over bathing suits.

In the malls, widening waistlines have spawned a booming market for plus-size clothes. In the schools, kids are fatter and less fit than previous generations.

We are a nation gone to potbelly.

Obesity is Public Enemy Number Two—right after smoking, say public health officials, who blame this serious and growing health problem for 300,000 deaths in the United States each year. Linked to a host of diseases

including heart disease, diabetes, hypertension, sleep apnea, stroke, gall bladder disease, arthritis, and certain cancers, obesity and overweight consume a huge portion of the nation's health care resources: By 2000, the economic cost of obesity in the United States had climbed to about \$117 billion. Meanwhile, the number of too-heavy Americans skyrockets. Nearly two in three adults in the U.S. are now over-



health, from behavioral support to pharmaceuticals to surgery. Many of the new treatment options are admittedly radical—sometimes even counterintuitive. But with the supersizing of America, experts say, it's time for solutions that work in real life.

REALISTIC EXPECTATIONS

For starters, throw the old notion of an "ideal body weight" out the window, suggests Duke Diet and Fitness Center Director Howard J. Eisenson, MD. Indeed, one of the most significant changes in obesity treatment is a new focus on realistic, sustainable weight loss. All too often, Eisenson says, the struggle to achieve a so-called "ideal weight" proves unattainable and demoralizing, with many of those who successfully shed pounds re-

gaining all they have lost—and more. "For the great majority of people, overweight is a chronic problem, caused by the interaction of our genes and an environment providing constant pressure to eat more and be less active," he says. "The great challenge is not only to lose some of our excess weight, but to keep it off. The modern goal for obesity treatment is to achieve and maintain a healthier weight."

Exactly what constitutes a "healthy weight" depends on the individual. But, as a rule of thumb, "Losing 5 to 15 percent of one's weight, and maintaining that loss, is considered a good medical result," Eisenson says. "Solid scientific evidence shows that losing as little as 5 to 10 percent of excess weight can produce significant health benefits, including lowered

"A lot of times when people get here, it's all they can do to walk across the street to the hotel—some even drive. But by the time they leave, they're walking back up the hill without difficulty. I've had people tell me that, for the first time in years, they can tie their own shoes and get in and out of a car."

—Howard J. Eisenson, MD

weight or obese, with North Carolina weighing in among the heaviest: More than 21 percent of the state's adults have a body mass index (BMI) of 30 or more, compared with 13 percent in 1991.* In fact, some experts say, if current trends continue, everyone in America will be obese in two centuries.

Yet, despite rising concern over widening waistlines, misconceptions about the problem abound. "The central issue is more calories in than out, but it's not as simple as pushing away from the table," notes Danny O. Jacobs, MD, the new chair of Duke's Department of Surgery and an expert on pioneering weight-loss procedures. "In the last 10 years, there's been a dramatic change in our thinking about obesity. Although

some people still think of it as a personal flaw, there's a new recognition of the strong genetic and environmental components involved and an emerging understanding of biochemical factors that influence hunger and satiety."

With obesity now recognized as a chronic disease with complex causes, he says, "The state-of-the-art treatment today is a multidisciplinary, collaborative program that brings together nutritionists, exercise physiologists, and medical, surgical, behavioral, and psychological professionals."

These professionals have more to offer their patients than ever. While the old mantra "eat less, exercise more" is still sound advice, recent research has yielded a wealth of additional strategies to help patients lose weight and improve



THE DIABETES CONNECTION

Disorder May Start in the Womb

AMERICA'S ALARMING EPIDEMIC of girth growth isn't restricted to adults. Nearly 15 percent of American children are now seriously overweight—compared with 5 percent in 1980.

"Our kids may be subject to heart disease as early as in their 20s and 30s," says Diet and Fitness Center director Howard J. Eisenson, MD. "A staggering number of children are developing type 2 diabetes, which was previously considered an adult disease. The implications of childhood obesity are going to be significant for our society, with a profound impact on health care in terms of cost and management of the disease."

Early identification of children at risk for obesity and related diseases is critical, says pediatric endocrinologist Michael Freemark, MD: The prevalence of type 2 diabetes in the US may increase as much as 65 percent during the next 50 years if societal trends in obesity are not controlled. "Type 2 diabetes is the end stage of a long process of metabolic decompensation," says Freemark, who heads the Insulin Resistance/Obesity and Endocrine Clinics at Duke's Lenox Baker Children's Hospital. "One can find precursors for adult, long-term chronic illness, including type 2 diabetes and cardiovascular disease, in childhood."

Some evidence suggests that certain events in utero, such as exposure to a diabetic environment from a mother with gestational diabetes, can predispose children to developing glucose intolerance, he says. The progression of disease from childhood to adulthood is often silent, however, so that by the time of diagnosis, many adults with type 2 diabetes already have complications from the disease.

"We need increased vigilance to identify children at earlier ages," says Freemark. Early warning signs include:

- Rapid, inappropriate weight gain in a young child
- Mild elevations in blood pressure
- Family history of diabetes and cardiovascular disease
- Acanthosis—a dark thickening of the skin under the base of the neck and under the arms.

"In the past, we haven't had the tools to identify these problems at a young age," Freemark says. "But now we can identify children at risk and begin management early. Early evidence suggests that lifestyle intervention and pharmacotherapy may reduce the rates of development of type 2 diabetes in children and adolescents at highest risk."

*Body mass index is a person's weight in kilograms divided by height in meters squared. Overweight is defined as BMI between 25 and 29.9; obesity as BMI 30 and above.

benefits that aren't necessarily registered on the scale. Most see improvements in blood pressure and blood sugar control and many report substantial lessening of arthritis pain, reduced need for medication, and an improvement in mood. In addition, he points out, those who go from being sedentary to becoming "moderately active" enjoy vastly improved quality of life.

improvements in function, and positive, lasting differences in quality of life. It's a big accomplishment."

DEMYSTIFYING DIET

A cornerstone of the DFC's approach is an effective diet—although what constitutes an effective diet is a matter of intense debate. After years of dismissing high-protein, low-carbohydrate plans as

the long-term risks and benefits were not established. "Out of concern and curiosity, I wrote Dr. Atkins a letter saying, in essence, 'Where's your data?'" recalls Westman. Atkins responded by funding Westman to study the diet—making Duke one of the nation's first research institutes to perform clinical trials evaluating the Atkins approach.

Westman and his colleagues followed 50 overweight or obese volunteers on the diet for six months, checking body weight and other metabolic parameters. Forty-one successfully completed the program—excellent compliance compared with about a 50 percent dropout rate on

other diets. Weight loss was also excellent, with decreases ranging from 6 to 10 percent of body weight. And contrary to predictions, cholesterol levels did not worsen. "It seems counterintuitive, but lipids actually got better," Westman says.

In a follow-up study, Westman and colleagues put 60 people on a low-carb diet and another 60 on the American Heart Association's (AHA) low-fat diet for six months. The results, presented at AHA's annual scientific meeting last year, again found that adherence and weight loss were good on the low-carb diet—better than in the low-fat group—and the change in blood cholesterol was similar or better. After six months, the low-carb dieters had lost 31 pounds, compared with 20 pounds on the AHA diet. Total cholesterol fell slightly in both groups—but the low-carb dieters had an 11 percent increase in HDL ("good") cholesterol and a 49 percent drop in

triglycerides, while the low-fat dieters had no change in HDL cholesterol and a 22 percent drop in triglycerides.

"The biochemistry of low-carbohydrate diets makes sense, but concern about the effect on heart disease risk factors has prejudiced us against this approach," says Westman. However, he cautions, "We don't know if these low-carbohydrate diets are safe or effective over time—one drawback may be an increased risk of kidney stones, for example. So I am not advocating these diets, I am advocating research. Only then will we know if the low-carb diet is a viable alternative to the proven low-fat diet that the medical and scientific community has recommended for years."

THE BEST DIET NOW

For caregivers, the take-home point is that "nutrition matters," Westman says. "In general, there has

been a strong bias towards using drugs in the treatment of obesity, thinking that diets aren't effective. Food is like religion and politics—people can be very irrational about it, very hard to change. But diets can be quite powerful. Physicians need to ask their patients what they're eating and offer support in making healthy changes."

Westman is continuing to study the effects of various diets as research director for the Diet and Fitness Center. But with so many important questions still unan-

swered, he says, "Our commitment is to provide a safe, effective, scientifically proven and medically sound weight management program. For this reason, the DFC continues to advocate a low-fat, reduced-calorie dietary approach, combined with moderate exercise, stress management, and medical monitoring, as the best route to reach health and weight goals."

Within those parameters, the best bet today for overall weight management and heart health is a Mediterranean-type diet, believes William S. Yancy Jr., MD,



William S. Yancy Jr., MD



"Food is like religion and politics—people can be very irrational about it, very hard to change. But diets can be quite powerful. Physicians need to ask their patients what they're eating and offer support in making healthy changes."

—Eric Westman, MD

"A lot of times when people get here, it's all they can do to walk across the street to the hotel—and some even drive that short distance," he says. "But by the time they leave, they're walking back up the hill to the apartments without difficulty. Many who come with canes or walkers leave without needing any assistive device. Sometimes people who required supplemental oxygen become able to exercise without it. I've had people tell me that, for the first time in years, they can tie their own shoes and get in and out of a car."

While not a cure for obesity, modest improvements in fitness and body composition "are significant and underappreciated," Eisenson says. "Many obese people—and some doctors—mistakenly think a 10- or 20-pound weight loss is a failure or not worth the effort. But we need to recognize its very real value in terms of health benefits, im-

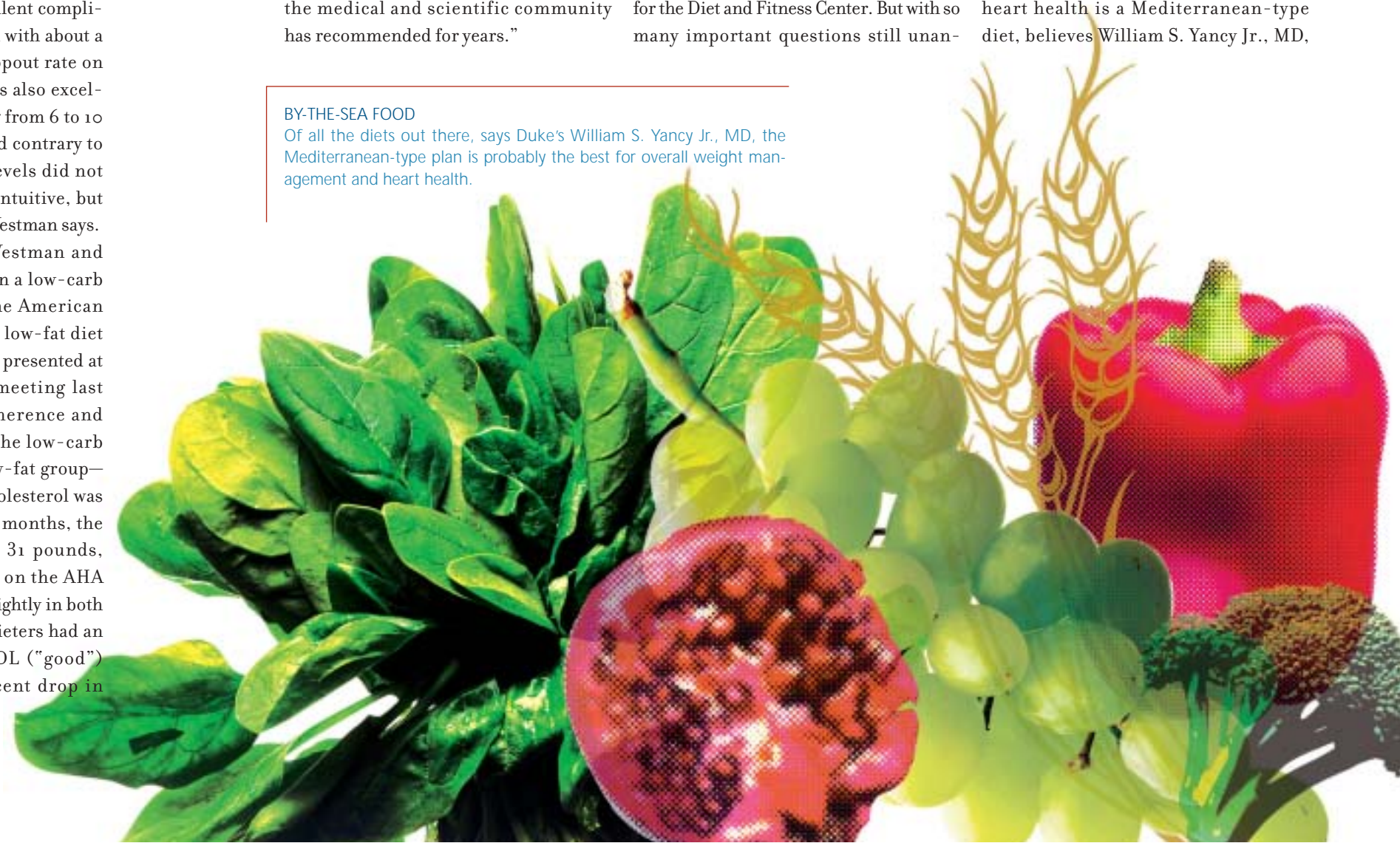
unhealthy, for example, the medical establishment received a jolt last year when research published in the *American Journal of Medicine* by associate professor of medicine Eric Westman, MD, suggested that these diets are extremely effective for weight loss.

"As a scientist, I feel that nothing should be unworthy of study," says Westman. He decided to examine the popular Atkins diet a few years ago after several patients tried it against his advice and lost about 20 pounds within two months. "I checked their cholesterol, sure it would go up, and was surprised to find it actually got better. So I decided that, even though the low-carbohydrate diet went against much of what I was taught in medical school, it was worth a closer look."

Reviewing the literature, Westman found some evidence that these diets can lead to significant metabolic changes—including weight loss—but that

BY-THE-SEA FOOD

Of all the diets out there, says Duke's William S. Yancy Jr., MD, the Mediterranean-type plan is probably the best for overall weight management and heart health.



assistant professor of medicine and lead author of a special review on diet and coronary events published in the January 2003 *Circulation*. "Current information about effective diet is incomplete, unscientific and often conflicting, but the Mediterranean approach has the strongest scientific support at present," says Yancy. "So what I recommend to my patients is an emphasis on lots of vegetables, fruits, and whole-grain foods, and cutting back on starches—especially potatoes and bleached or refined pastas, rice, or breads. Meat is okay as long as it's lean. Oils and fats should be mono- and polyunsaturated—solid, trans-fats like

margarine or shortening should be avoided. Fish should be emphasized and desserts should be kept to a minimum.

"I tell my patients to put less on their plates, and take home half at restaurants. Soda is a bad choice and should be avoided. Juices are also pretty high in calories, so should be consumed in moderation or watered down. But the best beverage choice is water—and people need to drink plenty of it."

GIVING OBESITY TREATMENT A BOOST

Of course, dieters often find it hard to abide by any restrictions on eating for long. For certain individuals, medica-

tions that manipulate the body's chemistry to decrease appetite or increase satiety can help, says psychiatrist Kishore Gadde, MD, director of obesity clinical trials at Duke.

"The central nervous system plays a powerful role in our desire to eat," he says. "Brain chemicals such as serotonin and norepinephrine are known to affect regulation of appetite and feeding behavior. Interestingly, many of the neurotransmitters and peptides that regulate appetite are the same ones that regulate mood."

Gadde discovered that weight loss was a surprising side effect of the antidepressant bupropion (trade name Wellbutrin) several years ago when he prescribed the medication for depressed obese patients, who reported feeling satisfied with smaller food portions and losing weight.

Subsequent research showed that women who took bupropion combined with a 1,600-calorie per day diet for eight weeks lost significantly more weight than women on placebo and the same diet. Sixty-seven percent taking bupropion lost more than 5 percent of their baseline body weight, while only 15 percent in the placebo group lost more than 5 percent. During the continuation phase, 14 bupropion participants completed 24 weeks on the program and achieved an average weight loss of 12.9 percent of their baseline body weight, with nearly 74 percent of the weight loss attributed to a loss of fatty tissue.

Gadde believes that bupropion is a valuable option in the management of obesity, especially as not all obese

"Medications may reduce craving for certain foods or reduce your appetite somewhat, but they won't close the refrigerator door for you."

—Kishore Gadde, MD

PROGRAM HIGHLIGHT

It Takes a COMMUNITY to Lose Weight



Jean Brown of Raleigh dropped 87 pounds after joining Project SELF Improvement and now helps others as a lay health leader with the program.

IN SWAIN COUNTY, the high school cafeteria replaced its deep-fat fryer with an oven. In Gaston County, 12 neighborhoods set up walking groups. In Alamance County, healthy lifestyle classes are offered in Spanish, and physical activity programs include salsa dancing and soccer. In Hertford County, eight churches purchased exercise equipment and sponsor grocery store tours highlighting nutritious, low-cost food choices.

These are just some of the healthy changes sweeping North Carolina as part of Project SELF Improvement, a grassroots initiative designed to lower rates of chronic disease like diabetes, heart disease, stroke, and cancer, all of which are associated with obesity. The program focuses on low-income areas, which have high rates of chronic disease: Women of lower socioeconomic status are about 50 percent more likely to be obese than those with higher incomes, for example.

Supported by \$10 million in grants from the Kate B. Reynolds Charitable Trust, SELF—an acronym for Smoking, Education, Lifestyle, Fitness—targets three core behaviors: lack of exercise, poor nutrition, and tobacco use. "Eighty percent of chronic disease is caused by those three things," says Lloyd Michener, MD, chair of Duke's Department of

Community and Family Medicine and director of the project. "And changing those behaviors can prevent or at least delay many health problems. But it's not particularly effective to just tell people what to do. Instead, our role is to serve as consultants, offering communities support as they figure out what will work to meet their residents' unique needs."

For example, something as simple as appealing music can be the spark that gets people moving. "People would tell me, 'I'd go to aerobics, but I don't like that kind of music,'" says Al Richmond, coordinator for Project SELF Improvement at Strengthening the Black Family in Raleigh. "So you put on some Gospel music, and now it's a Gospel-size class they enjoy. We know our community, and we're dedicated to finding out what it is that turns people on to healthy lifestyles."

Indeed, many SELF Improvement projects—which now number 16 across 21 counties—are faith-based programs that involve exercise and cooking classes held in churches, says project manager Maggie Sauer. "When your doctor tells you something and then your pastor tells you, too, it can have a powerful impact on behavior."

The program also relies on social support to help people adopt healthy habits, bringing in

community members to coach and inspire their neighbors. "Weight loss is far too difficult for people to go it alone," says Susan Yaggy, chief of Duke's division of community health. "It takes a lot of strength to alter fundamental behaviors like what you eat and how you exercise."

Lay health leader Jean Brown knows from experience that trying to lose weight by yourself can be tough. Concerned about heart disease in her family and increasingly uncomfortable as her weight climbed to 250, the 40-year-old accounting consultant joined the Raleigh program last year and has since dropped 87 pounds.

"Working as a lay health leader has helped me tremendously," says Brown, citing programs that taught her to recognize and eliminate "emotional eating" from fatigue or stress. "Now I want to provide inspiration and encouragement to others so our whole community will be stronger. I want them to realize that if I can lose weight and get fit, they can do it, too."

For more information, call 919-681-3023 or visit kbrselfimprove.mc.duke.edu/improve.html.

Weight-Loss Programs at Duke

People trying to lose weight—either a little or a lot—can find expert help through Duke's Center for Living, a local and national resource located on a 26-acre wooded site near Duke University's West Campus. Options include:

The Duke Health and Fitness Center

Members receive a fitness evaluation, support from a lifestyle counselor and access to a full range of fitness classes and state-of-the-art exercise equipment—plus options such as nutrition counseling, stress management, and personal training.

The Weight Management Program

The eight-week "Getting on Track" program features seven interactive classes focused on nutrition, exercise, medical, and behavioral change. Each class includes a healthy, low-fat dinner at the Innovations Café. The last session is a group meeting where the skills and knowledge are applied and discussed. After completion, participants may continue with group support sessions through the "Staying on Track" program.

For information call 919-660-6710 or visit www.dukefitness.org

Surgical options are offered through the **Duke Weight Loss Surgery Program**. For information, call 919-660-2229 or visit www.weightlossurgery.org

The Duke Diet & Fitness Center

Two, three, and four-week programs are offered at the newly renovated center near Duke's East Campus. Most popular is the four-week program, which includes medical and fitness evaluations, individual consultations with health psychology, fitness and nutrition staff, weekly check-ins with professional staff, three healthy meals and a snack each day, lectures on nutrition, fitness, psychology and medicine, small group workshops and discussions, cooking demonstrations, a restaurant experience and grocery store tour, daily fitness classes, and access to extensive fitness facilities, including a broad array of cardiovascular equipment and a large indoor lap pool.

For information, call 919-688-3079 or 1-800-235-3853 or visit www.dukedietscenter.org

patients benefit from the currently approved medications—phentermine, sibutramine, and orlistat—due to lack of efficacy, contraindications, or side effects. While seizure risk is a concern, bupropion is not addictive, treats depressive symptoms linked to obesity, and is generally tolerated well.

Recently, Duke researchers found that an antiepileptic drug, zonisamide (trade name Zonegran), may also help people lose weight. Among the various pharmacological actions of zonisamide, its effects on brain serotonin and dopamine are believed to be responsible for its potential as an anti-obesity drug, Gadde says. In a preliminary study published in the April 9 *Journal of the American Medical Association*, participants who took zonisamide and followed a low-calorie diet lost an average of 14.1 pounds over 16 weeks, compared to 2.2 pounds for people on a low-calorie diet and placebo. Moreover, extension phase data showed that participants were still losing weight when the study ended at eight months. "This is very interesting because with most other medications, as well as with other interventions, weight loss tapers off after the first four months," Gadde says. "We need to do more studies before we can safely recommend prescribing zonisamide for weight loss, but the results so far are encouraging."

No matter what the drug, medications work best in highly motivated people, he adds. "Medications may reduce craving for certain foods or reduce your appetite somewhat, but they won't close the refrigerator door for you."

SURGICAL SOLUTIONS

Indeed, for people who have dozens and dozens of pounds to lose, the diet-and-exercise route to a healthy weight can seem hopelessly long—even with the best medical and behavioral support. With celebrities such as TV weatherman Al Roker successfully undergoing weight-loss surgery, more and more extremely obese individuals are considering a different option—a procedure that reduces their stomach to the size of an egg.

"The demand is overwhelming," says professor of surgery John Grant, MD. Grant directs Duke's Weight Loss Surgery Program, which has a two-month wait just to attend its twice-weekly, free patient-education seminar. Created in the summer of 2000, the program moved to a newly renovated clinic on North Duke Street last November. The new headquarters is just down the road from Durham Regional Hospital, where Grant and Ross McMahon, MD, perform eight weight-loss surgeries a week—a number they hope to nearly double to 15 by summer.

Nationally, about 100,000 to 150,000 such procedures are performed annually, with mortality rates of 1 in 200. Duke's program has experienced two deaths in 350 patients. The procedure is painful and typically requires a four-day hospital stay. Post-procedure, patients consume a liquid or semi-liquid diet for the first three weeks, then gradually add soft and solid foods until they're eating three to eight small meals—totaling about 1,300 calories—per day. Patients may lose hair, which typically regrows, and will need to take certain supplements—including a multivitamin with iron—every day for the



"We're taking people who are morbidly obese and forcing them to make a behavior change by changing their anatomy. They're no longer going to overeat, because they can't."

—John Grant, MD

rest of their lives, plus walk at least five miles per week.

It's a drastic measure, to be sure—but so are the consequences of remaining obese, Grant says. "Obesity is a disabling disease. People with a BMI over 40 have only a third of the chance of living to 65 as normal-weight people.

"We're taking people who are morbidly obese and forcing them to make a behavior change by changing their anatomy. They're no longer going to overeat, because they can't. One or two bites will make them feel full, and they need to change the types of food they eat and increase their exercise. And unlike other weight-loss programs, you can't quit this one. It's not reversible."

Because of the risks, the procedure is best suited to highly motivated people who have been unsuccessful losing weight through a medically supervised program, he says. To qualify for surgery, patients must have a BMI greater than 40

for at least five years or greater than 35 with significant medical complications, but not weigh more than 400 pounds. Generally, patients must be between the ages of 21 and 65, undergo an interview by an eating disorder psychologist, and have a primary care physician willing to provide continuing care for nonsurgical medical problems and long-term follow-up. Many insurance companies now cover the surgery.

Average weight loss with the "gold standard" procedure, called a Roux-en-Y gastric bypass, is about 125 pounds or 60 to 70 percent of excess weight, according to Grant. Fifteen-year follow-up data suggests that most patients are able to maintain this weight loss. "Most see immediate improvement in respiratory function," he says. "Many eliminate the need for anti-hypertensive medication, reduce or eliminate need for insulin, normalize their serum lipids and experience an enhanced quality of life."



While it's clear that the procedure works for most patients, the exact mechanisms are still unknown. Grant says that changes in the production of ghrelin, a peptide hormone secreted by the stomach, may be the key. "This hormone is known to stimulate hunger," he says, "and after a Roux-en-Y gastric bypass, ghrelin levels in the blood are barely measurable, possibly accounting for the decreased sensation of hunger. So far, the only time ghrelin levels have been shown to fall is following the Roux-en-Y gastric bypass procedure."

THE METABOLIC FINGERPRINT

Ghrelin is among an intriguing array of recently identified biochemical factors that appear to play an important role in America's epidemic of overweight and obesity, says Christopher Newgard, PhD,

the recently appointed director of Duke's Sarah W. Stedman Nutrition and Metabolism Center.

"We're discovering a lot of players that seem to influence the sense of hunger and satiety," notes Newgard—and science is on the verge of discovering far more. New technologies allow researchers to perform comprehensive metabolic analysis in animals and humans, resulting in a unique "metabolic fingerprint" of patients, he says. "This sets us up to understand a great deal more about the biochemical process of weight loss. It may help us find markers to predict successful weight loss, learn more about the variables most strongly associated with weight loss, and hopefully learn how to manipulate those variables to enhance the process."

For example, he says, "We can seek to uncover what happens, in metabolic

terms, during the common and frustrating experience of 'hitting a plateau' during weight loss. We can then translate this data into practical strategies to help people get past that plateau."

Newgard recently launched a Metabolic Research Forum to bring together researchers and clinicians specializing in weight loss, and plans to apply to the National Institutes of Health for a National Obesity Research Center grant within the next year.

"We want to develop into a world-class center for nutrition and metabolism research to help us better understand—in biochemical and genetic terms—what's happening as people lose weight by different interventions," he says. "With new research techniques and the wealth of research and clinical weight-loss interventions already underway, we have a remarkable and unique opportunity to examine patients losing weight by different methodologies and translate that data into practical strategies to maximize success.

"The more we understand, the more we can do to help." □



FULL?

EMPTY OR FULL—HOW DO WE KNOW?

New technologies are helping scientists suss out the biochemical factors that influence hunger and satiety—such as ghrelin, a peptide hormone that stimulates appetite.