

DIET Redux

The latest diet drug was designed to fight extreme obesity, not help you fit into tight jeans. by Andrea Barnet



Imagine a drug that inhibits carbohydrate cravings, burns off fat, isn't addictive and has few side effects. These are the claims being made for dexfenfluramine, the first new diet drug to be approved by the FDA in 23 years. The drug, which suppresses appetite by boosting the levels of serotonin, a brain chemical affecting mood and behavior, is being marketed by Wyeth-Ayerst Laboratories under the

name of Redux. It is also being popularized by a new book, *The Serotonin Solution* (Fawcett), cowritten by Judith J. Wurtman, Ph.D., a biochemist at the Massachusetts Institute of Technology. Redux, which operates by altering signals sent to the brain, is the first in a new generation of anti-obesity drugs that regulate everything from appetite to the amount of food the intestines absorb.

Sound too good to be true? It may well be. Last November, when dexfenfluramine (also known as dex) came before an advisory panel to the FDA, many scientists raised serious concerns. George Ricaurte, M.D., Ph.D., a neurologist from the Johns Hopkins School of Medicine, reported: "When lab animals were given doses of dex that were sufficient to produce weight loss, those doses

produced serotonin brain damage." No matter what size the animal, the results were consistent. "We don't know if dexfenfluramine produces brain damage in humans," emphasizes Dr. Ricaurte. "But based on experiments on animals, I am concerned that it may."

To picture a serotonin nerve cell in the brain, imagine a tree. The nourishing root system is the cell
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WEIGHT-LOSS DRUGS: Where they stand

NAME	STATUS	USE	HOW IT WORKS	POTENTIAL RISKS
Fenfluramine (brand name: Pondimin)	Has been prescribed for more than 20 years	As a weight-loss drug appears most effective when used in combination with phentermine; combo referred to as fen-phen	Boosts serotonin by enhancing its release and delaying its return back to cells, thereby minimizing food cravings and promoting a feeling of satiety	May cause excessive drowsiness, as well as diarrhea and dry mouth
Phentermine resin (Ionamin)	Has been prescribed for more than 20 years for short-term use only	As weight-loss agent and stimulant for a maximum of three weeks, unless combined with fenfluramine	Stimulates the brain chemical dopamine, which inhibits appetite. Affects the brain chemical norepinephrine, which also suppresses appetite.	Insomnia, restlessness, anxiety, increased heart rate and increased blood pressure
Sibutramine (Meridia)	Currently under active review for FDA approval; all phases of clinical trials completed	Originally developed as an antidepressant, in clinical trials has been shown to reduce body weight	Reduces the amount of food eaten by enhancing the feeling of satiety; also increases metabolic rate. Maintains high levels of serotonin and affects norepinephrine	Dry mouth, constipation, insomnia and headache
Orlistat (Xenical)	Currently in FDA trials, not yet approved for use	Decreases the body's ability to absorb fat, producing weight loss	Blocks the digestion of fat by impeding certain enzymes that help "package" fat into digestible components	Symptoms of fat malabsorption, such as diarrhea and flatulence
Leptin	Potential anti-obesity drug; human studies may begin in 1997	Acts as an agent to reduce food intake and increase caloric expenditure	Increasing levels of leptin may signal the brain to stop eating. Mechanism varies depending on person's overall body fat	Too early to determine potential risks or side effects

—Susan Learner Barr, R.D.

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body, the trunk is the nerve fiber, and the branches are the nerve endings. What dex does is prune the nerve endings that employ serotonin, literally making stumps where once there were long, elegant fibers. As a consequence of pruning, everything that was in those nerve endings is lost. No one is sure how this damage manifests itself in terms of behavior. Serotonin, though, has been implicated in memory function, sleep disorders and panic attacks. It is unclear whether the nerve endings ever regrow. "There's simply not enough data," says Ricaurte.

There are also concerns about how dexfenfluramine affects the lungs and heart. In Europe, where the drug has been available since 1985, a study linked it to an increased incidence of a rare disorder called pri-

Dexfenfluramine was developed as a drug for the "morbidly obese"—those who are 30 percent or more above their ideal weight. Physicians such as Louis J. Aronne, M.D., who heads the respected weight-loss center at New York Hospital-Cornell Medical Center, feel the benefits of dex far outweigh the risks associated with obesity, such as diabetes, heart disease and many types of cancer. "If my patients go untreated," says Dr. Aronne, "most will develop life-threatening health complications." Dex is not, he stresses, "a miracle pill that is 100 percent safe."

Nor, it should be added, 100 percent effective. In clinical trials, people who took dex lost only about 10 percent of their weight, even in conjunction with diet and exercise regimes. And once taken off the drug, many gained back the pounds.

Like many of his colleagues, Aronne worries that dexfenfluramine, which

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mary pulmonary hypertension (PPH), which affects blood vessels that feed the lungs. It is almost always fatal. "In Europe no one was aware of the danger of dexfenfluramine," says Stuart Rich, M.D., a cardiologist at the University of Illinois in Chicago, who heads the largest PPH clinic in the U.S. "If you wanted to use it to lose 10 or 15 pounds it was no big deal." Since the link with PPH has been found, European sales of the drug have plummeted by 80 to 90 percent and restrictions have been placed on prescriptions.

is medically advisable for the truly obese, will be misused by healthy women for cosmetic purposes. With more diet drugs currently in the research and development pipeline (see "Weight-Loss Drugs: Where They Stand," page 98), there is a danger that many people will see these drugs as a magic bullet. "My advice to anyone considering dexfenfluramine is don't," cautions Dr. Rich. "There are a handful of people who are absolutely going to die because of their obesity. But for the rest of the population, it's not worth it." ❊



**THE SKINNY ON...
PUMPKIN**

FAMILY NAME *Cucurbitaceae*

NICKNAMES Big Moon, Ghost Rider, Jack-Be-Little (different varieties)

OCCUPATION Melon; largest of the gourd family

MOONLIGHTING JOB Ghoulish sentry. Ninety-nine percent of all pumpkins marketed domestically are used as jack-o'-lanterns.

BIRTHPLACE Mexico, 7000-5000 B.C. Indians living in caves in the Tamaulipas Mountains cultivated the squash for its nutritious seeds.

VITAL STATISTICS A ½-cup serving of canned pumpkin has 40 calories, 0 fat grams and more than three times the Daily Value for vitamin A.

The seeds are lower in fat than most nuts, second only to peanuts in protein content, and a good source of iron.

DISTINGUISHING FEATURES Ribbed gourd with a shell ranging from orange to red, filled with stringy orange flesh and large, flat seeds.

Although the smaller, sweeter pumpkins are used for cooking, they can easily grow to 20 pounds; zealous growers are in hot pursuit to set the 1,000-pound record.

FAMOUS RELATIVE The winter squash. Cousin to the cucumber.

FAVORITE HANGOUT Wherever it pleases. Can be a bit pushy in the garden, spreading out and snatching up soil nutrients and water.

LOVES To be gutted and carved; cooked into soups, breads and pies; canned; to have its seeds salted and oven-toasted.

HATES Jack Frost. Must be rescued from the garden before the first hard frost or the vines will turn black and the plant will die. A cozy blanket wrapped around the pumpkin will protect it.

CAREER HIGHLIGHTS In 1622, pumpkins helped the pilgrims survive in the New World. Pumpkin half shells were used as guides by barbers in seventeenth-century New England when the blue laws required all men to have round haircuts. Later went on to become the transportation of choice for Cinderella.

LEAST FAVORITE BAND Smashing Pumpkins

NOTORIETY The fat-laden grand finale of most Thanksgiving dinners. (One slice of pie gets 49 percent of its calories from fat.)

FAMOUS QUOTE "The coach has turned into a pumpkin, and the mice have all run away."—Lady Bird Johnson, after President Lyndon Johnson left office—Sally Kuzemchak

SPHON WATSON

