

# Diet Pills: Allure and Risk

By Gina Kolata

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Dr. Pietr Hitzig of Timonium, Md., is so impressed with the diet pill combination fenfluramine and phentermine that he has given it to 8,000 people. In fact, he advertises on his web page that if you cannot make it to his office, he will prescribe the drugs anyway over the phone. There are no contraindications, his web page says.

Dr. Ben Z. Krentzman, a family practitioner, said he had come out of retirement last year to prescribe the pills. He began by advertising on the Internet and seeing patients in his living room. Now he has an office in Culver City, Calif., and is about to open two more, one in San Luis Obispo, Calif., and the other in Hawaii. So far, he said in an interview, he has given the drugs to 800 people.

Not since the amphetamine craze of the 1970's have diet pills swept the country like fen-phen, as the drug combination is known. Patients got 18 million new prescriptions and refills last year, said IMS America, which tracks drug sales.

But now, in the wake of new hints that the drug combination might be dangerous, some medical experts are asking what the nation has wrought. What does it say about the American medical system when millions of healthy people rush to take an untested combination of drugs for long periods of time? What are people willing to risk to be slim?

The evidence that the drug combination may be dangerous is preliminary, but leading cardiologists and obesity experts say they are alarmed. Last week, doctors at the Mayo Clinic and elsewhere reported that 35 women who had taken fenfluramine and phentermine had developed an unusual and serious heart-valve defect. Previous studies have linked fenfluramine and dexfenfluramine, a chemically purer version of the drug, to primary pulmonary hypertension, an often fatal condition in which the artery that feeds

blood to the lungs becomes choked off.

Wyeth-Ayerst, one of two companies that make fenfluramine and the sole maker of dexfenfluramine, sold as Redux, sent out a news release saying it was working with the Mayo Clinic to further investigate the question of whether the fen-phen combination causes the heart valve defects but added that at this time the data were “limited and therefore not conclusive.” In addition, said the company, a unit of the American Home Products Corporation, obesity itself “is associated with serious health disorders.”

The Food and Drug Administration sent out a letter to thousands of doctors advising them of the valve defects but not telling doctors to take patients off the drugs.

Fenfluramine and phentermine are old drugs, approved two decades ago as short-term diet aids for the obese. Doctors started combining them only recently, after a four-year study of 121 obese people indicated that the combination could succeed where diets alone failed. Dr. Bernard Weintraub of the University of Rochester, who conducted the study, noted that the patients had not actually reached their ideal weights but that most had lost enough weight to lower their blood pressure and blood sugar levels. He suggested that obesity be treated as a chronic illness, with patients taking drugs for life.

But except for Dr. Weintraub’s small study, no one has tested fenfluramine and phentermine together, and no one has looked for adverse effects when people take the drugs for long periods of time. In effect, said Dr. Alan L. Hillman, an internist and economist who is associate dean of the University of Pennsylvania School of Medicine, when doctors began prescribing the drugs en masse, they were conducting an uncontrolled experiment on millions of Americans. That was legal because doctors are free to prescribe approved drugs for any uses they please, but Dr. Hillman and others question whether it was wise.

When a nearly untested drug combination enters the obesity market in a country where people are willing to try almost anything that promises to help them shed pounds, Dr. Hillman said, “you have a potential disaster on your hands.”

Of course, not every weight loss center freely prescribes the drugs. For example, Dr. Xavier Pi-Sunyer, director of the Van Itallie Center for Weight Loss and Maintenance at St. Luke’s-Roosevelt Hospital in New York City, said his center’s doctors had prescribed the drugs for fewer than 5 percent of their patients.

And Dr. Adam Drewnowski, director of the Center for Human Nutrition at the University of Michigan, said that an overweight but not obese friend of his had gone to a weight loss clinic near Atlanta looking for the drugs but that the doctor at the weight loss center had refused to prescribe fen-phen for him.

But there is no doubt that some clinics have prescribed the drugs to huge numbers of people.

About 10,000 people visiting the 16 Los Angeles area offices of California Medical Weight Loss Associates have taken the drugs, said Aaron Baumann, the group's administrator. "This is L.A.," Mr. Baumann said. "People tend to want to be thinner than in the rest of the country." He said the drugs "work like magic." He himself takes them.

Some commercial diet centers have used the drugs to attract customers. Nutri-System, for example, advertised two months of free medication with either fen-phen or dexfenfluramine to dieters who switched to them from Jenny Craig, a competing chain of diet centers. Jenny Craig Inc. said on Thursday that it was recommending that doctors at its centers stop prescribing fen-phen. Nutri-System's vice president for scientific affairs, Dr. Joseph Di Bartolomeo, said yesterday that his company's medical advisers were studying the new data and that, in the meantime, the company was still prescribing the drugs.

The Internet is bristling with fen-phen advertisements, including one that rather mysteriously quotes "L.D., San Diego" as saying, "I lost 40 pounds in six weeks on fen-phen and had to force myself to eat." The web page adds, "It was so easy," and promises to tell more for \$5.

Dr. Hitzig, Dr. Krentzman and others say they have prescribed the drugs to people with just a few pounds to lose. Dr. Hitzig's web page quotes a patient saying that until taking fen-phen, "no matter what I did, I could never shed that last 15 pounds." Dr. Hitzig also said he prescribed the drugs for people with eating disorders, who may not be overweight, as well as for alcoholics, cocaine addicts and people complaining of gulf war syndrome. But he noted that the vast majority of his patients wanted to lose weight.

Mr. Baumann, of California Medical Weight Loss Associates, said that doctors there prescribed the pills for people who are at least 20 percent above their ideal weights. "A lady who weighs 120 and should weigh 100 pounds is obese," he said. But he added, "You might not look at her and say she is obese."

Mr. Baumann and others whose medical centers have prescribed the drugs

widely said they had not seen any patients with heart damage. But cardiologists say the damage is not easy to spot.

“The first step is that you have to be aware of the connection,” said Dr. Jeffrey Isner, a cardiologist at Tufts University School of Medicine. If a young woman comes in complaining of shortness of breath and fatigue—signs of a heart valve defect—most primary care doctors would look at other possible causes first. The woman would most likely be overweight, which could account for her symptoms, Dr. Isner said. “You may not think to inspect the cardiac system that carefully,” he added. Now, of course, examining a fen-phen patient’s heart “jumps to the top of the list,” and doctors would be likely to order echocardiograms to examine patients’ heart valves.

The same goes for primary pulmonary hypertension, Dr. Isner added. The initial symptom is shortness of breath. Since the condition is so rare that doctors may have never seen it, few would think to do an angiogram—injecting dye into the arteries—which is the only definitive test for pulmonary hypertension. In a recent study in France documenting the association between fenfluramine alone or dexfenfluramine and primary pulmonary hypertension, the researchers noted that it took a year, on average, from the onset of symptoms until a correct diagnosis.

Doctors at some medical centers say they are starting to examine fen-phen patients for heart valve problems. “We’ve called all our patients who were on it,” said Dr. Albert Stunkard, an obesity researcher at the University of Pennsylvania who said that the university’s obesity center had prescribed the drugs for 20 patients.

But some doctors who enthusiastically prescribe the drugs say they are not worried. “It’s stupid to bring patients in for an echocardiogram,” Dr. Krentzman said. “That’s a very expensive procedure.” The risk is not established, he said, adding that none of his patients had experienced problems with the drugs.

Dr. Christian Renna, a doctor with offices in Dallas and in Los Angeles, who says he has prescribed fen-phen for hundreds of patients, said, “I am not worried about the use of these medications.” Rather, he said, “I am worried about the public’s reaction.”

Dr. Hitzig said he simply modified the dose of the medications if people start to have problems, thereby preventing serious ill effects. “Every side effect I’ve seen, to my current state of knowledge, is an indicator to modify the dose,” he said. When it comes to serious problems, he said, “we abort them before they happen.”