Anti-depression device implanted in hundreds
But the big question remains: Does vagus nerve stimulator actually work?

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The pocket-watch-sized device is billed as "a pacemaker for the brain," the newest cutting-edge treatment for as many as 4 million adults whose severe depression is not relieved by psychotherapy, drugs or even shock treatments.

Since its approval under unusual circumstances eight months ago by the Food and Drug Administration (FDA), more than 550 Americans have undergone surgery to have a vagus nerve stimulator (VNS) implanted in their chests to activate parts of their brains. Another 7,000 people -- aided by a network of nurses hired by Cyberonics, the Houston-based manufacturer of the device -- are seeking approval from their insurance companies for the $25,000 operation.

More than 3,700 psychiatrists, including doctors affiliated with Suburban, Georgetown, Sheppard Pratt and Howard University hospitals, have been trained in the use of VNS, the first device ever approved to treat depression. It consists of a battery-operated generator attached to an electrode implanted in the vagus nerve in the neck. The generator emits regular pulses of electricity that are supposed to stimulate serotonin and other brain chemicals believed to regulate mood, according to Cyberonics.

Yet despite the imprimatur of the FDA and an aggressive marketing campaign mounted by the company, the most basic question about the treatment remains unanswered: Does it work? Is VNS a lifesaving treatment for chronic depression, as some patients and doctors maintain, or an unproven and potentially harmful treatment based on flimsy science, as critics contend?

At the heart of the debate is this: The only rigorous clinical trial of the device -- which is approved to treat severe epilepsy -- failed to demonstrate effectiveness in alleviating depression. That study involved 235 patients, all of whom received the device, which was turned on in only half the group. At the end of three months, there was no statistically significant difference between the two groups.

A second study of 174 VNS recipients found that 30 percent showed significant improvement after one year. Because that study lacked a control group and because patients received other depression treatments after the device was implanted, there is no way to know whether the device was responsible. For years experts have known that depression -- unlike, say, type 1 diabetes -- can get better without treatment.

Last July, a top FDA official, citing the lack of alternatives for severely depressed patients, overruled unanimous opposition by 20 members of his staff and approved the device as a depression treatment for adults who had failed four other treatments.
FDA spokesman Stephen King said that VNS met federal standards for medical devices, which are less stringent than those governing drugs, and might help adults who had exhausted other options and were at a high risk of suicide. Cyberonics officials testified that 30,000 people commit suicide annually, most of whom were diagnosed with severe depression. The same rationale had led an FDA advisory panel in 2004 to approve the device by a 5-2 vote.

To Philadelphia psychiatrist Richard P. Malone, a member of the panel who voted against approval, such arguments are specious.

"Pancreatic cancer is a hopeless condition" with a much higher death rate than chronic depression, said Malone, a professor of psychiatry at Drexel University. "And we have as much evidence that this works for pancreatic cancer as it does for depression. Why not use it for that?"

Avoiding stigma
Some patients with chronic depression say they were willing to try anything that promised relief. Graphic artist Colleen Kelly decided in 2000 that she had nothing to lose by enrolling in an experimental study of VNS. Now 42, Kelly, who lives in Prince George's County, said dozens of medications had not helped her for long or had caused severe reactions. Nearly three dozen electroshock treatments failed to work and wiped out years of memories, she said.

VNS gave Kelly three "very good years," she said, and then her depression returned. "The past year has been abysmal," said Kelly, who urged the FDA advisory panel to approve the device. "I still keep hoping it's going to help me in some way."

But critics say they are not persuaded by Cyberonics's theory of how VNS works. The company's Web site says that "preliminary imaging studies suggest that VNS Therapy affects many areas of the brain implicated in mood regulation."

But Malone called the theory "all speculative."

"This almost has a feel of 18th-century psychiatry -- having a device and not being able to show how it works," he said.

Washington psychiatrist Wayne Blackmon agreed. "Psychiatry has been burned again and again by overextravagant claims" about devices and psychosurgery, said Blackmon, a lawyer and a past president of the D.C. Medical Society. "The history of psychiatry is plagued by psychiatrists jumping the gun because these poor people are suffering and the argument is we have to do something."

The device has also attracted attention on Capitol Hill, where the Senate Finance Committee has spent two years looking into decision-making at the FDA.

Last month committee chairman Charles E. Grassley (R-Iowa), whose panel issued a report highly critical of the agency's approval of VNS, said he was concerned that patients and their doctors were not being adequately informed about the risks of VNS, which include cardiovascular problems that can be life-threatening.
Grassley questioned whether Medicare and Medicaid should pay for the device, which costs $15,000 and must be replaced every five years or so when the battery runs low. So far neither the federal government nor private insurers have agreed to cover VNS for depression on a routine basis, although many have approved individual cases.

Last week, BlueCross BlueShield of Alabama announced it would pay for VNS treatment in chronically depressed patients who had failed four previous treatments.

Two recent technology assessments by major insurance companies have concluded there is insufficient evidence to find that VNS works for depression. A report by Harvard Pilgrim Health Care, an influential mental health insurer in Boston, called it "experimental, investigational and unproven."

Robert "Skip" Cummins, Cyberonics's CEO, dismissed such criticism and said his company, whose sole product is VNS, faced similar skepticism after the device was approved for epilepsy in 1997.

He noted that VNS is now accepted by insurers as a treatment for intractable seizures, which can be fatal if they are not controlled. About 35,000 epilepsy patients have received the implant.

Many FDA "regulators, politicians and third-party payers" know little about resistant depression, Cummins said. "Hundreds of psychiatric thought leaders and patients are rallying around the device" for "the worst of the worst" cases of depression, he said.

"There is nothing out there as safe and effective," Cummins said, adding that a company-financed study showed that the effectiveness of VNS improved over time. He added that he has a personal interest in intractable depression because his mother and grandfather committed suicide.

New York psychiatrist T. Byram Karasu, chairman of the task force that writes the section on depression for psychiatry's diagnostic and statistical manual, said that even though the effectiveness of VNS is uncertain, it appeals to patients and their psychiatrists.

In its marketing campaign, Cyberonics notes that VNS treatment does not cause the weight gain associated with antidepressants and the confusion and memory loss common after electroconvulsive therapy (ECT), psychiatry's term for shock treatments.

"VNS has a quality of cardiac surgery to it, a certain cachet," and it lacks the stigma of shock treatments, said Karasu, adding that six of his patients adamantly refused ECT and opted instead for VNS. "No one would know you didn't get a defibrillator."

**Option of last resort**

For Paulo Negro's patients, the issue is not stigma, but options. Negro, chief of behavioral health services at Suburban Hospital in Bethesda, said his VNS patients have tried everything, but their depression always recurred.
"What would you do if you've not been getting better for years?" asked Negro. "It's a chance to get better. I'd take it."

That's what Charles E. Donovan III did. The St. Louis resident credits the implant he received five years ago with saving his life. At the time, the Georgetown University graduate said he was so depressed he told his doctor he hoped to die on the operating table.

But in the weeks after surgery, Donovan said, he started to feel better. Although he takes antidepressants, Donovan said, he is sure drugs are not responsible, because they hadn't helped him previously.

Donovan, who is featured on the Cyberonics Web site, said he has no financial relationship with the company. He recently self-published a book about his experiences, entitled "Out of the Black Hole," and runs a pro-VNS Web site for patients. "I am so humbled by this treatment and grateful," he said.

Others have had far less positive experiences. Among them is Katherine V. Coram, 58, of Silver Spring who got the implant in the same study as Donovan. Coram said she knew she was in the group with the activated device because she could feel it going off, she said. She frequently lost her voice while she was talking and felt a persistent constriction in the back of her throat. Both are common side effects of VNS treatment.

Coram said the device seemed to help a bit at first, but when the doctor turned up the settings, she felt suicidal for the first time in years. Worsening depression and suicide attempts were reported by one-third of patients in one study funded by Cyberonics, according to data presented to the FDA.

Last year Coram said she had the generator removed from her chest because it wasn't helping. The electrodes in her neck must remain forever; doctors tell VNS patients that removing them is too risky because tissue grows around them. As a result, VNS recipients cannot undergo a full body MRI or therapeutic ultrasound.

"I'm still angry about the whole thing," said Coram, who said she regrets getting the implant and currently relies on the standby treatments: psychotherapy and antidepressants.

"You get desperate when you've been depressed for years," she said. "This sounds benign, like a pacemaker. My crusade is for people to know a lot more about it before they sign up."

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