FDA to probe safety of popular heart stents
Drug-coated devices may raise the risk of possibly fatal blood clots

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Millions of chest pain and heart attack sufferers thought they were getting a phenomenal medical advance when tiny coils that ooze medicine were placed in their arteries to keep them from squeezing shut again.

These gizmos, called drug-coated stents, worked so much better than plain old metal ones that 6 million people worldwide received them in the few years they have been available. It was a modern record for any medical device.
Now their long-term safety is in question.
Doctors think these stents may raise the risk of life-threatening blood clots months and even years later unless people stay on Plavix, an anti-clotting drug whose long-term safety in stent patients has not been established.
Thousands of people are being urged to take the $4-a-day drug until more is known.
Thousands of others each day who develop new blockages are being treated by doctors no longer sure of what to do. Many are returning to the old metal stents, and some are fundamentally rethinking when to use stents at all and are considering alternatives like bypass surgery or medications.
A Food and Drug Administration panel will meet on the issue Thursday and Friday. Medical journals are rushing studies into print, and powerful doctor groups are reconsidering treatment guidelines.
“It’s such a huge public health issue with so many people involved,” said Dr. Robert Califf of Duke University, who worked on one study to be presented to the FDA.

Doctors also worry about overreacting to a risk that appears small — five or fewer clots in every 1,000 patients.

“The benefit of having a drug-eluting stent is tremendous,” said Dr. Elizabeth Nabel, director of the National Heart, Lung and Blood Institute. Stents are used in angioplasty. Through a blood vessel in the groin, doctors push a tube to a blocked heart artery, inflate a balloon to flatten the clog, and prop the artery open with a stent.

**Maybe too aggressive**

About 652,000 Americans had angioplasty in 2003 — more than twice the 268,000 who had bypass operations, which are riskier, costlier and take far longer to heal. Angioplasty became more popular when the first drug-coated stent came out that year, virtually eliminating the procedure’s main drawback: scar tissue requiring a repeat effort to reopen the vessel.

Two brands are sold in the United States — Taxus, by Boston Scientific Corp., and Cypher, by Johnson & Johnson’s Cordis Corp. Labels say patients should take baby aspirin and Plavix for three months with Cypher and six months with Taxus, based on how long the stents release medication and how long doctors believed it took for the artery to repair itself by forming a new lining. Many doctors prescribe Plavix for up to a year.

Now it seems the coated stents may keep this essential artery lining from forming for a long time, maybe permanently. Without the lining or Plavix, clots can form and stick to stents.
It happened in May to David Reinhart, a 41-year-old legal secretary in Manhattan who collapsed two weeks after finishing the year of Plavix his doctor recommended.

“I feel a bit of a guinea pig,” he said of the stent situation. “It’s obvious there’s a lot they really don’t know about it yet.”
If it weren’t for Swiss efficiency, the risk might not be known. Switzerland’s government required a study to prove the new stents were worth their cost — $2,200 to $2,700 versus $600 to $800 for old ones — and to test how long Plavix should be taken. This produced the bombshell finding that patients with coated stents had double the risk of cardiac problems after stopping Plavix than those with plain metal stents.

“Everyone has been scrambling around looking in their databases” to see if it’s true in their patients, said Dr. Christopher Cannon of Brigham and Women’s Hospital in Boston, who consults for Sanofi-Aventis SA, which sells Plavix in the U.S. with Bristol-Myers Squibb.
Many such hospital registry studies have now been reported. Two presented at a recent American Heart Association meeting were provocative.

Dr. Joseph B. Muhlestein at the University of Utah found that deaths and heart attacks were higher with coated stents after three years and that their advantage for preventing artery reclosure disappeared by that time. Doctors in the Netherlands found that the devices were comparable after three years.

“It’s led me to wonder maybe we’re being too aggressive” in using the new stents, Muhlestein said.

Hospital registries help, but are not solid proof like randomized studies where similar patients are assigned to get one treatment or another. The best picture yet of risk may come from an analysis of pooled results from 14 randomized studies by Dr. Deepak Bhatt at the Cleveland Clinic. Published Wednesday in the American Journal of Medicine, it found that coated stents had five times the risk of clots as plain metal ones.
Some doctors say stents were approved based on studies that were too small, too short and in low-risk patients. Doctors also have used them for cases other than the types of blockages for which they were approved. Success is being further undermined by many patients quitting Plavix too soon.

“They just don’t understand how important it is to continue,” said Dr. Sidney Smith of the University of North Carolina, past president of the American Heart Association.

Longer Plavix treatment now is being urged “a little bit to get the doctor off the hook,” said Dr. David Williams of Brown University. “We’re saying indefinite for some patients even though we have no idea what that means” in terms of safety, he acknowledged.

“I find that a very unsettling recommendation,” said Dr. Spencer King, a cardiologist at Fuqua Heart Center in Piedmont Hospital in Atlanta and past president of the American College of Cardiology.

Plavix carries a risk of serious bleeding, he noted. Requiring coated stent patients to take it indefinitely puts them at risk of a clot if they have to temporarily stop Plavix to prevent excessive bleeding before a hip replacement or other surgery. Already, there are reports of people suffering such clots when going off Plavix for colonoscopies.

Many people can’t afford Plavix. Medicare doesn’t cover it unless people have the supplemental drug benefit, and half of angioplasties are done in people over 65.

“In the whole saga, the most important thing comes down to whether the patient is going to take Plavix or not,” said Dr. Samin Sharma of Mount Sinai Medical Center in New York.

More research is needed to clarify the drug’s role, Cannon said.

“There’s a risk that’s there when you don’t have (Plavix). What we don’t have are studies that show what’s the risk with it,” he said.