

How Safe Are Your Prescription Pills?

First a popular cholesterol drug gets the ax. Now there are concerns about arthritis medications

By CHRISTINE GORMAN

BECKY LONG, 63, OF TAMPA, FLA., HAS been taking the prescription drug Celebrex for her arthritis for the past two years. So when she heard the news last week that the drug, along with another painkiller called Vioxx, might be associated with an increased risk of heart attack, she called her doctor right away. Her biggest concern was not what you might expect, however. "The first thing I thought of was that Celebrex gave me my life back," says Long, who used to find climbing stairs impossible but has since felt well enough to travel to Nepal. "What would I do without it?"

Long is not the only one asking questions. Patients with a variety of concerns have been flooding physicians' phone lines with inquiries about Celebrex and Vioxx, two examples of a heavily advertised new class of analgesics called COX-2 inhibitors that are supposed to

be easier on the stomach than aspirin. Some folks wanted to discontinue their medication; others just needed to hear that the potential cardiac threat was only theoretical and not proved.

Certainly, second thoughts about the safety of new prescription drugs, not just Celebrex and Vioxx, are understandable. Three weeks ago, Baycol, one of the popular group of cholesterol-lowering drugs known as statins, was recalled because of an increased risk of rare but potentially fatal muscle problems. The same side effect—albeit at even lower rates—has been seen with the five other statins that remain on the market. But so few doctors and patients seem to know about the risk that last week, the Public Citizen Health Research Group, a consumer-advocacy organization, petitioned the Food and Drug Administration to require more prominent warnings on all the statins.

The truth is that no medication—not even a nonprescription drug like aspirin—

is 100% safe. Whether you realize it or not, whenever you take a drug, you are weighing the potential benefits against the possibility that the medicine can hurt you. So it pays to find out as much as you can about any drugs—including herbal remedies—you are taking.

When the COX-2 inhibitors hit the market in 1999, doctors and patients alike expected a lot from the little painkillers. The old standbys—which include aspirin and ibuprofen (Advil)—can tear up the lining of the stomach and cause serious bleeding disorders. These side effects occur when a protective enzyme called cyclo-oxygenase 1, or COX-1, is suppressed. Because the COX-2 inhibitors don't affect COX-1, it was expected that they would have fewer side effects.

Scientists are still debating whether that is the case. When the FDA approved the COX-2 inhibitors, it required Merck, the manufacturer of Vioxx, and Pharmacia, which markets Celebrex jointly with Pfizer, to include warnings about potential gastrointestinal problems.

Merck and Pharmacia were convinced that their medications had a better side-effect profile and submitted additional data to an FDA advisory panel last February. But the extra information raised new red flags for Dr. Steven Nissen, a cardiologist at the Cleveland Clinic who was consulted by the FDA. Nissen noticed what seemed like a high number of heart attacks and other cardiovascular problems in the companies' data. Together with Dr. Eric Topol and Dr. Debabrata Mukherjee, Nissen decided to look into the matter further.

The doctors combined the data from several studies about COX-2 inhibitors in a statistical process called meta-analysis. Then they looked to see if the information could tell them anything about heart-attack risk—something that the original trials had not been designed to explore. Such after-the-fact, or retrospective, analysis falls pretty low on the scale of scientific reliability. But sometimes it provides good clues about where problem areas may lie.

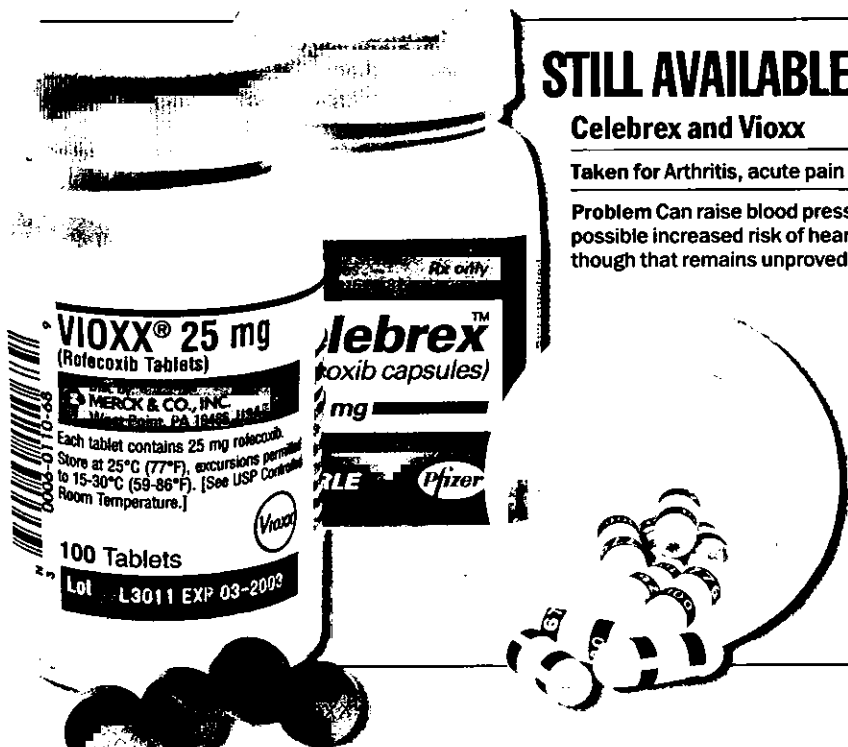
The meta-analysis, published in last week's *Journal of the American Medical Association*, showed that those who took COX-2 inhibitors suffered slightly more heart attacks than those who took older, aspirin-like drugs. The authors considered several explanations. Since the older drugs help prevent heart disease, the *JAMA* study might only be picking up the absence of a protective effect in the COX-2 inhibitors. Or the new painkillers might actually promote the creation of blood clots. Or both processes might be at

STILL AVAILABLE

Celebrex and Vioxx

Taken for Arthritis, acute pain

Problem Can raise blood pressure; possible increased risk of heart attack, though that remains unproved



work. The point, Topol says, is that “the cardiovascular effects of the [COX-2 inhibitors are] woefully understudied.”

For their part, the drug manufacturers stand firmly behind their products. Merck says its own meta-analysis, which contains data that weren't included in the *JAMA* study, shows that Vioxx is safe for the heart. Others have focused on the study's admitted limitations, including its direct comparisons of dissimilar patient groups. Says Dr. Michael Friedman, a senior vice president of Pharmacia: “The *JAMA* article is based on theory, not on solid data.”

So where does that leave the patient or doctor? For now, it's best to focus on what's known. If you already have heart disease, make sure it gets treated—whether or not you're taking a COX-2 inhibitor. If your blood pressure creeps up, which sometimes happens with Celebrex and Vioxx, make sure your doctor knows about it.

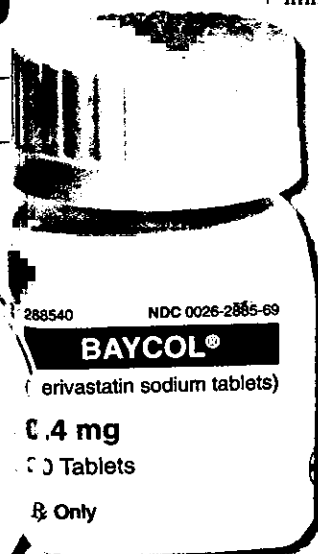
And be wary of side effects. Doctors have long known that the statins can trigger a rare breakdown of muscle tissue. (Stopping the drugs at the first sign of trouble usually halts the breakdown.) For some reason, patients who took Baycol—especially at higher doses or with another drug called gemfibrozil—were at greater risk. Bayer decided to drop Baycol in part because its attempts to alert doctors to those situations didn't always work. Drugs like the statins have the potential to save thousands of lives, and COX-2 inhibitors can relieve untold suffering. The trick, as always, is in figuring out how to use them wisely. —Reported by Alice Park and Andrea Dorfman/New York and Rochelle Renford/Tampa

RECALLED

Baycol

Taken for High cholesterol

Problem Can cause potentially fatal muscle breakdown



CHEAP LAUGHS: Like many victims of immune-deficiency disease, Jason Shuman, right, with his mother Lisa, says Disney's film makes a mockery of a serious illness

TOUCHSTONE PICTURES, MARIO TAMM—GETTY IMAGES

Bubble Boy Brouhaha

Real-life victims of immune-system disease are unamused by Disney's new gross-out comedy

By MICHAEL D. LEMONICK

NOBODY WOULD MISTAKE *BUBBLE BOY*, the Disney Touchstone movie that opened last week, for high art. It's full of the tasteless humor and crude pratfalls that appeal to fifth-grade boys. Critics have called it a “gross-out comedy.” But at least one boy was not amused. “I was just furious,” says Jason Shuman, 10, of Sudbury, Mass. “I thought it was a movie that shouldn't have been out in the first place.” No wonder. Like the film's hero, Jimmy Livingston, Jason suffers from an immune-system disorder that makes him highly susceptible to infections. And he and his family don't think the illness is funny at all.

He's not alone. All over the country, victims of similar diseases and their families and friends are outraged by *Bubble Boy*, which they say trivializes and misrepresents a life-threatening condition. They have asked Disney to add public-service announcements to all screenings and to contribute to immune-disease organizations; some are asking consumers to boycott the film. “It's really crossing the line,” says Marcia Boyle, founder of the Immune Deficiency Foundation in Towson, Md. “Can you imagine a movie

that makes fun of kids with cancer or HIV?”

Worse yet, says Boyle, the film specifically, if inadvertently, trashes the memory of the only person who has actually lived inside a bubble. David Vetter, of Woodlands, Texas, died in 1984 at age 12 from severe combined immune deficiency (SCID), the most serious form of the disease. Doctors tried to keep David germ-free by putting a plastic barrier between him and the world. It ultimately proved ineffective,



ONE OF A KIND: David Vetter, history's only bubble boy

and soon afterward, new treatments, including bone-marrow transplants, came along to make such experiments less urgent. Nonetheless, about half the 50 kids born each year with this type of immune deficiency still die before reaching adulthood.

Disney is not the first to exploit Vetter's story for

laughs. In an episode of *Seinfeld* (a production of Castle Rock Entertainment, an AOL Time Warner company), the character George famously ripped open an obnoxious bubble boy's capsule. Disney's position is that *Bubble Boy* makes fun of nobody and that Jimmy Livingston is “a resourceful, courageous and heroic character.” Realizing their predicament, however, company officials have privately told victims' groups that Disney may be prepared to aid them in their public-awareness campaigns. —Reported by Nadia Mustafa/New York