

The Painkiller Panic

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If there's silver lining to the sudden rash of unsettling news about painkillers, it's that just maybe it will force the American body politic to think twice about whether it really wants to destroy the pharmaceutical industry through an excess of litigation and reactionary over-regulation.

If it were just Vioxx that caused occasional cardiovascular problems, after all, it would be easier to convince the ignorant and the opportunistic -- i.e., likely jurors and Congressmen -- that the FDA and the drug industry had erred so badly with a widely taken drug that truly drastic measures should be taken with both.

But now that Celebrex and Aleve (also known as naproxen) have joined the list of drugs that might -- we stress might -- cause cardiovascular problems, people may be forced to come to terms with the fact that all drugs have side effects, especially when taken in large doses and over the long term. We already knew that more than 15,000 people die -- yes, die -- annually from gastrointestinal bleeding caused by drugs like naproxen and ibuprofen, the side effect newer drugs like Vioxx and Celebrex were designed to avoid.

Of course, drugs also have huge benefits. And this page has long argued that in almost all cases the right people to weigh them against the risks are doctors and patients, not courts and regulators.

One of the most frustrating things about the latest news on painkillers is that almost none of the people reporting it understand the concept of relative risk -- i.e., that a doubling of adverse events like heart attacks still doesn't mean that event is very likely. A doubled risk might well be a chance worth taking, especially if the baseline risk is low to begin with and the drug's benefits are significant for the patient in question. All of us implicitly accept this proposition with chemotherapy, for example, which poisons the entire body to kill a few cancer cells.

Why shouldn't we look at painkillers the same way? If you suffered from disabling arthritis and understood that your baseline risk for heart attack or stroke over a given time period was less than 1%, you might be willing to accept a doubling to a mere 1.5%. That's in fact what the study leading to the withdrawal of Vioxx in September found: 7.5 events per 1,000 in the placebo groups versus 15 per 1,000 among those taking the drug (and only after 18 months at a high dose).

Think patients don't actually approach their treatment this way? Consider Dave Ellis, who was featured in a Journal news story on Tuesday. The 66-year-old Mr.

The numbers on Celebrex and Aleve are likewise no reason for unnecessary alarm. In one trial patients taking very high doses of Celebrex experienced a 2.5-fold increase in the rate of cardiovascular events versus those on placebo. Other studies, including the one now raising the alarm about Aleve, have shown no risk. In that trial -- which had Aleve, Celebrex and placebo groups -- patients on Aleve saw a 50% increase in cardiovascular events. But we're talking about only 70 events (including 23 deaths) out of a sample of 2,500 patients who were already over 70 years old. We don't even know yet if that's significant in a statistical sense.

There is no reason to assume the Aleve alarm will pan out in other studies. But one of the ironies here is that it shows there never was solid evidence to prove that older-generation anti-inflammatories of its class were safer than the newer Cox-2 inhibitors, as has been asserted everywhere in recent months by critics accusing the drug industry of pursuing profits on newer patented drugs when patients would have been better off taking generics. The likes of Drs. Marcia Angell, Eric Topol, and David Graham have been shown up for the Luddites they are, willing to make grand pronouncements about the public health with nothing more than their anti-industry reflexes to support them.

Meanwhile, Merck's decision to withdraw Vioxx is looking worse by the day. It was irresponsible vis-a-vis the public health because the drug provided relief some patients couldn't find elsewhere, and because the extreme measure has made a rational national discussion about drug risk that much harder. Withdrawal was also irresponsible toward Merck's shareholders because it has placed Vioxx in a different class when it comes to litigation -- needlessly conceding the drug has no place in the pharmacopeia -- from drugs that shouldn't be withdrawn but which may carry similar risks.

We understand our hopeful scenario above -- that the latest news on Aleve may ultimately prove an antidote to anti-drug industry hysteria -- may not be the way things pan out. For the moment, America's trial lawyers are emboldened by all the blood in the water. If there are many people outside this publication putting the risks in proper perspective, we haven't seen them. But the possibility that Aleve (and who knows, maybe ibuprofen?) can have cardiovascular effects should change the political and legal environment in which the Vioxx drama plays out. By now just about every adult in America has experienced the near-miraculous healing powers of one non-steroidal anti-inflammatory or another for at least one episode of acute pain. We're guessing they won't want to find themselves without the option of relief should they ever be in pain again.