

The mystery of medications linked to suicide

As number of drug warnings rise, investigators search for reasons why

By Fran Kritz

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When Kate Miller of Queensbury, N.Y., filled a new allergy drug prescription for her 15-year-old son, Cody, last July, she hoped it would improve his bothersome allergy symptoms. Now, Miller is wondering whether a possible side effect of the drug, Singulair, caused Cody — who she describes as a happy, athletic teenager — to take his own life about a month later.

Miller isn't alone. Physicians or patients have filed anecdotal reports with drug companies or the Food and Drug Administration on at least six drugs or drug classes that may have been linked to episodes of suicidal thoughts or actions. In just the past few months, the FDA has released several advisory notices to both doctors and the public about drugs linked to suicidal thoughts or actions, including [Singulair](#), epilepsy drugs and the smoking-cessation drug [Chantix](#). Reports have also been filed on antidepressants, the influenza drug Tamiflu and the acne medicine Accutane.

It's a medical quandary that has doctors, drugmakers, federal health officials and patients confused and understandably concerned. Are the links between these medications and the risk of suicide real? And if so, how can drugs that are intended to help people instead potentially prompt them to end their lives?

Experts say there aren't many clear answers but medication links to suicide, if in fact real, could possibly result from the drug itself, an underlying disease or condition that predisposes someone to depression, or a combination of factors.

"The brain is a complex organ, and most of the drugs are complex as well," says Dr. Thomas Laughren, head of the division of psychiatric products at the FDA. "It's not unreasonable to think that a drug that gets into the brain may have effects other than you hope they would have ... but in some cases, it's just a background event. That's why it's so important to follow up with an analysis of the clinical trials."

After concerns were first raised about possible links between antidepressants and suicide about four years ago, the FDA commissioned researcher Kelly Posner, the principal investigator at the Center for Suicide Risk Assessment at Columbia University in New York, to help determine any suicidal risk posed by medications. Her quantitative tools and questionnaires to assess suicide risk are being applied to drugs already on the market and those still in testing.

"We know that whether or not these drugs actually cause suicidal thought or action is a question we have to answer, but up until now, none of the clinical trials for the drugs were set up to address the question," says Posner. "Either way we have to get the right

answers. It's critical to know about drugs that pose risk, but debunking false notions of risk is equally important to the public health."

Finding a link can present other issues. This became evident when the FDA, based on a review of antidepressant clinical trials, found a slight increase in suicidal thinking among children and young adults taking antidepressants such as Paxil and Prozac. The rate in those taking antidepressants was 4 percent, twice the rate of those taking a placebo. The information was added to the label of antidepressants within the last few years, pushing many doctors to stop prescribing the drugs for many of their patients.

"Use of antidepressants went down, and the suicide rate went up," says Dr. Paula Clayton, medical director of the American Foundation for Suicide Prevention in New York.

The drug? The diagnosis? Neither?

Laughren says the FDA hopes that by using Posner's methods, they may be able to find categories of people who might be at risk for suicide on a particular drug and more carefully determine who should stay clear of the drug and in whom it can safely be prescribed.

At least in theory, there are some possible explanations for why some of the drugs in question might be associated with suicidal thoughts or action, says Jason Noel, director of clinical pharmacy services at Rosewood Center in Owings Mills, Md., a residential facility for people with developmental disabilities. Singulair, for example, has a similar chemical pathway to steroids, which are drugs that can affect behavior and mood.

The FDA is conducting a safety review of Singulair, which is also used to treat asthma, that is expected to take about another eight months. Last week, Kate Miller and her husband, David, met with FDA officials in the office of Congresswoman Kirsten Gillibrand (D-N.Y.), who is pushing to help find answers on Singulair and other drugs that have been linked to suicide.

In the meantime, says Ron Rogers, a spokesperson for Merck, which makes the drug, a cause-and-effect link between Singulair and suicide has not been proven, and patients on the drug who are worried should consult their doctors. "If patients have any concerns about Singulair, the most appropriate course of action to take is to speak with their physician, not to stop taking their medicine," he says. "Each patient's doctor is in the best position to determine whether or not a person should continue to take the medicine."

Regarding antidepressants, Laughren and other experts say one possible explanation for the link may be that fatigue is one of the symptoms of depression and that the initial benefit of an antidepressant is increased energy. Improving depression symptoms can take a few weeks, but in the meantime, some patients may use their extra energy to act on their suicidal thoughts.

While some patients can take a drug and have no risk of suicide, in others, chemical factors in the drug combined with specific factors in the patient, or an underlying disease they have, may combine to influence depression or suicidal thinking or behavior, Noel says. Suicidal thoughts in patients taking epilepsy drugs, for example, have been reported in patients on the drugs for epilepsy, depression or other psychiatric conditions, but generally not in patients taking the drug for migraine headaches, for which they are sometimes also prescribed, says Noel.

"In some cases, the conditions being treated, even asthma, can be its own risk factor for suicidal thinking — confounding the impact a drug may have," says Posner. Asthma symptoms can impair daily living, such as being unable to walk far because of difficulty breathing, or having to cart oxygen around. Having your life hampered in this way can make some people with asthma think about suicide, experts say.

When it comes to Chantix, one theory is that the smoking-cessation drug, which works to block the pleasure pathways in the brain that make nicotine so satisfying, also suppresses other types of pleasure and happiness, leading to depression. But at the same time, stopping smoking, the goal for patients taking Chantix, can itself be a risk factor for depression, says Posner, and smoking itself is a risk factor for suicide.

A spokesperson for Pfizer, the maker of Chantix, says the company is continuing to investigate the association between the drug and suicide risk, and urges patients considering Chantix to talk frankly with a doctor about what to expect when getting off cigarettes.

A representative of the Pharmaceutical Research and Manufacturers of America in Washington, D.C., says the trade group is hoping for more answers soon.

"We looked at this with SSRIs [antidepressants] and the other drugs that have received warnings," says Alan Goldhammer, deputy vice president of scientific and regulatory affairs. "We're keenly interested to move forward and better understand what is the number being observed in the case of true suicides and how does that relate to the age group and population at large."

'A common background event'

Adding to the confusion of how to determine the possibility that a drug can cause suicidal thinking or action is the fact that suicide and suicidal thinking is, sadly, fairly common in the United States. Suicide is the fourth leading cause of death for adults between the ages of 18 and 65, according to the most recent data from the National Center for Health Statistics, accounting for about 26,500 deaths in that age group in 2005. For those ages 15 to 24, suicide is the third leading cause of death.

For all ages, suicide rates increased just under 1 percent between 2000 and 2005, but children and young adults ages 10 to 24 experienced an 8 percent increase between 2000 and 2004, following a decrease in the 15 years prior to 2000, according to the Centers for Disease Control and Prevention in Atlanta. Ileana Arias, head of the CDC's National Center for Injury Prevention and Control, says the agency doesn't have an explanation for the increase.

"What makes this so difficult is that suicidal thinking is a common background event," says Laughren, citing data from the CDC which found that one out of five young adults ages 13 to 19 admits to thinking about suicide.

Experts say recent increases in the reporting of medication side effects may be bringing attention to the issue of drugs possibly linked to suicide, but that doesn't prove a connection.

"Whenever an alert is issued by the FDA, the notice reminds patients and doctors to report side effects to the agency or drug company, and so we are getting more reports, which are then dispatched to health care professionals and consumers. That's a good thing, but it doesn't tell us enough," says Michael Cohen, head of the Institute for Safe Medication Practices in Horsham, Pa. "It's only after the reports have been investigated, which takes time, that we can know for sure if a reported side effect is actually related to the drug."

When a suicide occurs, says Clayton, families and friends look for answers, and because prescription medications are so prevalent, they may well find that their friend or loved one was taking one or more medications and often make the connection. "But that doesn't mean that the drug was a factor in the death," Clayton says.

Clayton and other psychiatric experts worry about listing suicidal thinking as a possible side effect on medications because, understandably, patients or their families are likely to see that and decide not to take a drug that could be beneficial for a medical condition.

Insufficient information

While investigators try to sort out the data and reports, family members of people who have committed suicide have said they didn't have enough information when choosing a drug to determine whether it was a safe choice.

Although Cody Miller had no history of depression or suicidal thinking, his mother says that if she had known that Singulair was linked to feelings of sadness, she might not have let him take the drug.

In fact, Merck voluntarily added depression to the drug's label in April 2007, three months before Cody's doctor prescribed the drug, because a number of doctors and patients reported the side effect to the company or the FDA. But Miller says her doctor did not tell them the drug could cause depression, nor was depression listed as a side effect of the

drug on the company Web site, which she checked when the drug was first prescribed, and wasn't in the information that came stapled to the prescription from the pharmacy.

Insufficient patient and doctor information on side effects of prescription drugs is hardly a new issue. At a 2002 Congressional hearing, Congressman Bart Stupak (D-Mich.) reported a similar lack of information on the acne drug Accutane that his teenage son B.J. was taking. B.J. killed himself in 1999, after several months on Accutane, and his parents have linked his death with the drug.

At the hearing, Stupak said that in 1998 the FDA publicly noted reports of depression, psychosis and suicidal thoughts and actions with the drug, but a year later when B.J. got the drug their doctor had not informed them of the risk, and the patient information that came with the medication did not include it. A spokesman for Stupak says the congressman is looking into current drugs that have been linked to suicidal thoughts and actions.

Consumer advocacy groups such as Public Citizen in Washington, D.C., say there can be lags in getting information to consumers about new warnings on drugs. Refill prescriptions don't necessarily highlight new information, and patient information that pharmacies staple to the prescription bag don't always include all necessary information, says Ray Bullman, head of the National Council on Patient Information and Education in Bethesda, Md., which educates consumers and health professionals on safe medication use.

The FDA is looking into the quality and timeliness of the information consumers receive with their prescription drugs, and Congresswoman Gillibrand would like to see a mechanism put in place by the FDA to alert physicians directly whenever a serious drug side effect is announced.

Ask questions, follow up

Medication experts including Cohen, of the Institute for Safe Medication Practices, says that asking whether any medication might cause suicidal thinking or action is a reasonable question when a drug is prescribed, and if the answer is yes, that should be weighed, with your doctors, against the benefits of the drug.

Posner and other experts say a drug should not be dismissed out of hand because it has suicidal thinking and/or behavior as a side effect, without thoroughly discussing the risk-benefit profile of the drug.

Cohen urges family members to monitor children and young adults for behavior changes when any new drug is started and to contact the doctor immediately if they are concerned. He suggests that adults who are taking a drug that has been linked to behavior changes let a friend or family know about the prescription and ask them to stay attuned to any changes.

"Suicide ideation is incredibly common, and is addressable, if needed," says Posner. "In almost all cases when you measure the risk against the benefit, it almost always favors treatment with the drug in question for conditions ranging from asthma to depression."

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