THE PILL PARADOX

Are antidepressants killing teens, or saving their lives? A father searches for answers.

Six years ago, my daughter, then in the sixth grade, tried to commit suicide. Under assault by the so-called "popular" girls at school, Alicia could no longer face the ordeal of getting up in the morning and going to class. She swallowed most of a bottle of Tylenol and went to bed. A few hours later, she started vomiting violently. At the time, I had no idea that she had tried to commit suicide. I thought she just had food poisoning. But a few months later, it happened again, and the truth came out. I took her to a psychiatrist, who immediately started her on an antidepressant. Since then, she has had ups and downs, but no more suicide attempts. She's now doing well in high school and will soon leave home for college. The antidepressants, I was convinced, saved her life.

Now I realize that maybe she was just lucky. In the past six months, under pressure from critics, politicians and regulatory agencies here and in the U.K., several pharmaceutical companies have released internal data showing that the class of drugs most often used to treat depression in kids—Prozac, Zoloft, Paxil, Lexapro, Wellbutrin and a few others—may not work very well. Even in adults, they aren't magic bullets: Only about 60 percent of depressed patients respond to these drugs, which include the well-known selective serotonin reuptake inhibitors. By comparison, roughly 40 percent respond to a placebo. (*Response*, in these studies, is defined as a 50 percent improvement in symptoms—a far cry from a return to health.) In adolescents the picture is even more complex. Since minors generally don't participate in clinical trials, most of these drugs have not been closely studied for them. And there's some new science suggesting that because adolescent brains are still maturing, depression may develop quite differently in young people. >>

What's worse, old concerns that some of these drugs might cause suicidal impulses have been reawakened by reports of a potential link between antidepressant treatment and suicidal thoughts. The evidence is mixed. Because depression itself can lead adults and teens to suicide, it's hard to tease out cause and effect. One theory is that antidepressants lift the fatigue and passivity of the disorder before they change feelings of despair, resulting in a still-very-unhappy but now-energized patient. One recent analysis of previously unpublished data indicated that young people being treated with antidepressants may be at a higher risk for suicidal thoughts.

The link to suicide is far from being proved, but even the possibility that the drugs might be harmful is profoundly disturbing. A study in the *British Medical Journal* in April concluded that researchers have exaggerated the benefits of antidepressants in children and adolescents, and that as a consequence, nondrug treatments like talk therapy may have been overlooked.

My daughter has been through a lot of turmoil. Could it be that the antidepressant she's taking might one day drive her to another suicide attempt? Should I take her off the drugs that seem to have helped her so much? What am I—and other parents in my situation—supposed to do?

Antidepressants are among the most heavily prescribed drugs on the pharmacist's shelf. Among American children under 18, antidepressant use rose 49 percent in just four years, from 1998 to 2002, according to a study published in April. Even so, government drug regulators in this country have reacted cautiously to these concerns. British regulators went as far as to ban the use of antidepressants for children, with the exception of Prozac, the most thoroughly studied of the group. By contrast, the U.S. Food and Drug Administration last spring merely asked the makers of 10 antidepressants to add a warning label urging doctors to "carefully monitor patients receiving antidepressants for possible worsening of depression or suicidal [tendencies]." The FDA is continuing to study the issue, but has offered no further advice.

Parents who have worked hard to find the best psychiatric care for their children are now confused. According to a poll conducted in May 2004 by Columbia University, nearly a third of parents say they think antidepressants are harmful. The same number say they aren't. But even more—the remaining 38 percent—aren't sure what to think. Psychiatrists and researchers are worried too. "There are a lot of sick kids whose lives we've saved with medication," says Richard Sarles, a child psychiatrist at the University of Maryland and the president of the American Academy of Child and Adolescent Psychiatry. "If parents became reluctant to use these medications, a significant number of children and adolescents would be in trouble again."

One thing is for sure: Children or adults on antidepressants who decide to quit the drugs should taper off gradually under the supervision of a doctor. Going cold turkey may cause serious withdrawal symptoms. Yet teens being teens, these recommendations may not be so easy to apply in the real world. While I was wrestling with the problem of what to do with my daughter, she quit taking her medication—without any advice from me or her psychiatrist. "I don't need it any more," she told me. "I'm feeling fine." By the time she admitted it, it was too late to do anything except to tell her that she should not have made that decision on her own. Six months after she quit, she was sorry she had stopped. She began to feel a little shaky emotionally, and she visited her psychiatrist. He put her back on an antidepressant, and she's doing better. Maybe she has now learned not to make medication decisions on her own; maybe not.

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One promising alternative to drug treatment is cognitive >>

behavioral therapy, which has been shown to be roughly as effective as drugs in treating teen depression. (Drugs and therapy together seem to be even more effective.) I asked James McCracken, the director of child and adolescent psychiatry at UCLA's Neuropsychiatric Institute, how many kids are willing to talk to a therapist. "More than you would expect," he said. "When it's very clear to the child that it's his or her therapy—and not [his or her] parents'—often that melts away a lot of the psychological barriers. The majority, when given the opportunity to meet with a generally skilled therapist, gain from it."

The frontal lobes of the brain—the centers of decision making—are the last parts of the brain to mature.

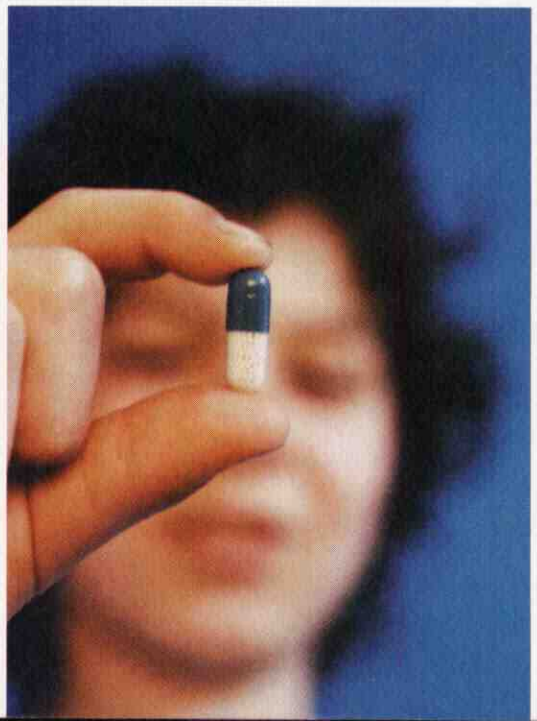
But it doesn't work for every kid. After I persuaded my daughter to begin therapy, she stuck with it for only a couple of months. She complained that her mother, with whom she lives, was not available to take her to her appointments, so I made it my job to pick her up and get her there. She went to therapy for another couple of months, and she dropped out again, despite my efforts. I was disappointed, but it wasn't a big surprise. Teenagers are working hard to become independent of the adults in their lives, and despite McCracken's confidence, I don't think it is possible to convince some teens to confide their most personal thoughts and feelings to any adult, even a skilled and understanding therapist.

Now, I'm beginning to hope that my daughter's darkest days are behind her. During the past few years, she's gradually become more stable, although she's continued to go through emotional ups and downs. At 17, she's still within an age range that carries a high risk of depression, especially for girls. (Beginning around puberty, women have about twice the risk of depression as men.) Yet she is consistently doing better, without therapy and with only intermittent medication. Why? For one thing, the disease may simply be waning, as it does from time to time.

There is another speculative but intriguing explanation: Perhaps as Alicia's brain matures, her susceptibility to depression declines. Until a few years ago, researchers believed that the brain finished developing at around age 12. The wiring was more or less complete, and the various parts of the brain had completed their growth. But the development of new brain scanners has led to a startling finding. It is now clear that the brain continues to grow and develop until about age 25. And the last area to develop is the so-called executive center of the brain, the site of mature decision making. It is possible that Alicia's improvement is due to the continuing development of her brain.

Researchers have believed for a long time that the brain produces too many neurons, or gray matter, early in life. These neurons are whittled away as the brain matures, leaving those that we have cultivated (through the study of Italian or jazz piano, for example) and dropping those we no longer need. But the story is not so simple. A few years ago, Jay Giedd of the National Institute of Mental Health (NIMH) showed that there is another burst of gray matter production just before puberty, and a second whittling during the teenage years, which ends in the early to mid-20s. In May, researchers at NIMH and at UCLA released a fascinating "movie" showing the development of the human brain from the ages of 4 to 21. It shows that the neurons at the back of the brain are the first to undergo this pruning process. The frontal areas of the brain—the centers of decision making—are the last to mature.

In one series of studies, Deborah Yurgelun-Todd at Harvard University's McLean Hospital in Belmont, Massachusetts found that teenagers' brains process emotions differently than those of adults. When young teenagers are shown emotions on faces displayed on computer screens, their amygdalas become active. The amygdala is a brain center related to fear and other instinctual reactions. As the teens grow older, the same pictures trigger activity in the frontal lobes of their brains, areas responsible for reasoned decisions.



Researchers do not yet know whether mental illness is related to a disruption of the developmental process that >

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Teen Troubles Or a Troubled Teen:

How can parents tell?

Adolescence is a time of huge social and emotional changes for kids, when they enter into complicated social webs at school and begin, sometimes in the most unpleasant ways, to assert their independence from their parents. They can be grouchy and withdrawn, they seem to sleep all weekend (except when it's time to go out at night), and they can be stubborn and unresponsive to even the simplest parental demands.

But take those normal hallmarks of adolescence, turn up the volume on all of them just a bit, and you have many of the symptoms of depression: withdrawal, sullen demeanor and irrational behavior. How is a parent to distinguish normal adolescence from the signs of emerging depression?

James McCracken of the University of California, Los Angeles Neuropsychiatric Institute has several rules of thumb to apply: a drop in academic performance; a change in activity, such as losing interest in a favorite sport; a big change in friendships or socializing; and difficulty with the family that goes beyond a bad day now and then. All of these things can happen to normal adolescents, says McCracken, but a sign of trouble is a change in many of these things at the same time. "A lot of it is the persistence of the change, and the impact," he says. Watch for family life that is "strained day in and day out due to the youngster's mood, withdrawal or refusal to follow the guidelines parents are trying to set," he says.

If teens are spending more time alone in their room, that can be a normal thing, part of the push for independence. "The substitute is that their peer world becomes much more important," McCracken says. If the child is withdrawing from peers, too, "that's when you get concerned."

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Further reading:

"Questions and Answers on Antidepressant Use in Children, Adolescents and Adults," U.S.F.D.A., March 2004: www.fda.gov/cder/drug/antidepressants/Q&A_antidepressants.htm

Help me, I'm Sad: Recognizing, Treating and Preventing Childhood and Adolescent Depression, by David G. Fassler, M.D., and Lynne S. Dumas (Penguin, 1997).

leads to mature reasoning, but they have hints. In yet another study, NIMH researchers found an exaggerated loss of gray matter in the brains of teens with schizophrenia. And children with autism also show an altered pattern of brain development. Could some disruption in brain maturation explain my daughter's depression? It might explain why it came on so intensely—and why she seems to be getting better.

In the meantime, the controversy over the risks of treating teens with antidepressants continues. In June, under the pressure of a lawsuit filed by New York Attorney General Eliot Spitzer, Paxil manufacturer GlaxoSmithKline released internal data which indicated that the drug was no better than a placebo for treating teen depression. Other research may ultimately provide better advice on the best treatment. At a medical meeting in June, child psychiatrist John March of Duke University announced preliminary results of a large study that showed that Prozac is effective in teens with depression. (In his study, drug and talk therapy combined were even more effective.) A report of the study appeared in *The New York Times*, but March will not discuss the early results or release any further details—not even to other psychiatrists—until the study is published.

Many psychiatrists believe that even if antidepressants do trigger suicide attempts in a few teenagers, the drugs save many more kids overall. The statistics seem to back up that thinking. Between 1992 and 2001, as the number of depressed kids taking antidepressants rose sharply, suicides among children aged 10 to 19 in the United States dropped by about 25 percent, reports the federal Centers for Disease Control and Depression in Atlanta. "We really need further large-scale clinical studies, where we are asking these questions up front," says David Fassler, a psychiatrist in Burlington, Vermont, and a member of the board of the American Academy of Child and Adolescent Psychiatry. But until that happens, it's tempting to conclude that the antidepressants are indeed saving young lives.

After a lot of soul-searching, I've urged my daughter to continue taking her medication, and most psychiatrists say that's the right course. She still refuses to see a therapist, but I'm hoping that will change. Along with millions of other parents, I'm making decisions about my child's care on the basis of conflicting reports. For now, we have no other choice.

Paul Raeburn is author of Acquainted with the Night: A Parent's Quest to Understand Depression and Bipolar Disorder in His Children *(Broadway Books, 2004).*