



The Antidepressant Dilemma

By JONATHAN MAHLER

Looking back, Mark and Cheryl Miller would have done a lot of things differently with their 13-year-old son, Matt. They probably would never have left Lenexa, Kan. They would have sent him to a different school, and they certainly would have chosen a different therapist. But most of all, they wouldn't have given him Zoloft. "It's not a pleasant thing living with the thought that you had a hand in your son's death," Mark Miller told me recently. "Making him take those pills was done out of love for Matt, but it was still the wrong thing to do."

We were on our way back from Mark and Cheryl's Wednesday-night Bible-study class. I was riding with Mark, who had come straight from the advertising agency where he works as a vice president and creative director. A young-looking 55, with neatly combed hair and wire-rimmed glasses, he was wearing a striped Polo button-down and pressed blue jeans. A few minutes later Mark eased his white Volvo into the garage of their home, a meticulously decorated two-story Tudor in Overland Park, Kan. The Millers moved here from Lenexa, like Overland Park a suburb of Kansas City, in the summer of 1996, though they'd been talking about relocating for years. They liked Lenexa, but Mark was doing well, and they could afford a bigger house in a more upscale neighborhood.

Their new home was only 30 minutes away from their old one, but it meant a new school district for their two children. Their 15-year-old, Jenny, was going to be a freshman in high school and was nervous about the move. Her 12-year-old brother, Matt, a slight, fair-haired boy who wore skateboard-style clothing, was excited. As a Cub Scout, he had built the fastest pine-wood derby car in his age division, and he was looking forward to taking flying lessons at a flight school near their house when he turned 14.

School started, and Jenny was doing fine. She tried out for the drill team, and while she didn't make it, she did meet some new friends at the auditions. Things were a little harder for Matt at Harmony Middle School. First of all, it was big; the Overland Park area had become very popular in recent years, and Harmony had been forced to temporarily accommodate 700 students, nearly twice as many as it had been designed to. Starting in the seventh grade also put Matt at a disadvantage, as most of his classmates had already been together for a year. Though he was small for his age, Matt was popular with the girls. Still, he was clinging to his old friends more tightly than the Millers had hoped. On weekends, Mark and Cheryl often found themselves driving him to and from Lenexa.

For a while, the Millers thought Matt was just going through a normal period of adjustment; a few months in, though, they noticed a change. "At the beginning of the school year, Matt was getting calls from girls all the time," Cheryl, a petite woman in a stylish gray jacket and black pants, told me. "But around Christmas we saw things weren't connecting for him as well. The kids weren't letting him in. He started getting quiet, withdrawn." The Millers' theory is that the other boys were jealous. "We think some of the guys were blocking him out because all of the girls were calling him," Mark said. "He probably crossed somebody with someone's girlfriend."

By midwinter the signs were more pronounced. His grades were falling. Always an A-B student -- he had excelled in math in particular -- he now had a D and an F. In February, Matt was caught forging his father's signature on several midterm progress reports. The Millers were called to the school for a conference. As the second semester continued, Matt's problems multiplied. One of his teachers reported that Matt was breaking pencils in class and failing to interact with his classmates. Several instances of "unsatisfactory conduct" were brought to the attention of the principal.

In April, the school put Matt in a special-needs class for an hour every afternoon. Neither his attitude nor his behavior improved, though he did start going steady with a girl in May. Around that time, a counselor at Harmony suggested to Mark and Cheryl that they seek therapy for Matt during the summer. The Millers, who knew by now that Matt was unhappy though they weren't sure why, thought this was a good idea. They were eager to help Matt while school was not in session; that way, he could start fresh in the fall. They initially wanted Matt to see a social worker recommended by the school, but their insurance did not cover that therapist. In the end, they chose a psychiatrist, telling themselves that this might be for the best in case medication was required. Matt didn't want to go. "He said to me, 'Mom, I'm not crazy,'" Cheryl recalled. Mark added: "I remember telling him, 'Matt, this is good.' We would all love to pay someone to help us work through our problems."

On June 30, 1997, the Millers took Matt to see Dr. Douglas Geenens, a child psychiatrist referred to them by Matt's primary-care physician. In addition to the doctor and the Millers, both Mark and Cheryl remember there being two other people in the room, who Dr. Geenens explained were his trainees. Matt sat silently for almost the entire 50-minute session. Cheryl did most of the talking, sketching out Matt's emotional deterioration since the start of the calendar year.

Matt's next appointment with Dr. Geenens was scheduled for July 21, a Monday. Mark and Cheryl recalled the details for me: Matt took a 30-minute test for attention deficit disorder and spent 15 minutes filling out a Children's Depression Inventory form, a standard tool for measuring depression in kids. At the end of the session, Dr. Geenens suggested that Matt try Zoloft. He gave the Millers three sample bottles with seven 50-milligram tablets in each and told them to make sure that Matt took one a day. The Millers had never heard of it. "The only thing I was aware of was Prozac," Cheryl told me. "I asked him why are you prescribing Zoloft?" Dr. Geenens answered that Zoloft was newer and more refined than Prozac. Cheryl asked if there were any possible side effects. Dr. Geenens said they should be on the lookout for stomachaches or insomnia. The doctor had no appointments available until the middle of August, but he wanted the Millers to call in a week and let him know how Matt was doing.

Two days later, Mark took the kids to visit his mother at her apartment in Sioux City, Iowa. Their plan was to spend a few days there, then bring Mark's mom back to Overland Park for the weekend -- they had tickets to a play in Kansas City -- before dropping her back home on their way to a family vacation on a lake in Wisconsin. Matt spent much of his time in Sioux City swimming in the pool at his grandmother's apartment complex. They came back on Friday and all went out to dinner. "He was sitting across from me, and I remember asking him to quit stomping on my feet," Cheryl told me. "I think back to that now -- he couldn't sit still." At lunch after church a couple of days later, Matt's grandmother also noticed that he seemed restless and agitated.

The Millers were leaving early Monday morning for Wisconsin. On Sunday night, July 27, at around 11:30, Matt was still on the phone with his girlfriend. Mark went to his son's room to tell him to hang up and go to bed. "I didn't yell at him, but I was firm," Mark recalled. Matt threw the phone down and angrily slammed the door in his father's face, something he'd never done before. Mark went back to his room and asked Cheryl if he should go back in and talk to him. Cheryl thought they ought to wait until the morning. "He's finally just getting settled," she told Mark. "We don't want to rile him up again." When Cheryl went in to wake Matt up the following morning, she found him hanging by a belt from a laundry hook in his closet.

It didn't take long for Mark's thoughts to turn to the Zoloft: "It was the only thing that had changed that week. What else could we attribute it to? He's on a new medication, and he takes his life." When he spoke with Dr. Geenens later that morning, Mark asked if there was something in the drug that might have triggered suicidal behavior. The doctor told him that he wasn't aware of anything.

At the time, there wasn't much reason for Dr. Geenens to have known otherwise. Over the course of the past two years, however, the debate over whether antidepressants, particularly those known as S.S.R.I.'s -- selective serotonin reuptake inhibitors -- can trigger suicidal behavior in teenagers has migrated from the margins of the medical community to the front pages of newspapers. Adding to the controversy was public outrage at revelations that a number of pharmaceutical companies had deliberately withheld damning information about S.S.R.I.'s -- specifically, data from clinical trials that suggested that these drugs were both more dangerous and less effective for adolescents than millions of consumers had been led to believe.

Beneath the rancor was a complicated question. Patients who were being prescribed antidepressants were, by definition, vulnerable to suicidal behavior; it was difficult to determine where the effects of depression ended and the effects of the drug began. What's more, psychiatrists had been aware for decades that the risk of suicide increases when patients first start emerging from depression. Rollback, as this is known, is thought to be caused by a depressed patient's energy level rising ahead of his or her mood. No longer lethargic but still deeply unhappy, for a brief period some patients who had been too apathetic before to harm themselves now had the wherewithal to do so. Were patients taking S.S.R.I.'s experiencing rollback? Or was there something specific about S.S.R.I.'s that triggered suicidal impulses?

Things came to a head this fall with the F.D.A.'s affirmation of a link between antidepressants and suicide "ideation," or suicidal thoughts, in adolescents. Now all antidepressants, including S.S.R.I.'s like Prozac, Zoloft, Paxil, Lexapro, Luvox and Celexa, must carry a black-box warning label, the regulatory agency's strongest kind, making a possible suicide link explicit and all but ensuring a significant decrease in their use among young people. Far from providing closure on this complicated issue, though, the F.D.A. ruling may ultimately raise more questions than it answers.

Many child psychiatrists, who as a group have come to rely on S.S.R.I.'s to treat adolescent depression, seem to think the F.D.A. overreached. Studies have shown that one out of every 20 teenagers has suffered at least one bout of severe depression in his or her life, and adolescent depression can be especially difficult for doctors to manage. Teenagers are often resistant to psychotherapy, and unlike adults, who can quit a job or leave a marriage that might be aggravating their unhappiness, adolescents are almost always stuck with their lots. Doctors who treat young people -- child psychiatrists, pediatricians and general practitioners alike -- were wary of tricyclics, the previous generation of antidepressants, because of the risk of overdose. (The difference between an effective dose and a lethal one could be as small as six tablets.) But it is much harder to OD on S.S.R.I.'s. While the F.D.A. has approved only Prozac for depression in children and adolescents, doctors are free to prescribe any of these drugs "off label" for a patient group not specified on the packaging. And they have: between the early 90's and 2001, the prescription rate of antidepressants for those under 18 more than tripled. In 2002, 11 million antidepressant prescriptions were written for children and adolescents in the United States. Doctors recommended the drugs primarily to treat depression, but also for other emotional problems, from anxiety to shyness to obsessive-compulsive disorder.

The pharmaceutical companies are clearly making a product that most psychiatrists consider critical to treating depressed adolescents. Not prescribing these drugs may very well pose a greater threat than prescribing them. Studies have shown that areas in which antidepressant use among young people is widespread have experienced a dip in teenage suicide rates; according to Dr. John Mann, a suicide expert at Columbia University, fewer than 20 percent of the 4,000 adolescents who commit suicide in America each year are taking or have ever taken antidepressants. "It would be ludicrous to think that antidepressants could actually contribute to suicide in the United States in any kind of significant way," Mann told me. "The vast majority of teen suicides are actually committed in the absence of antidepressants."

The F.D.A. was essentially forced to strike a balance between the cost of the few and the good of the many. Did the agency give too much weight to the few? "For a family who has lost a child shortly after going on Prozac or some other S.S.R.I., I don't know what I can say to them," Dr. John Walkup, a child psychiatrist in Baltimore, told me. "But it's dangerous to make public policy based on rare and tragic events." Still, as Mark and Cheryl Miller will tell you, it's no less dangerous to ignore them.

In the months after Matt's death, the Millers confronted a sort of grief that most parents cannot begin to imagine. Both of them took a month off from work. They started every day with an early-morning walk around a lake near their house. They talked about Matt and all of the things they might have done differently. Jenny made the drill team that fall, and the Millers attended every Friday-night football game to watch her perform at halftime. They found that they felt better when they were out of the house, so they took lots of weekend trips and visited family members on Thanksgiving and over Christmas. They also went out with friends and colleagues as much as possible. "We both strived for normalcy again, which we knew would never be quite the same," Mark told me. Always religious people, the Millers immersed themselves even deeper in Christianity and met weekly with a Christian grief counselor.

But Mark was also hunting for answers. He soon found what he was looking for, or rather whom. During one Internet search, he happened across the Web site of Ann Blake Tracy, author of "Prozac: Panacea or Pandora?" a self-published 424-page screed against S.S.R.I.'s. Unless you are desperate, as most people typing words like "suicide" and "antidepressants" into Google most likely are, Tracy's Web site does not invite lingering. A picture of her in what looks like an out-of-focus 70's yearbook photo is surrounded by text that is the online equivalent of someone yelling outside the gate of the White House -- angry black-and-red type interrupted with WARNINGS about the dangers of going off these drugs cold turkey, and invitations to "click here" to read more personal horror stories.

Even among the most ardent opponents of S.S.R.I.'s, Tracy is an extremist. When I met her this fall, she told me that she began her campaign against antidepressants in 1989, when two friends in Salt Lake City, both Mormons, became alcoholics shortly after going

on Prozac. Since then, she has come to believe that antidepressants have played a role in just about every high-profile act of violence the world has seen, from the death of the Princess of Wales ("When Princess Di was killed," she said, "I called the police in Paris and said you've got a driver on Prozac") to the 1999 shootings at Columbine High School to the terrorist attacks of Sept. 11. But as an early anti-S.S.R.I. activist, Tracy was a godsend to families like the Millers, who were relieved to discover someone who could vindicate their hunch about these drugs.

Mark pulled Tracy's number from her Web site and called her. After hearing Matt's story, she steered Mark to some other sources, and he continued his research. He soon learned that the possibility of a link between S.S.R.I.'s and suicide had first been raised many years earlier by two Harvard Medical School psychiatrists, Dr. Martin Teicher and Dr. Jonathan Cole, in a paper published in early 1990 in *The American Journal of Psychiatry* titled "Emergence of Intense Suicidal Preoccupation During Fluoxetine Treatment." The doctors observed that six of their adult patients experienced "intense, violent suicidal preoccupation" within two to seven weeks of starting on fluoxetine, the generic name for Prozac, the first of the S.S.R.I.'s to reach the American market.

Teicher and Cole didn't want to overstate the significance of their findings -- five of the six patients had entertained thoughts of killing themselves at some point earlier in their lives -- but the onset of suicidal thinking had occurred so suddenly after the beginning of treatment that a prospective link was hard to ignore. "The purpose of this report is to suggest the surprising possibility that fluoxetine may induce suicidal ideation in some patients," the doctors wrote, reporting that the phenomenon appeared in about 3.5 percent of their patients taking the drug.

About a year later, Dr. Robert A. King, a child and adolescent psychiatrist at the Child Study Center at Yale Medical School, noticed something similar in several of his patients between ages 10 and 17. Dr. King had prescribed Prozac for 42 of his young patients suffering from obsessive-compulsive disorder (but not depression), 6 of whom experienced what he later described in *The Journal of the American Academy of Child and Adolescent Psychiatry* as "self-injurious ideation or behavior" -- behavior that none of them had ever experienced before. This was too small a sample to rule out the possibility of coincidence, but large enough for Dr. King to conclude that a narrow, still poorly defined group of patients on Prozac do seem to experience a range of adverse side effects from restlessness to self-destructive acts.

In September 1991, the F.D.A. convened a committee of 10 psychiatrists and psychologists to weigh in on the issue. After listening to hours of testimony from victims, depression experts and mental-health professionals, the panel decided that more research was needed but that for now there was no "credible evidence" of a link.

To Mark, this hardly sounded like a clean bill of health. Other things troubled him as well. He learned, for instance, that the F.D.A. had never approved Zoloft as a pediatric antidepressant -- and indeed that the drug's maker, Pfizer, had not been compelled to prove that it was safe for young people. He read about a phenomenon known as akathisia, or activation, a state of extreme agitation that can be induced by some psychotropic medications and can cause patients to behave in an uncharacteristically violent manner, which seemed to describe perfectly Matt's condition before his suicide.

Armed with this new information, Mark contacted Matt's psychiatrist, with whom he hadn't spoken since the morning of his son's death, and suggested that they meet. Mark knew that most psychiatrists would also have prescribed antidepressants for Matt, but he wanted to encourage the doctor to reconsider his approach to these drugs. To that end, he brought along all of his S.S.R.I. files. They ordered iced teas, and Mark said a short prayer asking that they honor Matt in their approach to this very difficult meeting. He began by telling Dr. Geenens that he and Cheryl blamed themselves for being too quick to embrace a "solution in a bottle" to Matt's unhappiness. "We wanted a miracle," Mark said to the doctor, "and we were willing to accept anything offered which promised an end to his depression, and to our agony." Mark explained to Dr. Geenens that he and Cheryl wanted him as a partner, not an adversary, and urged him to join their anti-S.S.R.I. cause by using his professional influence to encourage other physicians to exercise restraint when it came to antidepressants. In Mark's recollection, Dr. Geenens was polite but visibly uncomfortable. When the hour-and-15-minute meeting was over, Mark didn't get the feeling the doctor was going to change his prescription habits, let alone enlist in their fight against antidepressants. "He was relieved to know I wasn't planning a malpractice suit," Mark later reflected in an e-mail message to Ann Tracy. (Dr. Geenens did not respond to phone calls seeking comment.)

Mark and Cheryl did, however, decide to sue Pfizer. The next time Mark saw Dr. Geenens, two years had passed and the doctor had just given his deposition in the case. By this point, any lingering hopes that Dr. Geenens might emerge as an ally had long vanished. Not only had the doctor not responded to letters from the Millers' lawyer; he had also signed an affidavit for Pfizer in which he maintained that he had relied solely on his own professional judgment when prescribing Zoloft for Matt. At his deposition, Dr. Geenens also acknowledged that he was a member of Pfizer's Speakers Bureau, and that he gave -- and was still giving -- on the order of 50 Pfizer-sponsored talks a year for between \$300 and \$750 each.

By the time of Matt Miller's death in 1997, there had been hundreds of adult antidepressant lawsuits focusing on both violence and suicide, the vast majority of which were either dismissed or resolved out of court. Drug makers are rarely eager to settle these cases, largely because they don't want to encourage the small cadre of trial lawyers who make a living suing them. At the same time, the publicity involved with going to court, in addition to the risk of confronting a guilty verdict, is even less appealing. A result is a great many 11th-hour settlements. Indeed, as of 1997, only one antidepressant case, that of Joseph Wesbecker, a former employee at a printing plant in Louisville who went on a shooting spree about a month after starting to take Prozac in 1989, had ever gone to trial.

For all of the adult suits, however, there had been relatively few adolescent cases before *Miller v. Pfizer Inc.* Unlike product-liability lawsuits, which focus on whether a particular item malfunctioned, it's the psychic state of an individual that is contested in S.S.R.I. lawsuits. For the parents of that individual, the prospect of subjecting themselves to a grueling emotional autopsy of their lost child can be too much to bear.

The Millers agonized over the decision to sue Pfizer, waiting until August 1999, two years after Matt's death and fewer than 24 hours before the statute of limitations would expire, before finally filing the papers. They knew that pursuing the case was going to require considerable financial and emotional investments. While their lawyer was working on contingency, Mark had to cover all of the court fees, which would run into the tens of thousands of dollars. "We knew it was going to be painful, that we were going to be reopening all sorts of wounds," Mark told me, reflecting on the decision now. "I don't regret it. I don't think I'd be able to live with myself if I didn't feel like we had done everything we could for Matt. But I would tell anyone who asks me, don't do it. It's not worth it."

Mark and Cheryl hired Andy Vickery to represent them. A stocky and excitable Georgia-born, Yale-educated plaintiff's lawyer who wears black cowboy boots under his dark suits and drives a Jaguar, Vickery has handled little besides antidepressant cases for the past decade. This preoccupation has not made for the most stable existence. A few years ago, after a devastating defeat at the hands of Eli Lilly & Company -- "The verdict came down on Good Friday, and I felt like I'd been crucified" -- and a succession of costly dismissals, Vickery almost lost the ranch-style house he and his second wife bought and renovated in Houston's tony Tanglewood section, a few blocks away from former President Bush.

But there have been some big victories since. In addition to dozens of settlements -- the out-of-court agreements always stipulate that the terms remain undisclosed -- Vickery took GlaxoSmithKline to court on behalf of the relatives of Donald Schell, who went on a violent rampage hours after starting on the company's S.S.R.I. Paxil, murdering his wife, his daughter and his granddaughter before turning the gun on himself. In 2001 a Wyoming jury ordered the company to pay \$6.4 million to Schell's relatives, 40 percent of which went to Vickery, who paid off his mortgage.

Like any good trial lawyer, Vickery has internalized his clients' traumas and converted them into a cause. "We're on the right side, we've been on the right side all along and now the world is starting to realize that we are on the right side," he told me in his office in a Houston skyscraper last month. "I've believed it from the bottom of my heart all along."

The basic facts of the Miller case looked compelling to Vickery. It was a violent suicide, which fit the pattern he had observed in previous antidepressant cases. Also, Matt had hanged himself from a low-hanging hook; all he had to do was lower his feet to the floor and he would have saved himself. To Vickery, this suggested a sudden, drug-induced mania. "Matt Miller went from zero to 60 and hanged himself in a way that took Herculean effort," he told me.

Miller v. Pfizer Inc. was Vickery's second adolescent suit and his first suit against Pfizer. He had tangled with enough drug companies to know it wasn't going to be easy, but he soon found himself grappling with a uniquely ferocious enemy. In addition to interviewing virtually everyone whom Matt had come into contact with in the year leading up to his death, Pfizer burrowed deep into Mark and Cheryl's private life. The company's lawyers deposed the Millers' pastor and grief counselor, and subpoenaed the handwritten journal that Cheryl kept after her son's suicide as well as their daughter Jenny's diary. Pfizer even hired Park Dietz, a forensic psychiatrist and an expert in autoerotic asphyxiation, to file a report contending that Matt's suicide may have been a case of masturbation gone awry. Among the numerous other possible causes Pfizer raised during the pretrial proceedings, according to Vickery, was Matt's relationship with his father. Malcolm Wheeler, Pfizer's lead attorney, "said in open court that Matt Miller hated his father," Vickery said. "That's as low a blow as I've ever seen by any lawyer. . . . They are subhuman. I hate Pfizer."

Pfizer doesn't think much more of Vickery. "Andy is a very clever, articulate guy," Wheeler told me recently. "But he just throws stuff out there, and unless you compel him to provide the backup data and calculations, he'll just talk you to death."

The Millers' story of Matt's life, until its abrupt end, is one of a more or less normal adolescent boy experiencing more or less normal adolescent problems. The Pfizer lawyers set out to build a counternarrative. In the thousands of pages of depositions and expert-witness reports, there are moments when it seems that the Millers might not have grasped the depth of their son's emotional problems. "Matt Miller was a very, very tragically disturbed child who just didn't get help in time," as Wheeler put it.

That said, many of the details that Pfizer's lawyers brought out can be seen either as a serious indication of severe emotional problems or as standard teenage acting out. The only thing that's truly beyond dispute is that the emotional life of an adolescent boy is virtually impossible to parse.

Matt was clearly having trouble making friends at Harmony Middle School. One of his guidance counselors testified that other students described him as "weird," and noted that Matt had a tendency to alienate the more popular kids and to pick on the less popular ones. Still, a good deal of his behavior seems fairly typical for an attention-seeking teenage boy, things like baiting other students, joking about defecation, drawing lewd pictures. Matt's special-needs instructor, Roxana Rogers, recalled Matt breaking into tears during a conversation in the hallway because he felt so much pressure at home to be "perfect," also not an entirely unusual sentiment for the child of ambitious upper-middle-class parents.

Yet there were hints of violence and self-destructiveness as well. Matt was disciplined several times at school, once for hitting a classmate with a chain, another time for supposedly threatening a fellow student with a piece of a plastic mirror. Rogers once saw Matt banging his head against his locker and remarked in her deposition that he shuffled his feet and walked around the classroom at inappropriate times -- which sounds a lot like the sort of restlessness that Cheryl observed the week he was on Zoloft.

There was every indication that Matt was depressed. He scored a 13 on the Children's Depression Inventory, which Dr. Geenens considered "significant" and indicative of moderate depression. There was also evidence that he had talked about taking his own life before doing so. Chad Brownel, Matt's only close friend at Harmony, said that Matt mentioned suicide "hundreds of times" during the six months that they'd known each other. And toward the end of the school year, when Roxana Rogers asked Matt about his plans for the summer, Matt said that if his parents sent him away to camp, he would kill them and then kill himself. Rogers considered the remark and his behavior problematic enough to call his mother and schedule a meeting.

What's more difficult to determine is whether Matt would have acted on these thoughts had he not taken Zoloft. Suicidal ideation is common among depressed adolescents, but completed suicides are rare; some child psychiatrists have come to see suicide attempts more as appeals for help than as expressions of a determination to die. One question on Matt's Children's Depression Inventory asked him to choose one of the following: "I do not think about killing myself"; "I think about killing myself, but I would not do it"; "I want to kill myself." Matt answered that he thought about killing himself but would not do it.

After going on the medication, Matt told his friend Chad that the pills were giving him insomnia. Chad also noticed that Matt seemed "a little more wild" and more energetic. Instead of watching "Beavis and Butt-head" or playing the video game Mario Kart, which they usually did, Matt wanted to ride bikes to Taco Bell. Matt could have been going through rollback, a relatively common reaction in the early stages of treatment. Or he might have been experiencing activation, the dangerous side effect that Mark had read about online. Was it the Zoloft per se? Or was Matt's suicide a tragic by-product of the process of getting better?

Those were questions for the jury to wrestle with. But before *Miller v. Pfizer Inc.* could go to trial, Vickery had to show general causation -- in other words, that S.S.R.I.'s cause some people to become violent or suicidal. He had done this in all of his previous antidepressant cases. There had been no shortage of hard-fought battles -- for the drug makers, causality was their first line of defense -- but he had never failed to clear that hurdle.

Vickery turned to Dr. David Healy, an expert witness whom he had used several times before, to present the court with proof of a plausible link between S.S.R.I.'s and suicide ideation. A specialist in psychological medicine at Cardiff University in Wales, Dr. Healy had first warned about the potential for suicidal acts among patients on antidepressants in 1990. Since then he has published several provocative academic books on the subject, most recently "Let Them Eat Prozac"; as a frequent expert witness in S.S.R.I. cases, Dr. Healy has spent quite a bit of time rooting around in the basements of drug companies searching for suppressed information on antidepressants. Conversely, the drug companies have spent quite a bit of time and money attacking Dr. Healy's bona fides and trying to discredit his research as "junk science."

The judge appointed two independent medical experts to evaluate Dr. Healy's work. Dr. Healy submitted his data to the court. The experts were flown to Kansas City. Over two days of hearings, they raised questions about Dr. Healy's methodologies, and the judge ultimately barred his testimony. Without it, the Millers had no proof of a causal link. Their case was dismissed before it had even begun.

Last February, six months before the F.D.A. acknowledged a link between S.S.R.I.'s and suicidal thoughts, a Kansas appeals court affirmed the ruling. By this point, Vickery had spent more than \$200,000 on the Millers' suit. One final, long-shot option remained: the Supreme Court.

Mark and Cheryl's lawsuit may have been foundering, but they were finally making some headway in their public campaign against S.S.R.I.'s.

Not long after Matt's death, Mark helped Ann Tracy create a Web site for her nonprofit group, the International Coalition for Drug Awareness, where families with similar experiences could post their stories and learn more about the side effects of antidepressants. He soon found himself at the center of a growing community of "survivors." For several years, this loose network of families tried vainly to draw attention to their cause; but then in late 2003, when the Medicines and Healthcare products Regulatory Agency -- the U.K.'s equivalent of the F.D.A. -- advised against the use of all S.S.R.I.'s except Prozac in patients under 18, the outside world suddenly became interested.

The British decision had been the unintended consequence of GlaxoSmithKline's request to market Seroxat -- known as Paxil in the United States -- to children with social phobias and O.C.D. As part of the application process, GlaxoSmithKline submitted what it believed to be all the data required for approval. The M.H.R.A., however, wanted to see more, specifically all of the company's trials on Paxil and adolescent depression, many of which had never been published.

The trials were submitted, and the British regulatory agency did not like what it saw. Not only did the data suggest that Paxil caused an increased suicide risk in children; several of the trials also failed to demonstrate that the drug performed any better than a sugar pill. Within a matter of weeks, the M.H.R.A. publicly announced that Paxil should not be used in children. Not long after came the broader warning against all antidepressants except Prozac.

By this point the F.D.A. had also seen GlaxoSmithKline's unpublished Paxil data and was deep into an investigation of its own. Over the summer of 2003, the regulatory agency warned doctors against using Paxil in children under 18, and in the fall of that year it publicly acknowledged that it couldn't "rule out" the possibility that a number of other antidepressants might also increase the risk of suicide in adolescents.

For the most part, though, the F.D.A. approached the issue more gingerly than its British counterpart. Agency officials wanted to see additional data before taking any further action. The problem was that no large-scale studies existed. Until they did, the F.D.A.'s only option was to combine a number of small, disparate trials conducted by drug makers in the late 90's and try to draw some meta-conclusions. None of those trials had been designed to assess suicide risk, but for the time being they were all that the agency had to go on.

In late 2003, the F.D.A. asked the pharmaceutical companies for all relevant information on every so-called adverse event in each of these pediatric antidepressant trials. A group of independent researchers from Columbia University was commissioned to review the 427 cases the companies produced. With the help of a separate team of suicide experts, the Columbia researchers set about classifying them as suicidal or not.

It was not an easy task. There wasn't a single successfully completed suicide among the cases provided, which meant that the researchers had to decipher suicidal thoughts or actions based on brief, vague narratives. Also, the information the researchers were given was often misleading. For instance, one child had taken 11 pills impulsively before going to school; this was classified a medication error. Another had wrapped a cord around his neck; this was labeled "hostility." At the same time, relatively harmless acts -- including a girl slapping herself in the face -- had been listed as "suicidal." But the biggest challenge was a theoretical one. "There's a lack of conceptual clarity about how you even define a suicide attempt," said the principal investigator of the Columbia team, Kelly Posner. Self-mutilation, for example, is common among depressed children, but how can you know whether it was done with suicidal intent?

The F.D.A. did not want to issue a ruling until the Columbia group finished, but one F.D.A. drug-safety analyst, Andrew Mosholder, did not want to wait. Mosholder was assigned to review GlaxoSmithKline's Paxil trials many months earlier and noticed that a number of events that looked a lot like suicide attempts had been subsumed under the euphemistic term "emotional lability." Since then he had conducted his own analysis on several antidepressants and determined that children on them were almost twice as likely to experience suicidal thoughts or exhibit suicidal behavior as those taking placebos. Mosholder wanted to go public, but the F.D.A. wouldn't allow it, out of concern that his conclusions would only further fan the flames.

Mosholder's findings were soon leaked to The San Francisco Chronicle. Before long, the story was splashed across the nation's newspapers. Families like the Millers had a new hero, a would-be whistle-blower who had been silenced by his own government.

The publicity surrounding Mosholder's conclusions also piqued the interest of several politicians, most notably Senator Charles Grassley of Iowa, who wondered if the F.D.A. might be deliberately suppressing information about the dangerous side effects of antidepressants. Tom Torlakson, a state senator in California whose niece had committed suicide after starting on Celexa, convened

his own hearings on the issue. In New York, Attorney General Eliot Spitzer sued GlaxoSmithKline for concealing vital information from the public about the safety and efficacy of Paxil. (The two parties settled, with the company agreeing to pay \$2.5 million to New York State.)

In the middle of September, with the Columbia study complete, the F.D.A. convened hearings on the issue. The anti-S.S.R.I. lobby was galvanized; dozens of families came to Maryland to tell their harrowing tales. (Only one mother rose to defend the drugs.) Kathleen Bodnar spoke about her 21-year-old daughter -- Torlakson's niece -- who threw herself in front of a BART train in San Francisco last spring, shortly after being prescribed Celexa. A number of families blasted the drug makers for suppressing data and chided the F.D.A. for not taking stronger steps earlier. "The blood of these children is on your hands," Mathy Downing, who found her 12-year-old daughter hanging from the valance above her bed in January, a few days after taking 100 milligrams of Zoloft, told the panel.

But for all of the impassioned testimony, the most important presentation came from an F.D.A. medical reviewer, who offered his analysis of the long-awaited Columbia review. The risk of depressed children engaging in suicidal acts was 1.78 times greater for those who had been treated with antidepressants than for those who had been given placebos. At the end of the hearings, the panel voted to add to all antidepressants black-box warnings cautioning that the drugs can trigger suicidal behavior in adolescents. "A 'BLACK BOX'! -- Wow," Mark wrote in a mass e-mail message to fellow survivors. "Could we have ever guessed they would go this far?"

When I visited Mark and Cheryl in late September, they were optimistic that the F.D.A. ruling would breathe new life into their lawsuit against Pfizer. "The whole summary judgment was granted based on us not being able to prove that there is evidence of suicidality," Mark told me. "Now the F.D.A. has basically validated our position."

A couple of weeks later, though, the Millers' five-year battle with Pfizer was over. The Supreme Court declined to review their case.

The black-box warning seems sure to put off parents, not to mention doctors, who will now have to assume a greater share of the responsibility when prescribing these drugs. "A black box is scary," Dr. Walkup, the Baltimore psychiatrist, told me. "In order for you to go against it, you've got to summon a certain amount of courage."

While many child psychiatrists are unlikely to change their attitude toward S.S.R.I.'s, most pediatricians and general practitioners, who until now have written the bulk of these prescriptions, no doubt will. This could mean a lot of untreated children. There are only 7,400 child and adolescent psychiatrists in America; even in areas with high per-capita concentrations, the average wait to see one is six weeks. There is also the matter of cost. Many child psychiatrists charge steep hourly rates that are only partly offset by health insurance providers.

For doctors who don't have much experience with S.S.R.I.'s, prescribing them for adolescents does seem daunting. Teenagers can't always be counted on to take their pills, and as with many medications, sudden withdrawal from S.S.R.I.'s can be dangerous. Perhaps an even bigger challenge is teasing out bipolar from unipolar depression, a critical distinction given that S.S.R.I.'s can trigger mania in a small number of bipolar adolescents. Even for those children who do respond well to S.S.R.I.'s, finding the right dose -- and, in some cases, the right combination of drugs -- can be tricky. Some children metabolize medicine more quickly than adults, others more slowly.

Still, over the past few months I have spoken with a number of teenagers (and their parents) whose lives have been saved by antidepressants. "Had it not been for these two medications, I would not be here," Kristen Conklin, a 21-year-old graduate student at Widener University in Pennsylvania, told me. Conklin started taking Wellbutrin five years ago after a failed suicide attempt. A year later, her doctor added Effexor as well. "I can look back on my life now and know that if I had to feel that way again, I probably would think it's a smart idea to commit suicide. It took some time to figure out what works, but they have helped me in ways that I can't even begin to explain."

The numerous antidepressant success stories have none of the drama of the comparatively few failures, but that doesn't necessarily make them any less important. Conklin's psychiatrist, Dr. Peter Kahn, told me that he and many of his colleagues have known from the beginning that S.S.R.I.'s are potent drugs. They always start with low doses and raise them gradually -- their mantra is "start low, go slow" -- and supervise their patients closely, particularly in the first few weeks after beginning treatment. (Kahn makes sure that all of his patients have his cellphone number.)

Child psychiatrists have an almost universal faith in S.S.R.I.'s; the problem is that there isn't much clinical data to support their conviction. Why? One explanation is that the limited number of studies that have been done on adolescents and antidepressants were almost all substandard. Most of them were conducted in response to a 1997 Congressional act intended to encourage drug makers to

undertake more pediatric trials. Companies could extend their patents for a drug for six months by testing it on children -- whether the trial demonstrated that the drug worked or not. There was, in other words, a powerful incentive to do the trials, but no incentive to do them well. Among other flaws, patients were enrolled at multiple sites in a number of different countries, which made quality control very difficult. In clinical parlance, the trials were susceptible to a lot of "noise," factors that obscure rather than illuminate the effects of a given drug.

A much more carefully conducted Prozac study was published this year in *The Journal of the American Medical Association*. The results pleased defenders of S.S.R.I.'s: 61 percent of the patients treated with Prozac improved, compared with only 35 percent of those given sugar pills. "This study should put to rest doubt about whether these drugs work in teenagers with severe depression," said one of the report's authors, Dr. Graham Emslie. (While the study was sponsored by the National Institute of Mental Health, Emslie has received money from a number of drug companies in the past.) What the study didn't do is put to rest concerns about suicidal side effects. No patients in the control group tried to commit suicide, while six of those treated with Prozac did.

More trials are under way now, but it may be years until the F.D.A. will have enough fresh data to revisit the subject. Until then, doctors will have to decide whether they want to go up against a black-box warning. And parents will have to decide whether they want to trust their doctor's judgment.

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Thirteen-year-old Matt Miller killed himself shortly after he started taking Zoloft. His parents and those of other teenage suicides recently won a victory when the F.D.A. issued a strong warning about adolescent use of antidepressants.



Collier Schorr for The New York Times

Mark and Cheryl Miller, Matt's parents, seven years later.