



pregnant pause

With a flurry of recent reports challenging the safety of antidepressants for unborn babies, doctors and concerned mothers-to-be are rethinking the guidelines. Alexis Jetter reports.

PRECIOUS CARGO
MANY DOCTORS ARE
REFINING THEIR DRUG
GUIDELINES FOR
EXPECTANT MOTHERS.

Oina Fromm can be absurdly cautious. She won't even talk on the phone during a thunderstorm. When she got pregnant in 2004, Fromm was so nervous about exposing her baby to drugs that she even balked at taking prenatal vitamins. "Are you sure these are OK?"

Fromm, then 38, asked her physician.

An engaging, green-eyed woman who lives in Columbus, Ohio, Fromm wasn't taking any chances with her pregnancy. She took only cold showers (to avoid overheating the baby), avoided yogurt (too much bacteria), and incinerated her chicken (to kill any lurking salmonella).

"I was very conscious of everything I put into my body," Fromm says—

including a small dose of Paxil, the antidepressant that she took daily to ward off panic attacks. But Fromm's doctors said she needn't worry. Her family physician opened a copy of the *Physicians' Desk Reference* to the entry on Paxil. "We read it together," Fromm recalls. "It said it was safe to take while pregnant."

But just two hours after Mark

was born, "we knew something wasn't right," Fromm says. When nurses wheeled her out of the recovery room, her husband met her with the bad news: Mark's heart wasn't normal. His tricuspid valve had never formed. To survive, he needed three risky operations to connect his right atrium to his pulmonary artery and close a hole in his heart.

Doctors could find no cause for Mark's malformed heart. But in late September 2005, Fromm flipped on the evening news—and caught her breath. "Across the bottom of the TV came a ticker," she recalls. "BABIES WHOSE MOTHERS TAKE PAXIL WHILE PREGNANT HAVE A HIGHER RISK OF HEART DEFECTS."

The U.S. Food and Drug Administration had just dropped a bombshell: A large Swedish study revealed that Paxil doubled the rate of heart defects in newborns. Some of the

abnormalities healed on their own, while others required major surgery. But FDA officials weren't taking any chances. In December 2005, the agency issued a public advisory urging doctors not to give Paxil to pregnant women.

Recent findings have sharply heightened those concerns. The U.S. Centers for Disease Control, Boston University, and the University of Montreal have all found that Paxil can triple a baby's risk of developing a heart defect like Mark Fromm's. "When my study on Paxil first came out, I was really walking on eggshells, and I was criticized," says Anick Bérard, Ph.D., professor of pharmacy at the University of Montreal. "But now other people have done the studies, too. And I'm much more comfortable saying that Paxil is a bad drug to take during pregnancy."

The increased likelihood of these defects is small: fewer than one in 500 births. "But if you're that one mother, it's devastating," says Carol Louik, Sc.D., an epidemiologist at Boston University's Slone Epidemiology Center. "So depending on the severity of your depression, you might opt for another drug—or no drug." That's because Paxil is not alone among antidepressants in its potential to harm infants. Prozac and Zoloft can also double the risk of heart abnormalities in babies, new research suggests. Some doctors aren't so sure: A few studies have found no proof that Paxil—or any antidepressant—poses a danger to infant hearts.

But birth defects aren't the only worry. There's mounting evidence that most of the top-selling antidepressants—the selective serotonin *health >148*

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reuptake inhibitors, known as SSRIs—dramatically increase the chances that a baby may be miscarried, be born prematurely or too small, suffer erratic heartbeats, and have trouble breathing. Yet SSRIs are the antidepressants most often prescribed for women of childbearing age.

Taken together, the new data have caught many experts by surprise—and some are changing course. Pregnant women with only mild depression, they now say, should think twice about using SSRIs.

“We’re refining our advice,” says Rita Suri, M.D., an associate professor of psychiatry at the University of California at Los Angeles. Antidepressants are still essential for expectant mothers who are unable to function without medication. “But for women with mild symptoms, we’re more likely to recommend nonpharmacological treatment first.”

That’s a potentially significant shift. In recent years, psychiatrists have been warning women that depression posed a greater threat to their unborn child than any medication they might take to relieve it. Depressed women are more likely to smoke, eat poorly, drink excessively, take drugs, and behave in other ways that might put them, and their fetuses, at risk. Studies have linked untreated depression with preterm birth, preeclampsia, and poor mother-infant bonding. Psychiatrists say the biggest danger is relapse—the possibility that women who quit their medications during pregnancy may sink back into despair that can linger for months, even years.

An increasingly vocal minority of doctors, however, says women have been misled about the benefits—and risks—of antidepressants during pregnancy. “Women and their providers have been told that even mild depression or anxiety will hurt their baby,” says Adam Urato, M.D., assistant professor of Maternal-Fetal Medicine at Tufts University School of Medicine. “And these antidepressants are portrayed almost like prenatal vitamins that will level out their mood and lead to a healthier baby. But antidepressants have not been shown to decrease rates of miscarriage

or birth defects or low birth weight. On the contrary, they’ve been shown to increase those problems.”

Since pregnant women are routinely excluded from clinical tests of new drugs—and, until this year, the FDA didn’t require drug companies to run clinical tests on their medications *after* they go on the market—we know aston-

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ishingly little about how most drugs affect the unborn child. “Pregnant women and the doctors who treat them are operating in a vast sea of ignorance,” says Boston University’s Louik.

What alarms doctors is the sheer number of pregnant women who use SSRI antidepressants—perhaps as many as 250,000 in the U.S. each year—when we still know so little about how the drugs affect babies. Until recently, for example, researchers couldn’t pinpoint what was causing birth complications in children born to depressed or anxious women: Was it the underlying malaise, the drugs used to treat it, or both?

Fortunately, scientists have begun to solve that riddle. Three years ago developmental pediatrician Tim Oberlander, M.D., at the University of British Columbia, traced the birth outcomes of nearly 120,000 women. His finding: Compared with babies born to depressed mothers who didn’t take SSRIs, infants prenatally exposed to the drugs were more likely to be born too small and have trouble breathing. “It’s not the mother’s mood,” Oberlander says. “It’s the medication.”

UCLA’s Suri didn’t initially believe that medication would have that effect. But after comparing two similar groups of depressed pregnant women at her own clinic, Suri found that infants born to women taking SSRIs were three times more likely to be premature, although, on average, the babies were born only a week early. The higher the antidepressant dose, the greater the risk. She found that untreated mild

depression, on the other hand, seemed to have no effect on prematurity.

Some of this is news—and some isn’t. Doctors have known since 1996 that SSRIs, which include Prozac, Paxil, Zoloft, Celexa, Luvox, and Lexapro, can trigger what’s called neonatal withdrawal syndrome in up to a third of exposed infants, causing respiratory

distress, hypoglycemia, jitteriness, irritability, and convulsions in infants for a few days or weeks after birth. “Physicians would have to be deaf and blind not to know about these birth complications,” says Tina Chambers, Ph.D., a birth-defects researcher at the University of California at San Diego. “The question is, Are there any long-term consequences, and are they severe?”

She has found at least one: Babies exposed to SSRIs in the second half of pregnancy are six times more likely to suffer from a life-threatening breathing disorder called persistent pulmonary hypertension of the newborn. The condition ordinarily strikes only one or two infants in 1,000. Among babies whose mothers took SSRIs, Chambers found, rates jumped to between six and twelve per 1,000.

Alexis McLaughlin’s youngest child, Evie, was born with the breathing disorder eleven years ago. McLaughlin, then 33, had been taking Paxil for three years to ease the crushing postpartum depression that had plagued her since she gave birth to her third child. But those crying jags, she says, were nothing compared to the shock of seeing her seven-pound daughter fighting for breath. “It was pretty horrifying,” recalls McLaughlin. “Evie couldn’t get air into her lungs. She was panting about 70 times a minute.”

Evie was placed on various respirators and, over time, recovered. But McLaughlin says she’s never gotten over the scare. “It’s difficult because you need good mental health and a healthy baby,” she says. “But if I had known this drug could cause *(continued on page 232)*

PREGNANT PAUSE

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problems, I would have found some other way to deal with my depression.”

Scientists aren't quite sure why antidepressants could so powerfully affect a developing fetus. But timing is everything, they say. Neonatal syndrome and persistent pulmonary hypertension appear to strike infants who've been exposed to antidepressants late in pregnancy, after their organs have formed normally. Birth defects, however, take root in the initial weeks and months of life—when, coincidentally, antidepressants first cross the placenta and reach the fetus.

It turns out that serotonin, the neurotransmitter that helps regulate mood, also sends crucial developmental signals to the fetal heart, lung, and brain. Some scientists think that SSRIs, which prevent the body's natural absorption of serotonin, could be tampering with essential cell growth. “Never before in human history have we artificially changed the architecture of brain development,” says Feng Zhou, Ph.D., of the Indiana University School of Medicine. “We always predicted that developmental exposure to these drugs would have some deleterious effects,” agrees Jean Lauder, Ph.D., of the University of North Carolina School of Medicine. “But no one was listening back then.”

Nancy Pekarek, a spokeswoman for GlaxoSmithKline, Paxil's maker, says the company has acted responsibly, noting that until 2005 there was no evidence that Paxil caused birth defects. “As soon as GlaxoSmithKline became aware of a potential increased risk, it notified the FDA, updated the Paxil label, and undertook further investigation.”

Doctors say there's no easy formula for figuring out what medication, if any, expectant mothers should take to control their depression. “It would be really nice if there was one clear answer, and if a drug was either completely good or completely bad,” says UCLA's Suri. “But it's not like that.” Even with Paxil, “you can always come up with a case where it makes much more sense to take it,” says Katherine Wisner, M.D., a professor of psychiatry and obstetrics at the University of Pittsburgh School of Medicine. “I had a patient who became suicidal every time she stopped taking Paxil. So when she got pregnant, she decided to stay on the drug.”

Many doctors say it's getting increasingly difficult to give good advice. A recent study in *The New England Journal of Medicine* found that drug companies

publish only two thirds of antidepressant studies—usually, the most positive ones—misleading doctors into thinking the drugs are more effective than they really are.

On top of that, argues Adam Urato, only one voice is reaching the ears of most women's health practitioners: that of a small coterie of influential doctors who he says underplay the dangers of antidepressants. Many of these physicians have accepted lucrative speaking fees and consulting contracts from the drug companies. And yet—sometimes without divulging those connections—these same doctors are shaping treatment guidelines. “We want and need expert opinion that's free from industry influence and from the appearance of bias,” Urato says. “It's just outrageous that doctors have to work without that.”

Gina Fromm says she'll never get over the sense that, somehow, her son's heart condition is her fault. “This person that I would have done anything to protect—how could I have harmed him?”

Mark Fromm, now four, is an energetic, cheerful boy who shows few outward signs of his weak heart. But he's smaller than most children his age, and he tires more easily. Mark has learned, instinctively, to stop and squat to increase the blood flow when he feels dizzy. But the big unknown is how long Mark Fromm will be healthy.

“If the drug company had provided the information that this medication may have these effects, I would never have done anything to jeopardize my son,” Fromm says. “But I was robbed of the ability to make that decision.”

The ultimate irony is that Fromm no longer needs the medication. She's alleviated much of her anxiety through a healthy diet and moderate exercise. “It's easier to take a pill,” she says. “But over the long run, that's not the best solution. It certainly hasn't been the best thing for my life.” □

THE GODFATHER

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worked at Halston for a summer, his very first job, where he met Stephen Sprouse, who became a lifelong friend (until his death in 2004); they bonded over their disdain for the older designer. “Everyone would be called into this room, and he would stand there like . . . like . . . Kay Thompson. ‘Think Pink!’ Oh, he drove me crazy.” Worse yet, Halston designed a uniform for his young charge to wear: a black ribbed short-sleeved shirt and

black slacks. “He would yell at me and say, ‘Don't just sit around, Pocahontas! You have to do something!’”

In the early 1970s, Meisel, drawings in hand, went literally across the street from Parsons to Fairchild Publications, where *Women's Wear Daily's* offices were, and met with the art director, who hired him. Ben Brantley, André Leon Talley, and Bonnie Fuller all worked there.

It was here that Meisel met the fashion illustrator Kenneth Paul Block, the closest he has ever come to a mentor. “He taught me so much about everything,” says Meisel. “He would sit there with this long cigarette holder and a polka-dot bow tie, always a sports jacket, immaculate. He never lost his temper. He had so much style, so much class, so much chic.” Block would sometimes draw Meisel, whose androgynous good looks allowed him to stand in for a woman. (In Block's fantastic book, *Drawing Fashion*, which came out in 2008, there is a spread devoted to Meisel that is titled simply “Steven.”)

While at *WWD*, Meisel started traveling back across the street to Parsons to teach illustration. A young student named Marc Jacobs tried to take his class. “I had seen Steven out and about in New York with his little entourage—Teri Toyne and Stephen Sprouse and Anna Sui—but I didn't know him,” says Jacobs. “But I was such a fan of his drawings and just thought he had a really great eye. I was very disappointed because the first night when I showed up, it was announced that he wasn't going to be teaching it, because he was off on a photography assignment for *W*. He had just started taking pictures.”

By the early eighties, Meisel intuited that fashion illustration was on its way out. “I needed to do more,” he says. He started by snapping pictures of his girlfriends. One day, he met a girl shopping and asked if she would sit for him. She was Valerie Cates, the sister of Phoebe Cates, then a model represented by Elite. “So I would shoot Valerie and Phoebe on the weekends,” says Meisel. The *B-girls*—the bookers—at Elite loved Meisel's photographs, so they asked him to do test shoots with other newly signed girls. Elite supplied him with film and processing, and Meisel began to hone his craft—while also learning how to make fourteen-year-old girls feel comfortable posing as women. From the very beginning, he did the hair, makeup, and styling all by himself. “I didn't know any different,” he says.

An editor at *Seventeen* saw his pictures in a model's portfolio and called to offer