

Exposure to SSRI Antidepressants In Utero Causes Birth Defects, Neonatal Withdrawal Symptoms, and Brain Damage

Peter R. Breggin, MD
Ginger Breggin

Founding Editors and Consultants, EHPP
Ithaca, New York

Pregnant mothers should avoid taking SSRI antidepressants—they are hazardous to the developing fetus, cause withdrawal symptoms in the newborn baby, and induce biochemical and morphological abnormalities in the brain. If pregnant mothers need help with sad or anxious feelings, they should seek counseling or psychotherapy, especially family therapy involving the child's father, as well as other sources of emotional support.

Keywords: antidepressants; birth defects; pregnancy; SSRIs; psychiatric drugs; depression

On June 28, 2007, more than 250 headlines around the world promised that SSRI antidepressants (such as Prozac, Paxil, Zoloft, and Celexa) were safe for pregnant mothers and their developing babies. "Mom's Antidepressant Use Poses Little Danger to Baby" heralded the *Washington Post* (Gardner, 2007). "Antidepressants Pose Low Birth Defect Risk" claimed *Boston Globe* (Donn, 2007). The *New York Times* ran with "Antidepressants Rated Low Risk in Pregnancy" (Carey, 2007). The *Wall Street Journal's* coverage was titled "Reassurance on Antidepressants in Pregnancy" (Seward, 2007). The day before the news stories broke, the Centers for Disease Control heralded the news in advance with a press release, "New Study Finds Few Risks of Birth Defects From Antidepressant Use During Pregnancy" (CDC Division of Media Relations, 2007).

The headlines and the CDC press release were misleading. In the CDC study, several severe birth defects were doubled or nearly tripled in frequency when SSRIs were taken in the first trimester.

SSRI antidepressant use by pregnant mothers in the first trimester of pregnancy was shown to have previously unidentified links to three birth defects in two new studies reported in the *New England Journal of Medicine*. One study was associated with the CDC (Alwan, Reefhuis, Rasmussen, Olney, & Friedman, 2007) and the other with Boston University (Louik, Lin, Werler, Hernandez-Diaz, & Mitchell, 2007).

The study led by Sura Alwan and colleagues involved the CDC and showed the following:

Anencephaly—birth without a forebrain—showed a 2.4 times greater occurrence in women who had taken SSRIs in the first trimester. This is a catastrophic, fatal birth defect that is not correctable.

The study examined histories of 9,622 cases of birth defects and 4,092 controls who were infants born without birth defects. Some stillbirths (occurring at 20-plus weeks gestation) were included, but if anencephaly resulted in a spontaneous miscarriage or a planned abortion, these events would not appear in this study's findings.

Omphalocele—babies born with organs outside the body—was found to be present 2.8 times as often in the SSRI-treated mothers compared to the control group. Some media portrayed this birth defect as a small hernia of the umbilical cord—but severity of the condition varies, usually requires surgery as well as weeks to years of adapting, and can be life-threatening.

Craniosynostosis—the premature closing of one or more sutures or fibrous joints knitting the bones of the infant's skull—showed 2.5 times more prevalence in infants exposed in utero to SSRIs. This condition also varies in severity. It can be primarily a bone condition of the skull or it can be secondary to an underdeveloped brain in the infant.

Craniosynostosis occurs in about 4 per 10,000 births according to the National Institutes of Health. A 2.8 times greater occurrence of this condition will cause 2,305 more U.S. babies to be born each year with this birth defect as a result of their mothers taking SSRIs in the first trimester of pregnancy.¹

In the abstract to the report, the CDC study claimed to find no association between SSRI use in pregnancy and heart defects in neonates. However, the study found that obese women who did not use SSRIs had an increased risk with heart defects and that *obese women who did use SSRIs had an even greater risk of neonatal heart defects with an adjusted odds ratio of 5.9 (95% CI, 2.4–14.3)*.

The second study, by Carol Louik and her colleagues, did *not* find an overall correlation between SSRI use and the two defects, craniosynostosis and omphalocele. It did, however, find an association between sertraline (Zoloft) and both omphalocele and septal defects in the heart, and between paroxetine (Paxil) and right ventricular outflow tract obstruction defects of the heart.

Louik made many reassuring statements to the press about the safety of SSRIs in regard to specific birth defects. Her study had funding from two pharmaceutical companies, including GlaxoSmithKline, the manufacturer of Paxil (Seward, 2007), one of the most implicated antidepressants in regard to birth defects. In part due to Louik's highly publicized comments, headlines throughout the country minimized the risk.

Nor are these the *only* birth defects related to SSRI consumption during pregnancy. In December of 2005, the FDA issued a Public Health Advisory warning that the risk of congenital malformation, especially of the heart, was increased by the consumption of Paxil in the first trimester of pregnancy. The American College of Obstetricians and Gynecologists (ACOG, 2006) warned pregnant women to avoid taking Paxil and also showed concern about any antidepressant exposure during pregnancy. Yet the CDC and researchers are using the new studies to exonerate SSRIs. This is clearly an orchestrated attempt to reassure the public after the FDA's and ACOG's earlier warnings.

The 2007 CDC study offers an illuminating discussion of other study findings concerning abnormal in utero development, including delayed ossification (bone development). "A specific role of serotonin in cardiac and craniofacial morphogenesis in the rodent embryo has also been established," according to Alwan et al. (2007) in the CDC study.

Newborns also go through withdrawal when their mothers have taken antidepressants during pregnancy. One study found a rate of 30% in neonates exposed in utero to SSRIs (Levinson-Castiel, Merlob, Linder, Sirota, & Klinger, 2006). Withdrawal symptoms in

infants reported in various studies include irritability, high-pitched or weak crying, tremors, poor muscle tone, disturbed sleep, rapid breathing and respiratory distress, and increased admissions to the neonatal intensive care unit.

In addition, children exposed in utero to SSRIs have an increased risk of developing persistent pulmonary hypertension at birth. This disorder, which is estimated to occur in 1 or 2 infants for every 1,000 live births, will occur six times more frequently in children exposed to SSRIs after the 20th week of pregnancy. The disorder causes “significant morbidity and mortality” (Food and Drug Administration, 2006, p. 1). These children have difficulty getting enough oxygen into their lungs. The two recent studies in the *New England Journal of Medicine* limited themselves to SSRI exposure during the first trimester; but the neonatal pulmonary hypertension studies show that some hazards will develop during exposure later in pregnancy. Again, the CDC and the researchers drew no attention to these hazards.

Withdrawal reactions confirm further potentially disastrous consequences of SSRIs to neonates that the CDC and the researchers failed to consider in their reassuring statements. Withdrawal reactions confirm that the brain of the fetus has been exposed to SSRIs and that it has suffered significant functional changes. Serotonin is intimately involved in the development of the brain in utero, and SSRIs inhibit normal brain cell development (Norrholm & Ouimet, 2000). It is also known that SSRIs cause myriad toxic effects on neurons in living animals, causing brain cells to grow abnormally (Kalia, O’Callaghan, Miller, & Kramer, 2000; Wegeer et al., 1999). Unavoidably, similar effects must be taking place in the human fetus exposed to SSRIs. In addition, the SSRIs cause measurable biochemical imbalances in the brain, many of them persistent or permanent (de Montigny, Chaput, & Blier, 1990; studies recently reviewed in detail in Breggin, 2008, pp. 174–180). At present we have no way of measuring the harmful impact on the growing brain and the future mental life of the fetus; but exposure to SSRIs is bound to be harmful in the long run.

Also alarming is the *Wall Street Journal* report that antidepressant use during pregnancy has jumped from 5.7% in 1999 to 13.4% in 2003 (Seward, 2007). The data was based on Medicaid patients and could be higher for the general population with its greater access to medical care.

The reassuring attitude promoted in the CDC’s press release flew in the face of evidence linking SSRI exposure during pregnancy to increased birth defects, and the additional evidence of SSRI toxicity in the developing brain. It proclaimed that the study “found no significant increase in the risks for the majority of birth defects assessed” (CDC Division of Media Relations, 2007, p. 1). But I am unaware of *any* prescribed medication that increases birth defects “for the majority of birth defects.”

Women and their doctors who only catch the headlines created by these studies are being misled. SSRIs should never be used during pregnancy.

Drug advocates, including the CDC, justify the use of SSRIs during pregnancy on the basis that depression has its own hazards. But these hazards pale in comparison to the upheaval that will befall new mothers, fathers, and the extended families of the children who are born with profound birth defects.

The worst hazards of depression in pregnancy are those of suicidality and, very rarely, infanticide. But the SSRIs are implicated in *increasing* the risks of both suicide and violence (Breggin, 2003; Breggin, 2008; Breggin & Breggin, 1994). In fact, the new FDA labels for antidepressants specifically warn about SSRI-induced suicidality in youth and in young adults, the very group most likely to become pregnant (Food and Drug Administration, 2007). Now we know that the SSRIs not only have the potential risk of death of the mother through suicide but the death of the child as well through lethal birth defects.

The CDC and other prodrug authorities urge pregnant mothers to speak with their doctors about the risk/benefit ratio of taking SSRI antidepressants. But doctors will have read the headlines inspired by the CDC and will imagine there is little risk. Furthermore, few physicians realize that meta-analyses have shown that antidepressants work no better than placebo at lifting depression (Kirsch, Moore, Scoboria, & Nicholls, 2002; Moncrieff & Kirsch, 2005). The risk/benefit ratio weighs a placebo effect against increased parental suicide and violence, and babies with congenital defects, babies undergoing withdrawal reactions, and babies whose brains have been modified by their exposure to SSRIs during their development.

There are many approaches to helping depressed people without resort to drugs (Breggin, 2001, 2008; Breggin & Breggin, 1994). Exercise has proven effective in alleviating depression (Babyak et al., 2000). Therapy and counseling can also be very helpful, and in the case of pregnant women, family therapy involving the father of the child and other family members can be especially supportive. Pregnant mothers need to stay in touch with other mothers-to-be or to form an informal support group, and they need to plan ahead for as much emotional support as they can find for several months or more after giving birth. Anticipating help and support after the birth is one of the best antidotes to depression during the pregnancy.

Given the casual attitudes displayed by the researchers and most of the media, it's appropriate to conclude with a condolence letter found on the Web site of the National Birth Defects Prevention Network (March of Dimes, University of South Florida, & Florida Department of Health, 2006). The letter notes that there is no treatment for babies with anencephaly, that they will be lost early or late in pregnancy or die shortly after birth, a few days at the most. Addressed to parents who have a baby with anencephaly, the letter shows a heart-rending drawing of a child with no forehead, and offers this emotional support:

We are so saddened to hear that your baby has anencephaly. We know this is not easy for you and you may not know how to feel. That's okay. Parents of babies with anencephaly feel shock, denial, grief, and even anger. It is all right to feel this way and no one will blame you.

No one can or should blame the parents of anencephalic children. However, when SSRI antidepressants are known to increase the risk by 240%, the medical profession must take responsibility for preventing fetal exposure to these medications. SSRIs should be contraindicated in pregnancy.

NOTE

1. The CDC reports 4,115,590 U.S. births in 2004. Four births per 10,000 births equal 1,646 births with craniosynostosis. Multiply 1,646 births by 2.4 times and the new total is 3,951 births with craniosynostosis.

REFERENCES

- Alwan, S., Reefhuis, J., Rasmussen, S., Olney, R., & Friedman, J. (2007). Use of selective serotonin-reuptake inhibitors in pregnancy and the risk of birth defects. *New England Journal of Medicine*, 356, 2684–2692.
- American College of Obstetrics and Gynecology. (2006, December 1). *Press release: ACOG issues opinion on SSRI antidepressant use during pregnancy*. Retrieved July 1, 2007, from www.ACOG.org/from_home/publications/press_releases/nr12-01-06-1.cfm

- Babyak, M., Blumenthal, J., Herman, S., Khatri, P., Doraiswamy, M., Moore, K., et al. (2000). Exercise treatment for major depression. *Psychosomatic Medicine*, 62, 663.
- Breggin, P. (2001). *The antidepressant fact book*. Cambridge, MA: Perseus Books.
- Breggin, P. (2003). Suicidality, violence and mania caused by selective serotonin reuptake inhibitors (SSRIs): A review and analysis. *Ethical Human Sciences and Services*, 5, 225–246.
- Breggin, P. (2008). *Brain-disabling treatments in psychiatry: Drugs, electroshock and the psychopharmaceutical complex*. New York: Springer Publishing Company.
- Breggin, P., & Breggin, G. (1994). *Talking back to Prozac: What doctors aren't telling you about today's most controversial drug*. New York: St. Martin's.
- Carey, B. (2007, June 28). Antidepressants rated low risk in pregnancy. *The New York Times*.
- CDC Division of Media Relations. (2007, June 27). *New study finds few risks of birth defects from antidepressant use during pregnancy*. Retrieved June 28, 2007, from www.phppo.cdc.gov/od/oc/media/pressrel/2007/r070627.htm
- CDC National Center for Health Statistics. (2006, December 20). *Births/Nativity*. NCHS-FASTATS. Retrieved June 28, 2007, from <http://www.cdc.gov/nchs.fastats/births.htm>
- de Montigny, C., Chaput, I., & Blier, P. (1990, December). Modification of serotonergic neuron properties by long-term treatment with serotonin reuptake blockers. *Journal of Clinical Psychiatry*, 51(12, Suppl. B), 4–9.
- Donn, J. (2007, June 28). Antidepressants pose low birth defect risk. *The Boston Globe*.
- Food and Drug Administration. (2005, December 8). *FDA public health advisory: Paroxetine*. Retrieved July 1, 2007, from www.fda.gov/cder/drug/advisory/paroxetine200512.htm
- Food and Drug Administration. (2006, July). *FDA alert: Increased risk of neonatal persistent pulmonary hypertension. FDA information for healthcare professionals*. Retrieved July 2007, from www.fda.gov
- Food and Drug Administration. (2007, May 2). *FDA news: FDA proposes new warnings about suicidal thinking, behavior in young adults who take antidepressant medications*. Retrieved May 3, 2007, from www.fda.gov/bbs/topics/NEWS/2007/NEW01624.html
- Gardner, A. (2007, June 27). Mom's antidepressant use poses little danger to baby. *The Washington Post*.
- Kalia, M., O'Callaghan, J., Miller, D., & Kramer, M. (2000). Comparative study of fluoxetine, sibutramine, sertraline and dextfenfluramine on the morphology of serotonergic nerve terminals using serotonin immunohistochemistry. *Brain Research*, 858, 92–105.
- Kirsch, I., Moore, T., Scoboria, A., & Nicholls, S. (2002). The emperor's new drugs: An analysis of antidepressant medication data submitted to the U.S. Food and Drug Administration. *Prevention & Treatment*, 5, article 23, posted July 15, 2002.
- Levinson-Castiel, R., Merlob, P., Linder, N., Sirota, L., & Klinger, G. (2006). Neonatal abstinence syndrome after in utero exposure to selective serotonin reuptake inhibitors in term infants. *Archives of Pediatrics & Adolescent Medicine*, 160, 173–176.
- Louik, C., Lin, A., Werler, M., Hernandez-Diaz, S., & Mitchell, A. (2007). First-trimester use of selective serotonin-reuptake inhibitors and the risk of birth defects. *New England Journal of Medicine*, 356, 2675–2683.
- March of Dimes, University of South Florida, & Florida Department of Health. (2006, October 22). *Anencephaly*. Retrieved July 1, 2007, from www.nbdpn.org/current/2007pdf/Anencephaly_Eng.pdf
- Moncrieff, J., & Kirsch, I. (2005). Efficacy of antidepressants in adults. *British Medical Journal*, 331, 155–157.
- Norrholm, S., & Ouimet, C. (2000). Chronic fluoxetine administration to juvenile rats prevents age-associated dendritic proliferation in hippocampus. *Brain Research*, 883, 205–215.
- Seward, Z. (2007, June 28). Reassurance on antidepressants in pregnancy. *Wall Street Journal*, p. D1.
- Wegerer, V., Moll, G., Bagli, M., Rothenberger, A., Ruther, F., & Huether, G. (1999). Persistently increased density of serotonin transporters in the frontal cortex of rats treated with fluoxetine during early juvenile life. *Journal of Child and Adolescent Psychopharmacology*, 9, 13–14.

Correspondence regarding this article should be directed to Peter R. Breggin, MD, or Ginger Breggin, 101 East State Street, No. 112, Ithaca, NY 14850.

Copyright of Ethical Human Psychology & Psychiatry is the property of Springer Publishing Company, Inc. and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.