

Depression During Pregnancy

Out of every 10 women who are pregnant, one or two have symptoms of major depression. Women who have been depressed before are at higher risk.

Depression is a serious medical condition. It poses risks for the woman and her baby. But a range of treatments are available. These include counseling, psychotherapy, support groups, therapy with light, and medications. Individual therapy is highly recommended.

It is usually best for a team of health care professionals to work with a pregnant woman who is depressed or who has a history of depression. Team members include:

- The provider who is caring for her during her pregnancy
- A mental health professional
- The provider who will take care of the baby after birth

Together, the team and the woman decide what is best for her and her baby. The team can connect her to support groups, help her consider counseling and psychotherapy, and assess the need for light therapy or medication.

Often a pregnant woman wonders whether antidepressant drugs, such as Zoloft and Prozac, will harm her baby or herself. There are no simple answers. Each woman and her health care providers must work together to make the best decision for her and her baby. The drugs used to treat depression have both risks and benefits.

IMPORTANT: If you are taking an antidepressant and find that you are pregnant, do not stop taking your medication without first talking to your health provider. Call him or her as soon as you discover that you are expecting. It may be unhealthy to stop taking an antidepressant suddenly.

What Is Depression?

Depression is an illness that involves the body, mood and thought. It affects the way a woman feels about herself and the way she thinks about things. This article addresses two types of depression:

Major depression: This serious illness interferes with a person's ability to work, study, sleep, eat and enjoy oneself. It may appear once in a person's life, but more often occurs several times.

Dysthymia: This is a less severe type of depression. Persons with this illness have long-term symptoms. They are able to conduct day-to-day activities, but they don't always function well or feel good. They may also have episodes of major depression.

Depression carries serious risks for the pregnant woman and her baby. These risks include:

- Poor weight gain
- Use of drugs or alcohol to self-medicate
- Suicidal Thoughts and/or Suicide
- Poor nutrition

The above symptoms can lead to premature birth, low birth weight and developmental problems. In addition, depressed mothers are often less able to care for themselves or their children, or to bond with their children.

What Are the Symptoms of Depression?

A woman who is depressed feels sad or “blue” and has other symptoms that last for two weeks or longer. The other symptoms include the following:

- Trouble sleeping
- Sleeping too much
- Lack of interest
- Feelings of guilt
- Loss of energy
- Difficulty concentrating
- Changes in appetite
- Restlessness, agitation or slowed movement
- Thoughts or ideas about suicide

Things other than depression can cause some of these symptoms. For instance, changes in appetite and trouble sleeping are common in pregnancy. Some medical conditions, such as anemia and hypothyroidism, can cause a pregnant woman to lack energy.

If you have any of these symptoms, talk to your health care provider. He or she will check to see what might be causing your symptoms. You need to be checked for depression if symptoms continue and interfere with your daily life and if your provider rules out other medical conditions.

Treatments

Depression can be treated in several ways. Support groups may help. Some women go to therapy or counseling with a mental health professional (such as a social worker, psychotherapist or psychiatrist).

Some people suffer from a type of depression that comes on during the fall or winter, when there is less sunlight. This is called Seasonal Affective Disorder (SAD). This condition can be treated with light therapy. In her home, the patient looks into a box with special light bulbs. To avoid injury to her eyes, she looks at the lights indirectly. Typically, the patient does this from 15 minutes to two hours every day. The health provider may recommend a different number of minutes over time.

Mental health professionals often talk with women about the risks and benefits of antidepressants.

Two Main Groups of Antidepressants

The most studied antidepressants can be categorized into one of two groups.

Group 1: Selective serotonin uptake inhibitors (SSRIs). This group of drugs includes:

- Prozac (fluoxetine)
- Zoloft (sertraline)
- Celexa (citalopram)

- Lexapro (escitalopram)
- Paxil (paroxetine) – not recommended in pregnancy (see below)
- Effexor (venlafaxine) – not actually an SSRI, but has similar serotonin effects

Group 2: Tricyclic antidepressants (TCAs). This group of drugs includes:

- Elavil (amitriptyline)
- Tofranil (imipramine)
- Pamelor (Aventyl, nortriptyline)

Like many drugs, antidepressants can have side effects. SSRIs usually have fewer side effects than TCAs. Women differ in the type and seriousness of the side effects that they have.

What Research Tells Us About Antidepressants

It is challenging to study and understand the risks of any drug given to pregnant women. During pregnancy, two patients—the mother and the fetus—are exposed to the drug. Medications that are safe for a woman are sometimes risky for a fetus. Because of this, researchers have not studied many drugs during pregnancy.

It is unethical to test a drug on a pregnant woman since we don't know how it might affect the fetus. Researchers get most of their information by studying drugs that have been approved for women who are not pregnant and that are then taken by pregnant women. Often these women are not aware that they are pregnant.

Several drugs have been used for many years without any obvious signs of serious risk to the baby. But some researchers have reported that some antidepressants may have increased risks. SSRIs are a newer group of drugs than TCAs. Researchers are continuing to study them.

Research has clearly shown that women who are not pregnant and are depressed are very likely to become ill again if they stop taking their medications. A recent study in 2006 suggests that the risk of depression relapse is high in pregnant women who discontinue their antidepressant during pregnancy.

Here are some other things that research tells us about the risks and benefits of taking SSRIs during pregnancy.

During Pregnancy:

- One study in 2006 found that pregnant women with major depression are very likely to become ill again during their pregnancy if they stop taking their medication. A depressed woman may have trouble taking care of herself during pregnancy. This could threaten the health of the fetus.
- Many studies have found no link between antidepressants and serious malformations in newborns. But in 2005, the U.S. Food and Drug Administration (FDA) issued a warning about Paxil (paroxetine) based on several studies. The warning said that taking the drug during the first three months of pregnancy may increase the risk of birth defects, particularly heart defects. Scientists do not yet know enough to draw a firm conclusion. Women and their health care providers should weigh the risks and benefits of using Paxil during pregnancy. But in general, Paxil is not advised during pregnancy.

- In one study in 2006, three of 60 infants exposed to SSRIs for the complete pregnancy had major congenital anomalies, including ventricular septal defect, hydronephrosis, and cleft palate (see below for more specific information).
- Two large studies in the June 28, 2007 issue of *The New England Journal of Medicine* found that despite some significant associations, any increase in birth defects associated with exposure to SSRIs is "likely to be small in terms of absolute risk." There was a small increased risk for right ventricular outflow tract lesions with Paxil and a small increased risk for septal defects with Zoloft (sertraline) (see below for more specific information).

During Delivery:

- **Neonatal Abstinence Syndrome (NAS):** Some babies born to mothers who are taking SSRI antidepressants show signs of "withdrawal." For instance, they may have breathing or feeding problems. Their movements may be jerky. Some have irritability, abnormal crying and tremor. There have been reports of some seizures and intubations, but no deaths. NAS can affect 10-30% of neonates exposed to SSRIs. Health providers who care for newborn babies are aware of these risks and can provide treatment. Symptoms usually subside from 48 hours to a few days. It is important for the baby's provider to know ahead of time that the mother has taken antidepressants during pregnancy (see below for more specific information).
- **Persistent Pulmonary Hypertension of the Newborn (PPHN):** Babies exposed to SSRIs in late pregnancy (after 20 weeks) may be more likely to have PPHN. This is a rare, but serious heart and lung disorder. Not enough studies have been done to know for certain if SSRIs cause the disorder, but in February 2006, Christina Chambers and her team came out with an important study (see below for more specific information).
- One study in the August 2007 issue of *The American Journal of Psychiatry* followed 90 pregnant women, and found that compared with lower SSRI doses, higher SSRI doses were significantly associated with earlier birth. Yet a second study in the August 2007 issue of *Psychosomatic Medicine* found that women with higher anxiety were significantly more likely to have spontaneous preterm birth than less anxious women (see below for more specific information).
- A more recent study published in October 2008 in the journal *Human Reproduction* found that "depression in pregnant women could help explain the growing problem of preterm delivery." A total of 791 women completed the screening and delivered a live baby. Overall, after accounting for other factors that might play a role, women with significant depressive symptoms were nearly twice as likely to deliver a baby preterm — or before 37 complete weeks' gestation — than those without significant depressive symptoms. The more severe the women's depression, the greater their risk of delivering preterm, the study found. The authors speculate that depression during pregnancy might interfere with placental hormones that help maintain a healthy pregnancy and ensure that labor doesn't start too early.

After Delivery:

- Some researchers have studied children whose mothers took antidepressants. They have found no link to serious problems with language, behavior or intelligence.
- There has been no data reported on long term effects of antidepressants on the baby's well being. So far, there is no evidence of long term effects.

Choosing an Antidepressant

This decision is difficult because we don't know all the answers. No drug is entirely safe. A woman and her health care team must look at her case and carefully weigh:

- The risks and benefits of various drugs
- The risks and benefits of other types of treatment
- The risk of untreated depression for the woman and her baby

Choosing an antidepressant needs to be done on a case by case basis. Of note, the literature changes frequently in this area.

Important Points

- Make sure that you are being followed closely by both your psychiatrist and an Ob/Gyn
- Take prenatal vitamins and folic acid
- Have your thyroid, blood count and other lab work checked to rule out medical reasons for low mood or energy
- It is a good idea to deliver your baby in a hospital versus at home by a midwife, as they can adequately monitor and assess any possible delivery complications
- Stress reduction techniques and individual therapy (at least weekly) are both encouraged
- It is always a good idea to be on the lowest number of medications possible, and on the lowest dose necessary
- With any medication during pregnancy, start low and go slow

The Latest Research

There are a variety of studies which show a small risk of increased side effects or birth defects in newborns who have been exposed to SSRIs during pregnancy or delivery. Below are the most recent studies.

Depression During Pregnancy Can Double the Risk of Preterm Delivery:

The study looked at 791 pregnant Kaiser Permanente members in San Francisco city and county from October 1996 through October 1998. Researchers interviewed the women around their 10th week of pregnancy and found that 41 percent of the women reported significant or severe depressive symptoms. The women with less severe depressive symptoms had a 60 percent higher risk of preterm delivery -- defined as delivery at less than 37 completed weeks of gestation -- compared with women without significant depressive symptoms, and the women with severe depressive symptoms had more than twice the risk. "Preterm delivery is the leading cause of infant mortality, and yet we don't know what causes it. What we do know is that a healthy pregnancy requires a healthy placenta, and that placental function is influenced by hormones, which are in turn influenced by the brain," said lead author Dr. De-Kun Li, a reproductive and perinatal epidemiologist at Kaiser Permanente's Division of Research in Oakland. The authors theorized that "depression during pregnancy might interfere with placental hormones that help maintain a healthy pregnancy and ensure that labor doesn't start too early."

Human Reproduction 2008 October; on-line journal.

No Association Between 1st Trimester SSRI Use and Major Congenital Malformations:

Using large medical, demographic, and public drug insurance registries in Quebec, researchers focused on women with psychiatric diagnoses (mostly mood or anxiety disorders) and antidepressant use for at least 1 month in the year before pregnancy. Researchers compared first-trimester antidepressant exposure and duration in 2140 healthy infants and 189 infants with any major congenital malformation in the year after birth. Antidepressants commonly used were paroxetine (42%), sertraline (15%), and venlafaxine (13%). The risk for congenital malformation (8%, vs. the usual population rate of 3%) was unrelated to first-trimester antidepressant use, its duration, or therapeutic class.

Br J Psychiatry 2008 May; 192:344.

Duration of Exposure to SSRI's Rather Than Timing of Dose Increased Risk for Side Effects:

Other researchers linked maternal and neonatal British Columbian health records to identify recipients of SSRI's (commonly, paroxetine, 39%; fluoxetine, 25%; or sertraline, 23%) during pregnancy and compared effects of early exposure only (first and/or second trimesters; n=1575) and of continued exposure (from first or second trimester through delivery; n=1925). Longer duration of exposure to SSRI's rather than timing increased the risks for lower birth weight, gestational age, weight for age, and for respiratory distress.

Br J Psychiatry 2008 May; 192:338.

The Risks of Earlier Birth with SSRI Use:

Suri et al. prospectively followed 90 pregnant women (mean age, 33.8). Forty-nine had major depression and received antidepressant medication, predominantly SSRIs (44 received medication in the first trimester, and all received medication in the second and third trimesters); 22 had major depression but minimal or no antidepressant treatment during pregnancy; and 19 were not depressed. The groups had similar mean numbers of previous births, miscarriages, and abortions. Apgar scores and birth weights did not differ significantly among the groups. However, women receiving antidepressants gave birth approximately 1 gestational week earlier than the others (38.5 weeks vs. 39.4 weeks in depressed controls and 39.7 weeks in healthy controls), had higher rates of preterm birth (14.3% vs. 0% and 5.3%), and had infants who were more likely to require admission to special-care nurseries (21% vs. 9% and 0%; these were *not* neonatal ICUs). Compared with lower SSRI doses, higher SSRI doses were significantly associated with earlier birth.

Am J Psychiatry 2007 Aug; 164:1206.

The Risks of Preterm Birth with Higher Anxiety:

Orr et al. prospectively examined rates of spontaneous preterm births (<37 weeks' gestation) among 1820 medication-free pregnant women reporting significant anxiety at a health clinic. The women self-rated their anxiety on a 6-point scale (median rating, 2). Results were adjusted for a host of potentially confounding factors, such as bleeding before the third trimester, drug use, employment, prior pregnancy outcomes, smoking, body-mass index, race, age, and education. Compared to women with self-rated anxiety of 3 or less, women with the two highest anxiety scores were significantly more likely to have spontaneous preterm delivery (adjusted odds ratios: score of 5, 1.70; score of 6, 2.73).

Psychosom Med 2007 Jul/Aug; 69:566.

Low Risk of Birth Defects:

Two large studies in the June 28, 2007 issue of *The New England Journal of Medicine* indicate a few very small increases in risks for particular defects. Earlier studies have reported that use of SSRIs —especially paroxetine — during early pregnancy increases the

incidence of cardiovascular birth defects markedly. These two large case-control studies challenge these findings.

Investigators from the U.S. and Canada identified 9622 infants with major birth defects, and 4092 controls without such defects, born between 1997 and 2002. No significant association was found between SSRI use in early pregnancy and congenital heart defects. However, there were small absolute increases in risks for anencephaly, craniosynostosis, and omphalocele with SSRI use, and all these risks — as well as the risk for ventricular outflow tract lesions — were increased most with paroxetine.

In a second study, funded in part by the manufacturer of paroxetine, 9849 infants with birth defects were compared with 5860 control infants born in five centers in the U.S. and Canada between 1993 and 2005. Use of SSRIs in early pregnancy was not associated with heart defects in general, but there was an increased risk for right ventricular outflow tract lesions with paroxetine and an increased risk for septal defects with sertraline. No evidence of increased risk was found for any other birth defects with paroxetine.

An accompanying editorial by Dr Michael F. Greene highlights the difficulties of interpreting the new findings. However, together with previous data, the results "[make] it clear that neither SSRIs as a group nor individual SSRIs are major teratogens on the order of thalidomide or isotretinoin," Dr. Greene writes. He concludes, "[A]ny increased risks of these malformations in association with the use of SSRIs are likely to be small in terms of absolute risks."

The absolute risk for right ventricular outflow tract lesions in the infant of a mother who uses paroxetine during pregnancy is likely less than 1%, and the risk for any congenital heart defect is unlikely to exceed 2%. These small risks must be weighed against the risks associated with discontinuing an SSRI during pregnancy.

N Engl J Med. 2007 Jun 28; 2675-2683, 2684-2692, 2732-2733.

Neonatal Abstinence Syndrome (NAS):

About one-third of infants in a recent study who were exposed to antidepressants while in the womb experienced symptoms of neonatal abstinence syndrome, which include tremors, disturbed sleep, gastrointestinal problems, and hypertonicity.

Most of the symptoms occurred within the first 48 hours after birth, but the long-term effects of neonatal abstinence syndrome, if any, are unknown, according to a report in the February 2006 Archives of Pediatric and Adolescent Medicine.

Researchers from the Schneider Children's Medical Center of Israel studied 120 infants born at the Rabin Medical Center in Israel between January 2002 and August 2004.

Half of the infants in the sample were born to mothers who took one of the selective serotonin reuptake inhibitors (SSRIs) either through the entire pregnancy or during the last trimester.

Of the mothers who took SSRIs, 37 took paroxetine, 12 took fluoxetine, eight took citalopram, two took venlafaxine, and one took sertraline. The remaining 60 infants were born to mothers who did not take an SSRI during pregnancy.

Researchers assessed the infants' health with blood tests and by monitoring cardiorespiratory functioning and temperature. In addition, they used the Finnegan Scale, which measures symptoms of neonatal abstinence syndrome (NAS).

Of the 60 infants exposed to SSRIs in utero, 30 percent (18) exhibited symptoms of NAS. None of the infants in the control group exhibited symptoms of NAS.

When researchers measured severity of symptoms among the 18 NAS infants, they found that eight had severe symptoms and 10 had mild symptoms. Six of the eight infants with severe symptoms had been exposed to Paxil (paroxetine) in utero.

In addition, three of the infants exposed to SSRIs for the complete pregnancy had major congenital anomalies, including ventricular septal defect, hydronephrosis, and cleft palate. One of the newborns in the control group had hydronephrosis.

Gil Klinger, M.D., one of the study's investigators, told *Psychiatric News* that most of the mild symptoms in newborns subsided within a few days. "Of the severely affected infants, two had seizures, which resolved without intervention." Klinger is a senior neonatologist at Schneider Children's Medical Center.

Though none of the short-term symptoms were life-threatening, he said, "the long-term effects of SSRIs on newborns are unknown."

Klinger acknowledged that "depression also entails a risk to a pregnant woman and her fetus and should also be controlled—we are not recommending discontinuation of medications during pregnancy; however, sometimes SSRIs are given for very mild indications, and in these circumstances the risk-benefit ratio may not be in favor of giving antidepressants."

Arch Pediatr Adolesc Med. 2006; 160:173-176.

Persistent Pulmonary Hypertension of the Newborn (PPHN):

In other research, a case-controlled study published in February 2006 by Christina Chambers, PhD, MPH and her group revealed a slight risk of a relatively serious health problem for newborns of mothers taking antidepressants during late pregnancy.

Researchers found that mothers who took SSRIs after the 20th week of gestation were six times as likely as those who did not take the antidepressants in late pregnancy to have newborns with persistent pulmonary hypertension.

Researchers recruited a sample of 377 women whose infants had pulmonary hypertension and 836 control women and their healthy infants from nearly 100 medical centers in Boston, Philadelphia, San Diego, and Toronto from 1998 to 2003. They gathered information on the mothers' medical and obstetrical histories and past antidepressant usage. They assessed infants for pulmonary hypertension.

The researchers found that 14 infants with pulmonary hypertension had been exposed to an SSRI during late pregnancy, while only six infants in the control group—those without the condition—had been exposed to SSRIs.

When researchers analyzed the association between SSRI use anytime during pregnancy and pulmonary hypertension in newborns, however, they found no elevated risk. Only use of SSRIs after the 20th week of gestation was significantly associated with pulmonary hypertension.

According to the report in the February 9, 2006 *New England Journal of Medicine*, newborns with the condition "are typically full-term or near-term infants without associated congenital anomalies who present shortly after birth with severe respiratory failure requiring intubation and mechanical ventilation."

Christina Chambers, PhD, MPH, the study's lead investigator, emphasized that the relative risk for infants is low—only about 6 to 12 women per 1,000 who use SSRIs late in pregnancy will have babies with pulmonary hypertension (vs. 1-2 per 1000 in the general

population) . "About 99 percent of women exposed to one of these medications late in pregnancy will deliver an infant unaffected by pulmonary hypertension," she told Psychiatric News.

Chambers is an assistant professor of pediatrics at the University of California, San Diego School of Medicine.

Though the findings could not prove a causal association between fetal exposure to SSRIs and pulmonary hypertension, Chambers noted that one effect of SSRIs is to reduce the production of nitric oxide, a vasodilator. "SSRIs also boost levels of serotonin," she added, "which has vasoconstrictive properties."

Chambers also noted that even though there is low risk of pulmonary hypertension among newborns of mothers who take SSRIs late in pregnancy, the finding "should be factored into the many things an expectant mother must consider when she is deciding whether to take an SSRI during pregnancy."

N Engl J Med. 2006 Feb 9; Volume 354(6):579-587.

Herbal Products

Herbal products, such as St. John's Wort, vary in strength and quality from product to product. We need more research to help us know whether St. John's Wort is useful and safe for treating depression in pregnant women.

Resources

- The Organization of Teratology Information Services (OTIS), (866) 626-6847. Provides fact sheets on pregnancy and specific antidepressants, including Prozac and Zoloft.
http://otispregnancy.org/otis_fact_sheets.asp
- LACT MED: A website that gives the latest research about medications and breast feeding.
<http://www.toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT>
- www.womensmentalhealth.org - Massachusetts General Hospital
- www.emorywomensprogram.org - Emory
- www.motherisk.org
- Parts of this handout were adapted from the following websites:
www.marchofdimes.com/pnhec/188_15663.asp
<http://pn.psychiatryonline.org/cgi/content/full/41/7/25>