# Special Populations: Women of Childbearing Age and Infants

Treatment decisions during pregnancy should be as collaborative as possible between health care providers and patients, and take into account the individualized risks and benefits of treatment options. In addition to the reproductive safety of psychopharmacologic treatments, the past course of illness and treatment responses should be strongly considered. Specifically, the potential risks of medications must be assessed along with the risks of untreated psychiatric disorders across pregnancy and the postpartum. Decision making around treatments for psychiatric disorders in pregnancy requires consideration of what is known about the medications in pregnancy, the course and severity of the woman's disorder being treated, and exposures to the baby of both untreated maternal illness and medication. Psychiatric mood and anxiety symptom burden during pregnancy is a major risk factor for serious postpartum illness.

Unplanned pregnancies are common, and the reproductive safety of treatments should be kept in consideration when treating women of reproductive potential. General recommendations for healthy pregnancies should be included in the treatment plan, as some elements are particularly relevant for individuals with mood disorders. These include getting regular exercise, abstaining from tobacco, alcohol, and illicit substances, and maintaining a healthy diet and weight.

For specific recommendations on the treatment of mood disorders in pregnancy, refer to the 2015 Florida Best Practice Psychotherapeutic Medications Guidelines for Adults, pages 33-40.[57]

## Treatment Goals and Management

- Optimal functioning of the mother, aiming for remission of illness, with a goal of achieving or maintaining euthymia, and relapse prevention and associated risks of morbidity and mortality, including risk of suicide.
- Managing risk of medication exposure to the infant.
- Individualized consideration of risk/benefit ratio for treatment options, realizing that untreated illness itself poses risks to the mother and baby.
- Wherever possible, multidisciplinary management involving the patient's obstetrician, mental health clinician, primary health care provider, and pediatrician is recommended to facilitate care.
- Prioritize medications that have worked for the mother in the past.
- Minimize polypharmacy, if possible, as multiple exposures may increase risk to the fetus.
- Maximize non-pharmacologic therapies if effective, either without pharmacotherapy or to augment pharmacotherapy (Psychotherapy is the most important effective non-medication treatment for mood disorders during pregnancy and the postpartum).

**Table 11. The Safety of Psychotherapeutic Medication in Pregnancy and Lactation[58, 59]**

| Medication Class | Safety and Management Issues* | | |
|---|---|---|---|
| | Pregnancy | Birth Defects and Other Neonatal Outcomes | Lactation** |
| Benzodiazepines | ✦ Ultrasonography for facial morphology | ✦ Possible increased incidence of cleft lip or palate<br>✦ Floppy infant syndrome<br>✦ Withdrawal syndrome | ✦ Infant sedation reported |
| SSRIs, SNRIs***, and tricyclic antidepressants | ✦ Decreased serum concentrations across pregnancy | ✦ No conclusive evidence of birth defects, with the exception of paroxetine<br>✦ Potential increased risk of congenital and cardiac defects in 1st trimester exposure to paroxetine†<br>✦ Prenatal antidepressant exposure syndrome | ✦ No conclusive evidence of adverse outcomes |
| Lithium | ✦ Ultrasonography, fetal echocardiography, or both for heart development<br>✦ Decreased serum concentrations across pregnancy<br>✦ Delivery - intravenous fluids; increased risk for lithium toxicity in mother | ✦ Increased incidence of cardiac malformations<br>✦ Increased risk for lithium toxicity in infant | ✦ Is incompatible with breastfeeding due to relatively high levels found in neonates, and multiple adverse event reports |

**Table 11. The Safety of Psychotherapeutic Medication in Pregnancy and Lactation[58, 59] *(continued)***

| Medication Class | Safety and Management Issues* | | |
|---|---|---|---|
| | **Pregnancy** | **Birth Defects and Other Neonatal Outcomes** | **Lactation**** |
| Antiepileptic drugs | ✦ Decreased serum concentrations across pregnancy<br>✦ Folate supplementation and Vitamin K for some drugs | ✦ Valproic acid in the 1st trimester is associated with numerous neural tube defects and congenital malformations.<br>✦ Carbamazepine in the first trimester is associated with fetal carbamazepine syndrome – dysmorphic features and major malformations<br>✦ Neonatal symptoms<br>✦ Long-term adverse neurobehavioral outcomes | ✦ Carbamazepine has relatively higher levels in breast milk, with measurable levels in the infant |
| First and second generation antipsychotics | ✦ Avoid anticholinergic medications for side effects | ✦ No conclusive evidence of birth defects<br>✦ Potential higher risk of preterm birth, low birthweight, and postnatal symptoms (e.g., jitteriness, somnolence) | ✦ Breastfeeding is not recommended for mothers on clozapine due to relatively high levels in breast milk that may affect the infant's complete blood count (CBC) |

*Note: SSRIs = Selective serotonin reuptake inhibitors; SNRIs = Serotonin–norepinephrine reuptake inhibitors.*

**Many challenges exist in interpreting and evaluating evidence regarding adverse effects of psychotropic medication use during pregnancy. Key limitations include lack of well-conducted robust studies in pregnant women. Use of registry data and cohort designs has inherent flaws of lack of control for confounding variables such as psychiatric diagnoses, comorbid health conditions, obesity, tobacco use and use of alcohol and illicit substances.*

** *Most medications can cross into breast milk but their levels vary. Formula feeding is an alternative that can allow the mother to use whichever medication works best for her.*

****Little is currently known about the safety of SNRIs, compared to SSRIs.*

*†Data also suggest that the risks of malformations associated with paroxetine use are inconsistent.[60]*

## Psychotherapeutic Medications Associated with Risks in Pregnancy

- Avoid benzodiazepines if possible, although the decision should be made on a case by case basis. There is inconsistent data suggesting that in the first trimester, there may be a small increased risk of oral clefts, and high doses in late pregnancy may be associated with a floppy infant syndrome at birth and withdrawal afterwards.
- Valproate exposure in pregnancy is associated with an increased risk of fetal anomalies, including neural tube defects, fetal valproate syndrome, and long-term adverse neurocognitive effects. It should be avoided in pregnancy, especially during the first trimester.
- Carbamazepine exposure in pregnancy is associated with fetal carbamazepine syndrome. It should be avoided during pregnancy, if possible, especially during the first trimester.
- Lithium exposure in pregnancy is associated with a small increase in a congenital cardiac malformation known as Epstein's anomaly. Risk of Ebstein's anomaly is estimated at 1/20,000 (0.005%) in the general population.[61] The relative risk of developing Ebstein's anomaly has been estimated at 7.7 in patients exposed to lithium in utero compared to those not exposed to lithium in utero.[62]
- Paroxetine use in pregnant women and women planning pregnancy should be avoided, if possible. Fetal echocardiography should be considered for women who are exposed to paroxetine in early pregnancy.

*Note. The U.S. Food and Drug Administration's (FDA) new labeling is detailed in the Pregnancy and Lactation Labeling Rule (PLLR) or "final rule" at -**http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Labeling/ucm093307.htm.** The use of letter labeling (i.e., A, B, C, D, X) for pregnancy categories is being phased out by the FDA. This change is based on the major limitations of the letter category system.*

## Lactation and Sleep

Breastfeeding is an important topic for women, as is sleep. Maternal mental health should be prioritized over breastfeeding. If a woman is exclusively breastfeeding, she is the only one that can feed the baby, and therefore her sleep will be greatly affected. Sleep deprivation is a major trigger for the relapse of mood episodes, particularly in bipolar disorder. It is strongly encouraged that women consider at least supplementing with bottles.

Most medications can cross into breast milk but their levels vary. The medications with relatively high levels found in neonates are lithium, carbamazepine, and clozapine. Formula feeding is an alternative that can allow the mother to use whichever medication works best for her.