

Using Psychotropic Medications during Pregnancy and Lactation

General Issues for all Psychotropic Medications ^{1,2,3,4}

- > **<u>Avoid</u>** medications in first trimester, if possible
- > Taper medications if discontinuing
- > Use monotherapy whenever possible
- ➢ Use the lowest <u>effective</u> dose

Psychotropic Medications in Pregnancy

First Trimester:

Antidepressants: 2,5,6,7

- Evidence indicates no increased risk of major malformation in the newborn or spontaneous abortion following exposure to antidepressants in early pregnancy
- > There is no indication to stop tricyclics or SSRIs as a matter of routine in early pregnancy
- If a pregnant woman becomes depressed antidepressant medication should be prescribed with caution
- Significant literature supports the safety of TCAs, especially Nortriptyline and Desipramine *Lithium:* ^{5,9,8}
 - ➢ Early studies suggest that the risk of malformations and Epstein Barr, from exposure to lithium early in pregnancy may have been overestimated.
 - Women with severe bipolar illness successfully maintained on lithium should carefully consider the risks and benefits of lithium.
 - The risks of lithium to the fetus and the effects of lithium withdrawal on the mother should be discussed before pregnancy

Anticonvulsants : ⁵

- Anticonvulsants (carbamazrpine, valproate, lamotrigine increase the risk of congenital malformations.
- > The risk is higher with valproate especially at doses over 1000 mg/day
- Several of these drugs are folate antagonists.
- > All women on anticonvulsants should receive extra folate
- > **<u>AVOID</u>** valproate as a mood stabilizer in pregnancy

Benzodiazepines: 4,5,10

- > Evidence suggests exposure may increase risk of cleft palate
- > **<u>AVOID</u>** benzodiazepines in the first trimester
- > **<u>AVOID</u>** diazepam especially because of its high milk to plasma ratio
- Lorazepam has lower milk to plasma ratio

Second and Third Trimester:

Antidepressants: 2,5,6,7

Neonates exposed to psychotropic medications during pregnancy should be monitored for withdrawal syndromes after delivery 12 out of 55 (22 percent) reported cases of treatment with paroxetine showed evidence of withdrawal requiring treatment

Lithium: 5,98

Newborn infants of women treated with lithium in later pregnancy face potential risks of neonatal toxicity, thyroid and renal dysfunction

Consideration should be given to dose reduction and/or discontinuation two to four weeks before the expected date of delivery with recommencement after delivery

Footnote: ^{7,11,12}

Because of the issues surrounding pregnancy and lactation there are:

- No controlled studies
- > Most information comes from case reports or pharmaceutical registry
- > The greatest amount of data exists for fluoxetine, TCAs and citalopram
- > There is no information on trazadone, mirtazapine or nefazadone
- > Sertraline has lower umbilical cord levels than fluoxetine

Psychotropic Medications in Lactation

If a breast-feeding mother is taking psychotropic medication, infant development should be monitored and a careful assessment made of the risks and benefits

Antidepressants: ^{13,14}

- > TCAs: Significant literature to supports safety especially Nortriptyline and Desipramine
- > Doxepin: One case of respiratory depression reported
- Sertraline, paroxetine and fluvoxamine: Relative infant dose of 0.3-0.5
- No adverse clinical effects have been reported in breast-fed infants of mothers taking paroxetine (also has the lowest milk plasma ratio of sertraline, paroxetine and fluvoxamine.
- Fluoxetine and Citalopram: Relative infant dose of 1-6 (two adverse drug reactions one infant adverse drug reaction with fluoxetine)
- Little evidence on Fluvoxamine
- Clomipramine Use with caution

Lithium: ^{13,14}

- > Lithium is excreted in breast milk at 40 percent of maternal serum levels
- Lithium toxicity has been described in breast-fed infants
- > **<u>AVOID</u>** breast feeding while taking lithium

Anticonvulsants: ^{13,14}

- Valproate is excreted at levels of 1to 2 percent maternal serum levels and no clinical adverse effects have been noted
- Carbamazepine is excreted in ranges from 6 to 65 percent of maternal serum levels
- Valproate, Carbamazepine both considered compatible with nursing by American Academy of Pediatrics.

Benzodiazepines:^{13,14}

- AVOID new prescriptions of benzodiazepines (except where there are concerns about drug dependence when breast feeding may be beneficial if the infant was exposed to benzodiazepines in utero)
- > Excreted in breast milk with low milk/plasma ratio
- > Clonazepam most commonly used during lactation. No adverse drug reactions reported

Anti-psychotic:s: 13,14

All antipsychotics are excreted in breast milk but there is no evidence to suggest that breast fed infants are at risk of toxicity or impaired development

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² McElhatton, P.R., Garbis, H.M., Elefant, E., Vial, T., Bellemin, B., Mastroiacovo, P., Aron, J., Rodriguez-Pinilla, E., Schaefer, C., Pexieder, T., Merlob, P., Dal Verme, S. The outcome of pregnancy in 689 women exposed to therapeutic doses of antidepressants: A collaborative study of the European Network of Teratology Information Services (ENTIS). *Reprodroductive Toxicology 1996;* 10: 285- 290.

³ Nulman, I., Rovet, J., Stewart, D.E., Wolpin, J., Gardner, H.A., Theis, J.G., Kulin, N., Koren, G: Neurodevelopment of children exposed in utero to antidepressant drugs. *New England Journal of Medicine* 1997; 336: 258-262.

⁴ Briggs, G., Freeman, R.K., Yaffe, S.J., Drugs in pregnancy and lactation. *A Reference Guide to Fetal and Neonatal Risk*, 1998; 5th Edition, Baltimore, Wilkins and Wilkins.

⁵ Altshuler, L.L., Cohen, L., Szuba, M.P., Burt, V.K., Gitlin, M., Mintz, J., Pharmacologic management of psychiatric illness during pregnancy: Delimmas and guidelines. *American Journal of Psychiatry* 1996; 153: 592-606.

⁶ Ericson, A., Kallen, B., Wiholm, B.E., Delivery outcome after the use of antidepressants in early pregnancy. *European Journal of Clinical Pharmacology* 1999; 55: 503-508.

⁷ Hendrick V., Altshuler, L., Management of major depression during pregnancy. *American Journal of Psychiatry* 2002; 159: 1667-1673.

⁸ Cohen, L.S., Altshuler, L.L., Pharmacologic management of psychiatric illness during pregnancy and the postpartum period. *Psychiatric Clinical North America* 1997; 4: 21-60.

¹ Alshuler, L.L., Cohen, L.S., Moline, M.L., Kahn, D.A., Carpenter, D., Docherty, J.P., Treatment of depression in women. *Post graduate Medicine: The Expert Consensus Guideline Series*, March 2001.

⁹ Cohen, L.S., Friedman, J.M., Jefferson, J.W., et al., A reevaluation of risk of in utero exposure to lithium. *Journal of the American Medical Association* 1994; 271: 146-150.

¹⁰ Dolovich, L. R., Addis, A., Vaillancourt, J.M., Power, J.D., Koren, G., Einarson, T.R., Benzodiazepine use in pregnancy and major malformations or oral cleft; Meta analysis of cohort and case-controlled studies. *British Medical Journal* 1998; 317: 839-843.

¹¹ Wisner, K.L., Zarin, D.A., Holmboe, E.S., et al., Risk-benefit decision making for treatment of depression during pregnancy. *American Journal of Psychiatry* 2000; 157: 1933-1940.

¹² Dwenda, G., The effectiveness of various postpartum depression treatments and the impact of antidepressant drugs on nursing infants. *American Board of Family Practice* 2003; 16: 372-382.

¹³ Winans, E.A., Antidepressant use during lactation. *Journal of Human Lactation* 2001; 17: 256-261.

¹⁴ Wisner, K.L., Perel, J.M., Findling, R.L., Antidepressant treatment during breast-feeding. *American Journal of Psychiatry* 1996; 153: 1132-1137.