INFORMATION FOR CLINICIANS ON ANTIDEPRESSANTS DURING PREGNANCY AND BREAST FEEDING - JUNE 2009

This chart is produced by the University of Illinois at Chicago (UIC) Perinatal Mental Health Project as a summary of research on antidepressants in human pregnancy and breastfeeding.

Sources of data:

- Pregnancy data: Data summarized here are from controlled studies in human pregnancy. The Food and Drug Administration (FDA) Pregnancy Risk Categories, as found in the Physician's Desk Reference[1], are based on both animal and human studies. No antidepressants are yet specifically FDA-approved for use during pregnancy. All antidepressants cross the placenta, so are never Category A ("no risk"). Medications that are non-teratogenic in animal studies but have never been studied in humans are classified as "Category B". Since teratogenicity does not generalize across species, a Category B classification does not imply greater safety in human pregnancy than a Category C or D classification. Several medications have been shifted from Category B to C or D as their risks became better known.
- Breastfeeding data: Data about antidepressant effects on breastfeeding babies are predominantly from case reports and case series. For medications with no reported side effects, that does not necessarily mean the medication is "safe"; often it means there are few case reports available. Reported per cents of maternal dose to breastfeeding babies are weight-adjusted estimates that include the agent and its active metabolite(s).
- Specific references are available on request.

General guideline:

- Optimal treatment is based on individual patient characteristics and clinical judgment, weighing medication risks against risks of untreated illness. Risks of untreated perinatal depression may include preterm birth and other obstetric complications, increased risk of infection and more difficult temperament in the infant, impaired parenting, and impaired cognitive development, emotional and behavioral problems and increased reactivity to stress in children.

Antidepressants as a group may be associated with following risks:

- Gestational age decreased by an average of one week.
- Possible increased risk of miscarriage, but rates within norms of the general population.

SSRI antidepressants as a group (citalopram, escitalopram, fluoxetine, paroxetine, sertraline) may be associated with the following risks:

- Neonatal side effects, including respiratory distress, excessive crying, changes in sleep and behavioral state, difficulty sleeping, increased or decreased muscle tone, hyperreflexia, seizures and/or cardiac arrhythmias.
- Most studies have found no increased risk of gestational hypertension. One retrospective study[2] found a possible increased risk of gestational hypertension
- Possible increased risk of persistent pulmonary hypertension in the newborn with exposure later in pregnancy.
- Most studies have found no increased risk of birth defects. One retrospective study[3] found a possible increased risk of anencephaly, craniosynostosis and omphalocele, another[4] found an increased risk of anomalies in general; absolute risks were small.

For dosing strategies during pregnancy please refer to: www.psych.uic.edu/research/perinatalmentalhealth/pdf/Miller_et_al_Balancing_Risks.pdf

For questions, references, or permission to reprint, call the UIC Perinatal Mental Health Project at 1-800-573-6121 or visit www.psych.uic.edu/research/perinatalmentalhealth/

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Anti-depressant	Advantages During Pregnancy	Teratogenicity	Other Disadvantages During Pregnancy	Estimated % of Maternal Dose to Breastfeeding Baby	Reported Side Effects to Breastfeeding Babies
Bupropion	• Fewer sexual side effects • Less risk of weight gain • Helps with smoking cessation	Morphologic – none found Behavioral – unknown	• Limited data available • Lowers seizure threshold • Can cause insomnia • May increase risk of miscarriage	2.0%	Seizures
Citalopram	• Few interactions with other medications	Morphologic – none found Behavioral – none found	• Limited data available	0.7% -9.0%	Uneasy sleep, drowsiness, irritability, weight loss
Desipramine	• More studies in human pregnancy, including neurodevelopmental follow-up	Morphologic – none found Behavioral – none found	• Maternal side effects additive to pregnancy effects (sedation, constipation, tachycardia) • Orthostatic hypotension, risking decreased placental perfusion • Fetal and neonatal side effects: tachycardia, urinary retention	1.0%	None
Duloxetine	• Also treats diabetic peripheral neuropathic pain	Morphologic – unknown Behavioral – unknown	• No systematic studies in human pregnancy	0.1%	Unknown
Escitalopram	• Few interactions with other medications	Morphologic – unknown Behavioral – unknown	• No systematic studies in human pregnancy	3.9% - 7.9%	Enterocolitis
Fluoxetine	• More studies in human pregnancy, including meta-analysis and neurodevelopmental follow-up	Morphologic – unlikely increased risk of cardiovascular malformations* Behavioral – none found	• More reports of neonatal side effects than most other antidepressants	1.2% - 12.0%	Excessive crying, irritability, vomiting, watery stools, difficulty sleeping, tremor, somnolence, hypotonia, decreased weight gain, hyperglycemia
Mirtazapine	• Fewer sexual side effects • Helps restore appetite in women who are not gaining weight • Less likely to exacerbate nausea and vomiting	Morphologic – none found Behavioral - unknown	• Limited data available • Can cause excessive weight gain • Tends to be sedating • May increase risk of preterm birth	0.6% - 2.8%	None
Nortriptyline	• More studies in human pregnancy, including neurodevelopmental follow-up	Morphologic – none found Behavioral – none found	• Maternal side effects additive to pregnancy effects (sedation, constipation, tachycardia) • Orthostatic hypotension, risking decreased placental perfusion • Fetal and neonatal side effects: tachycardia, urinary retention	1.3%	None
Paroxetine	• None specific, but may be optimal for some individual patients	Morphologic – Possible increased risk of cardio vascular malformations Behavioral – unknown	• More reports of neonatal side effects than most other antidepressants	0.1% -4.3%	Irritability, sleepiness, constipation, SIADH
Sertraline	• Relatively well-studied in human pregnancy • Fewer reports of neonatal side effects than other antidepressants	Morphologic – unlikey increased risk of omphalocele and septal defects* Behavioral – none found	• None specific	0.4% -2.3%	Benign sleep myoclonus, agitation
Venlafaxine	• None specific, but may be optimal for some individual patients	Morphologic – none found Behavioral – unknown	• Limited data available	5.2% -7.6%	Decreased weight gain
Desvenlafaxine	• None specific, but may be optimal for some individual patients	Morphologic – unknown Behavioral – unknown	• No systematic studies in human pregnancy	Unknown	Unknown

* Findings from one study at variance with other data, perhaps due to methodological flaws

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1: Physician's Desk reference. Thomson Reuters. Montvale, NJ. **2**: Toh et al. Selective serotonin reuptake inhibitor use and risk of gestational hypertension. Am J Psychiatry. 2009 Mar;166(3):320-8. **3:** Alwan S et al. Use of selective serotonin-reuptake inhibitors in pregnancy and the risk of birth defects. N Engl J Med. 2007 Jun 28;356(26):2684-92. **4**: Wogelius et al. Maternal use of selective serotonin reuptake inhibitors and risk of congenital malformations. Epidemiology. 2006 Nov;17(6):701-4.