Breastfeeding Safety: Antidepressants
INFORMATION BULLETIN

This information is intended to supplement your health care provider's advice.
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Reference books by Thomas Hale, *Medications and Mothers' Milk*, and Gerald Briggs and colleagues, *Drugs in Pregnancy and Lactation*, have emerged as the standard resources for rating breastfeeding safety. In this entry, we provide a summary of Hale's and Briggs' breastfeeding safety ratings and recommendations for **Antidepressants**.

Both references assign a 2-dimensional rating to each medicine. Medicines are rated both for their *volume of safety data* (newer and seldom-used medicines are often NOT well-studied) and the *potential for risk* suggested by that data. In addition, Hale includes a 5-category system of ***Lactation Risk Categories,*** which include:

- **L1 SAFEST** – Drug has been taken by many breastfeeding women without evidence of adverse effects in nursing infants OR controlled studies have failed to show evidence of risk.
- **L2 SAFER** – Drug has been studied in a limited number of breastfeeding women without evidence of adverse effects in nursing infants.
- **L3 MODERATELY SAFE** – Studies in breastfeeding have shown evidence for mild non-threatening adverse effects OR there are no studies in breastfeeding for a drug with possible adverse effects.
- **L4 POSSIBLY HAZARDOUS** – Studies have shown evidence for risk to a nursing infant, but in some circumstances the drug may be used during breastfeeding.
- **L5 CONTRAINDICATED** – Studies have shown significant risk to nursing infants. The drug should NOT be used during breastfeeding.

Another risk estimate is provided by quantifying a nursing infant's level of exposure. Hale reports the ***Relative Infant Dose (RID)*** as an index of the level of exposure. Expressed as a percentage, the RID is calculated by dividing the infant's total daily ingestion of a medicine via nursing (mg per kg infant body weight) by the mother's daily dose of the medicine (mg per kg maternal body weight). Hale advises that "a Relative Infant Dose of <10% is considered safe", though we would caution that this is a general observation that has never been objectively verified. Earlier studies had utilized milk:plasma ratio as an index of the level of exposure, but milk:plasma ratios because they do not provide an estimate of the total amount of a drug that is transferred to a nursing baby.

General Suggestions

- **Mother's Side Effects Predict Baby's Safety Concerns** – This intuitive observation helps direct the focus of your concern. For example, if a medicine is likely to cause sedation in adults, then observe your nursing infant for sedation. If it causes loss of appetite in adults, then carefully monitor your infants' growth.
- **Laboratory Monitoring for Mother Should Also Be Performed for Baby** – Some medicines require laboratory safety monitoring. For example, liver tests are monitored in women taking valproate, blood counts in women taking clozapine, and kidney tests in women taking lithium. If you are breastfeeding while taking a medicine that requires laboratory monitoring, ask for these laboratory tests for your baby as well.
- **Pregnancy Exposure Is Much Higher Than Breastfeeding Exposure** – Fetal exposure levels to a medicine are usually much higher than exposure via nursing. Thus, if your child was exposed to a medicine during pregnancy, then nursing simply continues exposure to that same medicine at a much lower level.
- **Long-Term Effects of Breastfeeding Exposure Are Not Well-Studied** – Breastfeeding safety ratings focus on risks that can be seen when your child is still nursing. However, keep in mind that there may be developmental effects of nursing exposure that will not be evident until much later.
- **Pumping and Dumping Can Reduce Exposure Levels to Occasional Medicines** – Peak breast milk levels of a medicine occur within the first hours after a dose. If taking an "as needed" dose of a medicine, you can reduce your baby's exposure by: 1) maintaining a supply of pumped/stored breast milk; 2) take the medicine immediately AFTER nursing; 3) use stored breast milk (or formula) at your baby's next feeding; 4) at this time, pump and discard milk from both breasts; 5) resume regular breastfeeding at the next feeding.

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Antidepressant	Briggs[1]	Hale[2]		
	Lactation Rating	Lactation Rating		Relative Infant Dose
Selective Serotonin Reuptake Inhibitors				
Citalopram	Limited Human Data, Potential Toxicity	L2	Limited Data / Probably Compatible	3.6 – 5.4%
Escitalopram	Limited Human Data, Potential Toxicity	L2	Limited Data / Probably Compatible	5.2 – 7.9%
Fluoxetine	Limited Human Data, Potential Toxicity	L2	Limited Data / Probably Compatible	1.6 – 14.6%
Fluvoxamine	Limited Human Data, Potential Toxicity	L2	Limited Data / Probably Compatible	0.3 – 1.4%
Paroxetine	Limited Human Data, Potential Toxicity	L2	Limited Data / Probably Compatible	1.2 – 2.8%
Sertraline	Limited Human Data, Potential Toxicity	L2	Limited Data / Probably Compatible	0.4 – 2.2%
Serotonin-Norepinephrine Reuptake Inhibitors				
Desvenlafaxine	Limited Human Data, Potential Toxicity	L3	Limited Data / Probably Compatible	5.9 – 9.3%
Duloxetine	Limited Human Data, Potential Toxicity	L3	Limited Data / Probably Compatible	0.1 – 1.1%
Levomilnacipran	--	L3	No Data / Probably Compatible	
Milnacipran	No Human Data, Potential Toxicity	L3	Limited Data / Probably Compatible	
Venlafaxine	Limited Human Data, Potential Toxicity	L2	Limited Data / Probably Compatible	6.8 – 8.1%
Atypical Antidepressants				
Agomelatine	--	--		
Bupropion	Limited Human Data, Potential Toxicity	L3	Limited Data / Probably Compatible	0.1 – 2.0%
Mianserin	--	--		
Mirtazapine	Limited Human Data, Potential Toxicity	L3	Limited Data / Probably Compatible	1.6 – 6.3%
Nefazodone	Limited Human Data, Potential Toxicity	L4	Limited Data / Possibly Hazardous	1.2%
Reboxetine	--	--		
Trazodone	Limited Human Data, Potential Toxicity	L2	Limited Data / Probably Compatible	2.8%
Vilazodone	No Human Data, Potential Toxicity	L3	No Data / Probably Compatible	
Vortioxetine	--	L3	No Data / Probably Compatible	
Tricyclic & Tetracyclic Antidepressants				
Amitriptyline	Limited Human Data, Potential Toxicity	L2	Limited Data / Probably Compatible	1.1 – 2.8%
Amoxapine	Limited Human Data, Potential Toxicity	L2	Limited Data / Probably Compatible	0.6%
Clomipramine	Limited Human Data, Probably Compatible	L2	Limited Data / Probably Compatible	2.8%
Desipramine	Limited Human Data, Potential Toxicity	L2	Limited Data / Probably Compatible	0.3 – 0.9%
Dothiepin	--	--		
Doxepin	Limited Human Data, Potential Toxicity	L5	Limited Data / Hazardous	0.3 – 3.0%
Imipramine	Limited Human Data, Potential Toxicity	L2	Limited Data / Probably Compatible	0.1 – 4.4%
Maprotiline	Limited Human Data, Potential Toxicity	L3	No Data / Probably Compatible	1.4%
Nortriptyline	Limited Human Data, Potential Toxicity	L2	Limited Data / Probably Compatible	1.7 – 3.4%
Protriptyline	No Human Data, Potential Toxicity	--		
Trimipramine	No Human Data, Potential Toxicity	--		
Monoamine Oxidase Inhibitors				
Isocarboxazid	No Human Data, Potential Toxicity			
Moclobemide	--	L4	Limited Data / Possibly Hazardous	3.4%
Phenelzine	No Human Data, Potential Toxicity	--		
Selegiline	Limited Human Data, Potential Toxicity	L4	No Data / Possibly Hazardous	
Tranylcypromine	No Human Data, Potential Toxicity	--		

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Medicine-Specific Suggestions

- **Bupropion & Milk Production** –Bupropion increases dopamine activity. Because dopamine blocks the effects of prolactin (i.e., the hormone that stimulates the breastmilk production), bupropion may, in theory, lower your breast milk production. While this is a *theoretical* concern, it has not been our experience that bupropion significantly lowers breast milk production.
- **Bupropion & Seizure Risk** – Bupropion is contraindicated for patients who are risk for having seizures. We recommend that you avoid nursing while taking bupropion if your baby has any history of seizures, including febrile seizures, or if there is any history of seizures in you, your baby's father, or any of your older children. It may also be advisable to temporarily suspend breastfeeding while taking bupropion if your baby has a high fever to decrease the risk of infant febrile seizures.
- **Nefazodone & Laboratory Monitoring** – Nefazodone requires laboratory monitoring of liver enzymes. We recommend that this laboratory testing should also be performed in your baby if you are nursing while taking nefazodone.

References
1. Briggs, G. G., Freeman, R. K., Towers, C. V., & Forinash, A. B. (2017). *Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk (11th edition).* Philadelphia, PA: Wolters Kluwer.
2. Hale, T. W. (2019). *Hale's Medications & Mothers' Milk 2019: A Manual of Lactational Pharmacology (18th edition).* New York, NY, Springer Publishing Company.

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