BREASTFEEDING AND WOMEN’S MENTAL HEALTH

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Disclosures

- Nothing to disclose, currently paid by Banner University Medical Center, and on faculty at University of Arizona.
Goals and Objectives

- Review the basic physiology involved in breastfeeding
- Learn about literature available regarding mood, sleep and breastfeeding
- Know the resources available to refer to regarding pharmacology and breastfeeding
- Understand principles of psychopharmacology involved in breastfeeding, including learning about some specific medications, to be able to counsel a woman and obtain informed consent
- Be aware of syndrome described as Dysphoric Milk Ejection Reflex
Lactation Physiology

Conception

16-22 weeks

BIRTH

30-40 hrs after birth

3 mo

Progestrone →

Prolactin

(not to scale)

Endocrine (Hormonal) Control

L I

Autocrine (Local) Control

L II

L III

Increased milk production triggers increased sucking by infant (positive feedback loop).

Suckling triggers sensory nerve impulses in the areola.

Brain receives sensory impulses from the areola and releases oxytocin (OT) from the hypothalamus and posterior pituitary.

Lactocytes in mammary alveoli produce milk in response to sensory nerve impulses.

Oxytocin (OT) triggers myoepithelial cells to squeeze milk from alveoli so it drains into lactiferous ducts.

Milk is pooled in lactiferous sinus before being discharged through nipple pores.

Milk transport

Alveolus

Lactiferous ducts

Lactiferous sinus

https://courses.lumenlearning.com/boundless-ap/chapter/lactation/
Why is breastfeeding so good for my baby?

Breastfeeding is good for your baby because:

1. Breastfeeding provides warmth and closeness. The physical contact helps create a special bond between you and your baby.

2. Human milk has many benefits.
   - It's easier for your baby to digest.
   - It doesn't need to be prepared.
   - It's always available.
   - It has all the nutrients, calories, and fluids your baby needs to be healthy.
   - It has growth factors that ensure the best development of your baby's organs.
   - It has many substances that formulas don't have that protect your baby from many diseases and infections. In fact, breastfed babies are less likely to have:
     - Ear infections
     - Diarrhea
     - Pneumonia, wheezing, and bronchiolitis
     - Other bacterial and viral infections, such as meningitis
   - Research also suggests that breastfeeding may help to protect against obesity, diabetes, sudden infant death syndrome (SIDS), asthma, eczema, colitis, and some cancers.
Why is breastfeeding good for me?

Breastfeeding is good for your health because it helps:

- Release hormones in your body that promote mothering behavior.
- Return your uterus to the size it was before pregnancy more quickly.
- Burn more calories, which may help you lose the weight you gained during pregnancy.
- Delay the return of your menstrual period to help keep iron in your body.
- Provide contraception, but only if these 3 conditions are met:
  - You are exclusively breastfeeding and not giving your baby any other supplements
  - It is within the first 6 months after birth
  - Your period has not returned
- Reduce the risk of ovarian cancer and breast cancer.
- Keep bones strong, which helps protect against bone fractures in older age.
i make milk...
what's your superpower?
A Few Numbers

- About 80% of US women breastfeed
- 10-15% of women suffer from post partum depression or anxiety
- 1-2/1000 suffer from post partum psychosis
Depressed mothers are:

- More likely to misread infant cues
- Less likely to read to infant
- Less likely to follow proper safety measures
- Less likely to follow preventative care advice
Depression is Associated with Decreased Chance of Breastfeeding

- A review of 75 articles found “women with depressive symptomatology in the early postpartum period may be at increased risk for negative infant-feeding outcomes including decreased breastfeeding duration, increased breastfeeding difficulties, and decreased levels of breastfeeding self-efficacy.” ¹
Depressive Symptoms and Risk of Formula Feeding

- An Italian study with 592 mothers participating by completing the Edinburgh Postnatal Depression Scale immediately after delivery and then feeding was assessed at 12-14 weeks where asked if breast, formula or combo feeding. Scores were significantly higher in the full bottle fed group than the fully breastfed group (but average of both groups was not in the depressive range). An increase of 1 point on the EPDS correlated to a 6% chance of bottle feeding.²

- Excluded mothers taking antidepressants,
Depression and Post Partum Sleep

- A Norwegian study aimed to estimate the prevalence of and risk factors for poor maternal sleep and depression among 2830 post-partum women.

- Pittsburgh Quality Sleep Index (PSQI) was used to self rate sleep complaints and the Edinburgh Postnatal Depression Scale (EPDS) was used to measure depressive symptoms. Demographic info was obtained from records. Moms would have been on maternity leave (44 weeks paid in Norway) and info about breastfeeding and sleeping arrangements were added.

- 57% above cut off for PQSI, and 16.5% for EPDS

- Multiple logistic regression showed depression was the variable most strongly associated with sleep problems.

- Went on to measure sleep using actigraphy in a subset of mothers and there was no difference in sleep between depressed and non depressed women despite differences in the PSQI.
How Do Babies Sleep?

- Henderson et al. studied natural pattern of infant sleep and found that by 3 months of age 50% of infants are sleeping from 24:00 until 05:00 AND sleeping for 8 hours straight.
Breastfeeding and Sleep

- Survey of sleep and fatigue administered to 6410 mothers in 59 countries.  
- Breastfeeding mothers reported significantly more sleep than mixed or formula only fed (6.6, 6.4, and 6.3 hours).
- Breast feeding mothers reported more energy than mixed or formula feeding.
Breastfeeding and Sleep Disturbances

- Doan et al studied parents of infants and found that parents who breastfed (vs. formula) actually got 40-45 min more sleep per night as measured by actigraphy and also self-reported less sleep disturbances.\(^6\)
## Contraindications to Breastfeeding

**Maternal**
- Abuse of street drugs
- HIV
- T-Cell lymphotropic virus infection or Brucellosis
- Untreated miliary TB
- Antimetabolite chemotherapy and ongoing radiation therapy
- Active herpetic breast lesions

**Infant**
- Galactosemia

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2012 revision of the American Academy of Pediatrics policy statement on breastfeeding and the use of human milk
Considerations When Prescribing Medications in Pregnancy

- The need for the drug by the mother
- The potential effects of the drug on milk production
- The amount of the drug excreted into breast milk
- The extent of absorption by the breast feeding infant
- The potential adverse effects on the breast feeding infant

AAP publication: The Transfer of Drugs and Therapeutics into Human Breast Milk: An Update on selected topics. Hari Cheryl Sachs and Committee on Drugs. Pediatrics 2013; 132; e796.
The amount of medication to which an infant is exposed depends on several factors: factors pertaining to the specific medication, the maternal dosage of medication, the frequency of maternal dosing as well as chronicity, frequency of infant feedings, and the rate of maternal drug metabolism.

Age of the infant, and health status of the infant: During the first few weeks of a full-term infant’s life, there is a lower capacity for hepatic drug metabolism, which is about one-third to one-fifth of the adult capacity. Over the next few months, the capacity for hepatic metabolism increases significantly and, by about 2 to 3 months of age, it surpasses that of adults.

Involve the pediatrician

Pump and Dump?
Lactation Risk Categories

- **L1 Compatible**: drug has been taken by a large number of breastfeeding women without any observed increase in adverse effects in the infant; controlled studies fail to demonstrate a risk to the infant, or the product is not orally bioavailable in an infant.

- **L2 Probably compatible**: drug has been studied in a limited number of breastfeeding women without an increase in adverse effects in the infant, and/or the evidence of a demonstrated risk is remote.

- **L3 Probably compatible**: there are no controlled studies in breastfeeding women; however, the risk of untoward effects to breastfed infant is possible, or controlled studies show only minimal non-threatening adverse effects; drugs should be given only if potential benefit justifies potential risk to infant; new medications that have no published data are automatically categorized in this category, regardless of how safe they may be.

- **L4 Possibly hazardous**: positive evidence of risk to breastfed infant or to breast milk production; benefits of use may be acceptable despite the risk to infant; e.g. if the drug is needed in a life-threatening situation or a serious disease for which safer drugs cannot be used or are ineffective.

- **L5 Hazardous**: studies in breastfeeding mothers have demonstrated significant and documented risk to the infant based on human experience, or is a medication that has a high risk of causing significant damage to infant; drug is contraindicated in women breastfeeding an infant.
Resources

- Infant Risk Center: infantrisk.com
- MGH: Womensmentalhealth.org
- Mothertobaby.org has fact sheets you can give to patient
Antidepressants and Lactation

- A small study compared milk secretory activation between mothers taking antidepressants and mothers who were not. Mothers taking antidepressants had a delay of 16 hours, but no difference in success of breastfeeding at 4 days.

- Online survey of 930 mothers who took an antidepressant during pregnancy compared those who nursed while taking an antidepressant to those who did not. Drug discontinuation was noted in 10% of infants, and it was much less likely if mother continued antidepressant while breastfeeding.
Antidepressants

- **MAOIs:** Insufficient evidence, and as such not recommended during nursing.

- **TCAs:**
  - Amitriptyline and nortriptyline found in variable concentrations. But no adverse effects reported. Also no adverse effects for the small number of infants exposed to imipramine, desipramine, clomipramine.

- **Doxepin:**
  - In a case report of 2 infants exposed to doxepin both had high levels in the milk, and one of those infants had respiratory depression that resolved within 24 hours of cessation of breastfeeding. In other cases doxepin has been linked to infant death.
  - Do not use DOXEPIN, linked with infant death in one case.
Antidepressants

- **Sertraline**: Considered preferred. Concentrations of 0.5% down to 0.04% of maternal dose in milk. Milk concentration did not correlate with maternal dose. Drug concentrations are higher in hind milk. Peak concentrations at 8-9 hours (pump and dump would reduce infant exposure by 17%).
  
  - Infant serum levels only detectable in 24% of infants, and correlated with mother’s dose and inversely with infant age.  
  - Meta-analysis found serum levels were nondetectable or negligible and no adverse events reported.
  - Once case of sleep myoclonus in a 4 month old, and one case of agitation that spontaneously resolved.
Antidepressants

- **Paroxetine:**
  - Preferred medication.
  - Undetectable or minimal concentration in breastmilk
  - Meta-analysis of 37 infants exposed. Infant serum levels were nondetectable in all but 3 cases which had low levels. No adverse effects were reported.
  - Multiple cases with no ill effect to infant.
  - In a study of mothers who took paroxetine in the 3rd trimester and breastfed, about a quarter reported side effects such as decreased alertness, constipation, sleepiness, and irritability.
  - One study found 12% of infants of mothers taking paroxetine had adverse events including insomnia, restlessness, crying and poor feeding, all of which resolved within 3 days of discontinuing paroxetine (or in one case decreasing the dose).
  - 36 mothers on an avg dose of 20.4mg daily of paroxetine had infants with normal 6 month weights and no abnormal effects.
  - One case report of an infant with detectable serum paroxetine levels who had 3 episodes of vomiting and dehydration. The infant was thriving 6 weeks after breastfeeding was discontinued.
Antidepressants

- **Fluoxetine:**
  - Meta-analysis compiled data from 238 infants on 15 antidepressants and found fluoxetine had a relatively high infant serum levels (18% had levels over 10% of maternal levels) \(^{11}\)
  - In a meta-analysis of 190 infants, serum levels varied from undetectable to very high. The infant with the “very high” level had excessive fussiness, decreased sleep, vomiting and diarrhea that stopped when breastfeeding stopped. Infant serum levels did not seem to correlate with maternal dose. 10 cases of adverse events which were transient or confounded by multiple medications.
  - One study looked at infants neurobehavioral development at 1 year of age and found it to be normal. \(^{9}\)
  - Despite higher levels in breast milk most experts do not recommend changing to breastfeed if on fluoxetine prenatally.
Antidepressants

- **Citalopram and escitalopram:**
  - Citalopram has relatively high infant serum levels.\(^{11}\)
  - Several small reports of mothers taking citalopram show generally low levels in infant serum, but with occasional higher levels which may relate to mother being a poor metabolizer of CYP2C19.\(^{17}\)
  - One study looked at infants breastfed by mothers taking citalopram and found normal weight and development at 1 year compared to controls.\(^{11}\)
  - Infant serum levels in infants whose mothers were taking escitalopram were undetectable or very low.\(^{11}\)
  - Several case reports of infants without adverse effects on escitalopram, but also one report of an infant with irritability, vomiting and fever with moderately elevated LFTs that improved 2 weeks after breastfeeding was discontinued and resolved 1 month later.\(^{20}\) Another report of a 5-day-old exposed to escitalopram both pre and postnatally admitted for necrotizing enterocolitis.\(^{21}\)
Antidepressants

- **Venlafaxine, Desvenlafaxine, Duloxetine:**
  - **Venlafaxine:** Infants had elevated rate of metabolites in all infants studied of up to 37%\(^{11}\)
    - In 10 cases, 2 infants had decreased weight gain and the others had no adverse effects.\(^9,23\)
  - **Desvenlafaxine:** Levels of desvenlafaxine are about half that of mothers who took venlafaxine. Babies exposed to desvenlafaxine (and polypharmacy) were found to have lower growth rate.\(^{22}\)
  - **Duloxetine:** has limited data looking at 2 infants. Thus far low levels in milk and infant serum.
  - Monitor infant growth rate
Antidepressants

- **Mirtazapine:**
  - Several case reports of infant serum levels that were either undetectable or low.
  - Case study of 8 infants found normal development at around 6 months of age. 

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Antidepressants

- **Bupropion:**
  - 8 case reports of which 7 found non detectable levels with both IR and SR dosage. 1 case report where the mother of a 6 month old was taking the XL formulation (along with escitalopram) and the infant had a seizure. The infant had detectable but low levels of bupropion and its metabolite hydroxybupropion \(^{25,26,27,28}\)
Antidepressants

- No data with vortioxetine, vilazodone, brexipiprazole and levomilnacipran
Neurostimulation for Depression

- ECT: Acceptable option as anesthetics and neuromuscular blockers such as propofol and succinylcholine are acceptable with breastfeeding as soon as the effects wear off.
- TMS: No data.
Mood Stabilizers

- **Lithium:**
  - Milk levels are nearly half of maternal levels\(^{29}\)
  - No difference between fore and hind milk \(^{31}\)
  - Levels reported in 13 infants were all high (10-50% of maternal levels), but no adverse effects reported except for one infant exposed in utero with heart murmur, T wave inversion, cyanosis and hypotonia whose mother was also on a diuretic
  - TSH elevated in 2 infants (one normalized despite continued breastfeeding) who were exposed during pregnancy \(^{32, 33}\)
  - Need to monitor infant lithium concentration, TSH, renal function and CBC
  - AAP recommends using caution
Mood Stabilizers

- **Valproate:**
  - If not exposed during pregnancy infant serum levels were less than 6% of maternal levels (studies complicated by polypharmacy) \(^{34}\)
  - 19 infants with no adverse effects, one infant with thrombocytopenia and anemia which resolved when nursing stopped (however could be explained by viral infection.) \(^{35}\)
  - One study compared IQ of children breastfed with valproic acid vs formula fed by mother on valproic acid and found a statistically different higher IQ in breastfed infants at age 6. \(^{36}\)
  - Monitor for bruising and jaundice, VPA level, platelets and liver enzymes
Mood Stabilizers

- **Carbamazepine:**
  - Levels are detectable but low in breastmilk, limited data on levels in infants not exposed during pregnancy. One study looked at 54 breastfed infants and infant serum levels ranged from undetectable to 70% of maternal levels of carbamazepine, no correlation was found with maternal and infant serum level. Of 25 infants exposed through nursing 2 had transient hepatic dysfunction (resolved when nursing was stopped) and both demonstrated normal development at 6 months.
  - Monitor for jaundice, drowsiness, weight gain, and developmental milestones. Check liver, bilirubin, CBC, and Carbamazepine levels.
Mood Stabilizers

- **Lamotrigine:**
  - Milk/Plasma ratio of 0.61 with infant serum concentration of 30% of maternal concentrations\(^3\)
  - No reports of infant SJS
  - Multiple case reports without adverse events
  - Of 8 infants who had platelets monitored, 7 were elevated with no adverse event\(^4\)
  - A mother on 850mg daily had an infant have a severe apneic spell requiring chest compressions.\(^4\)
  - Monitor for rash, respiratory depression, CBC, consider lamotrigine levels
Antipsychotics

- **Clozapine:**
  - Concentrated in breast milk
  - Infant serum levels 279% that of mother’s serum levels.
  - Case reports of infant with sedations, agranulocytosis, and cardiovascular instability.
  - Monitor for somnolence, CBC with diff (weekly), NMS. Infant would go on clozapine registry
  - Probably best to avoid
Antipsychotics

- **Olanzapine:**
  - Several reports of infant’s levels being undetectable for mothers with doses up to 20 mg daily, 1 case report with infant with detectable level.
  - The manufacture compiled 102 breastfed infants whose mother was taking olanzapine and 15% reported adverse events (somnolence, irritability, tremor and insomnia) though many exposed prenatally also. 46-47
  - A case control study compared mothers who took olanzapine and breastfed vs those who took the drug and did not breastfeed, vs those taking Tylenol. Mothers completed a survey 1-2 years later showing no statistical difference in the groups with regards to development. 66
  - Probably preferred antipsychotic in breastfeeding
Antipsychotics

- **Aripiprazole:**
  - Very limited data,
  - Can lower prolactin levels and several case reports of difficulty with establishing supply.
  - Only a handful of cases with doses around 15mg daily. One case where serum levels were detected the infant was exposed in utero. One case of a 3 month old infant who was growing normally, and one case a baby was partially breastfed and at 4 months was reaching normal developmental milestones. \(^{42-44}\)
  - One case of a 12 day old on lamotrigine, aripiprazole, sertraline and synthroid presented with severe weight loss and dehydration who developed DIC and required 5 toe amputation. \(^{45}\)
  - Probably pick another agent
Antipsychotics

- **Risperidone:**
  - 4 case reports of infants breastfed (mother’s dose up to 4mg daily) and infant levels where undetectable. 48
  - No reports of adverse events (except sedation in a infant with mother and significant polypharmacy). Several reports of normal development. 49-52
  - Can cause galactorrhea
Antipsychotics

- **Quetiapine:**
  - Probably a good choice during breastfeeding, at least at low doses.
  - Max milk levels 1 hour after dose and correlated with maternal dose. No difference in fore vs hind milk.
  - A lot of the cases were moms on very low doses
  - The few cases of infant levels were below 10%
  - All case reports did not note adverse events, and development was within normal limits for the cases in which it was reported.
Antipsychotics

- **Haloperidol:**
  - Levels in infants of mothers on 5-20mg collected. They had low levels present, not related to dose.
  - Several cases showed normal development and no adverse effects, but one study with haloperidol plus chlorpromazine showed 2 infants (out of 4) had a decline in developmental scores at 12-18 months.
Antipsychotics

- Ziprasidone has 1 case report of no adverse events\textsuperscript{54}
- Asenapine, paliperidone, lloperidone, and lurasidone have no data
Lactation on an Inpatient Psychiatric Unit

- Is it safe?
- Is it wise?
- Who gets to decide?
Insomnia

- Sleep hygiene
- Risk of mother falling asleep
  - **Diphenhydramine**: has surprisingly little data, but occasional use is acceptable
  - **Trazadone**: 0.6% maternal dose, and no reported adverse events
  - **Zolpidem**: variable levels in milk, one case of infant sedation
  - **Eszopiclone**: no data
  - **Melatonin**: Limited data on safety and infant plasma levels, but short term course is unlikely to have negative effect.
Anxiolytics

- **Buspirone**: has insufficient data. One case report with undetectable milk and infant serum levels.\(^\text{55}\)

- **Hydroxyzine**: Chronic use may effect milk supply, but occasional use probably will not. No data on milk or serum concentrations. Of 174 mothers taking hydroxyzine there were 8 adverse events noted, primarily sedation.\(^\text{68}\)

- **Motherisk Study included 124 infants exposed to benzodiazepines via breastmilk, only 1.6% experienced sedation**

- **Clonazepam**: Not a preferred choice, associated with multiple adverse events including serious adverse events.

- **Diazepam**: Infant serum levels are unpredictable and can range from unpredictable to very high. Associated with sedation and weight loss making diazepam a poor choice.\(^\text{56}\)

- **Lorazepam**: Low breast milk levels, safe to administer to infants, no adverse effects noted in breastfed infants (toxnet.nlm.nih.gov)

- **Oxazepam**: has a short half life and low levels in breast milk. It is also acceptable to give to infants. There are reports of sedation.

- **Alprazolam**: One case reported of withdrawal from alprazolam when medication was tapered.
ADHD Treatments

- **Guanfacine** has no data on serum levels or safety, but may lower prolactin
- **Strattera** has no published data
- **Clonidine**: infant levels ranged from undetectable to 66% of maternal levels. There have been several reports of infants without adverse effects, but one report of an infant with hypotonia, seizures and apnea that resolved 24 hours after breastfeeding was stopped. Possible galactorrhea. 57
- **Dextroamphetamine/amphetamine**: found up to 15% serum levels in infants. 4 cases published of mothers on 18-35mg daily where infant developed normally without adverse events. Some data to show a non statistical decrease in prolactin with IV amphetamines. Monitor for agitation and poor weight gain. 58-59
- **Methylphenidate**: 4 infants studied all (3 tested) had undetectable methylphenidate levels and no adverse effects were reported. Possible decrease prolactin levels. Monitor for agitation and poor weight gain. 60
Cannabis

- Neurodevelopmental effects, delayed motor development at 1y, lethargy, less frequent and shorter feeds, high milk-plasma ratio in heavy users
- New study 61 on transfer of inhaled cannabis into human breast milk.
- Looked at women who smoke cannabis regularly and are 2-5 months postpartum and breast feeding.
- 8 moms where told not to smoke for 24 hours and baseline levels where drawn. Then they were told to smoke 3-4 hits of cannabis and breastmilk samples were collected at 20 min, 1, 2 and 4 hours intervals afterwards and THC was quantified by high performance liquid chromatography tandem mass spectroscopy.
- THC detected at low concentrations at all time points beyond baseline. THC was transferred into mother’s milk such that exclusively breastfeeding infants ingested estimated 2.5% of maternal dose (range 0.4-8.7%)
Dysphoric milk ejection reflex (D-MER)

- Only recently described in the literature, with 3 publications found on pubmed.
- Websites, books and blogs.
- Negative feelings with each breastfeeding (milk let down) episode. Described as lasting 90-120 seconds with feeling worthless, poor concentration (effecting math skills and reading skills), feeling homesick, and feeling hollow.
- Resolves after weaning.
- Speculation that it may involve oxytocin or dopamine (dopamine could drop to increase prolactin). In one case a woman reported that pseudoephedrine was very helpful. 67
Conclusion

- Breastfeeding has many health benefits to mother and baby
- Traditional beliefs about breastfeeding and sleep are probably incorrect
- Psychopharmacology during breastfeeding is challenging due to limited data in most agents, but with only rare exception it is not a reason to prevent a mother from breastfeeding, albeit with close monitoring to the infant in some cases
  - Be sure about the diagnosis and severity of symptoms
  - Find out about what has worked in the past
  - Avoid polypharmacy whenever possible
  - Coordinate with the Pediatrician
- Mother should be able to provide informed consent without a sense of judgment from her physicians
- Use your resources!
Questions?

2. Gagliardi L, Petrozzi A Rusconi F. Symptoms of maternal depression immediately after delivery predict unsuccessful breast feeding. Archives of Disease in Childhood 2012; 97:355-357


38. Ohman I, Tomson T, Vitolš S. Lamotrigine levels in plasma and breast milk in nursing women and their infants (abstract). Epilepsia 1998; 21 (suppl 2):39


