

# Medications in Lactation



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I have no actual or potential conflict of interest in relationship to this presentation.

# Medications in Lactation

- Many common medications prescribed to breastfeeding mothers are safe to take while breastfeeding and providers may not realize this or may not have time to research each medication during a busy clinic/shift when seeing patients
- For each medication that the breastfeeding mother takes, it is important to weigh the benefit to the mother against the risk to the infant and mother's ability to breastfeed her infant

# Ethical Issues

- Unique dilemma compared to pregnancy as formula is considered a safe alternative by some
- Risk avoidance leading to lack of evidence and off label prescribing
- 2005 FDA recognizes need for improved labeling and research
- 2015 Pregnancy and Lactation Labeling Rule
- Working on more inclusive study groups
- Need to have more data to provide improved education to health professionals and consumers

# Remembering basic Pharmacology

- Pharmacokinetics – How drugs move through the body – absorption, distribution, metabolism, and excretion
- Pharmacodynamics – How drugs interact with the body and cells to elicit their effect (receptor and drug interaction)
- Half Life – the time it takes for a drug to become half of the level that it was previously
- Volume of Distribution – Not all drugs distribute evenly throughout the body – depends on many factors
- pKa – acid dissociation constant

# Lactational Pharmacology

- Milk/Plasma Ratio
- T<sub>max</sub> – time interval from drug administration to peak concentration in the mother's plasma
- Protein binding
- Molecular weight
- Oral bioavailability
- RID – Relative Infant Dose



# Physiology of Transfer

- Enters by passive diffusion – driven by equilibrium between maternal plasma and milk
- Drugs pass through capillaries into lactocytes, and must be able to pass through both bilayer lipid membranes of the alveolar cell
- Early on (first 72 hours pp) medications may pass more freely between the alveolar cells due to larger gaps
- By the end of week 1 pp, alveolar cells swell from prolactin and gaps close, reducing entry
- Although meds penetrate into milk more during colostrum period, absolute dose is still low as total volume of milk is low
- Mothers in late stage lactation (>1 year) have low milk production so dose of drug delivered is lower



# Drug Trapping in Milk

- High pKa (ion trapping) – lower pH of milk changes the ionic state of drug and prevents re-entry into maternal plasma, e.g. barbiturates
- Ionic forms of iodine or “iodides” - iodine pump, e.g. radioactive iodides





# Drugs more likely to transfer IF:

- Attain high concentrations in maternal plasma
- Are low in molecular weight (<800)
- Are low in protein binding (as those bound will stay in the maternal circulation)
- Cross the blood-brain barrier easily (typically more lipid solubility)

# Oral bioavailability

- Many drugs destroyed in infant's gut before achieving systemic circulation
- Many are not absorbed through gut wall preventing circulation
- Many are rapidly picked up by the liver where they are metabolized or stored but don't reach plasma

# Relative Infant Dose

- Infant's dose via milk in mg/kg/day over mother's dose in mg/kg/day
- If RID is less than 10%, most medications are considered relatively safe to use, but this is always dependent on **the type of drug**



# In General:

- If the drug is hazardous to mother, most likely hazardous to infant, e.g. radioactive iodide, cancer medications
- Choose drugs with short half-lives, high protein binding, low oral bioavailability, or high molecular weight
- Avoid drugs that alter mother's milk production – estrogens, ergot alkaloids, etc.

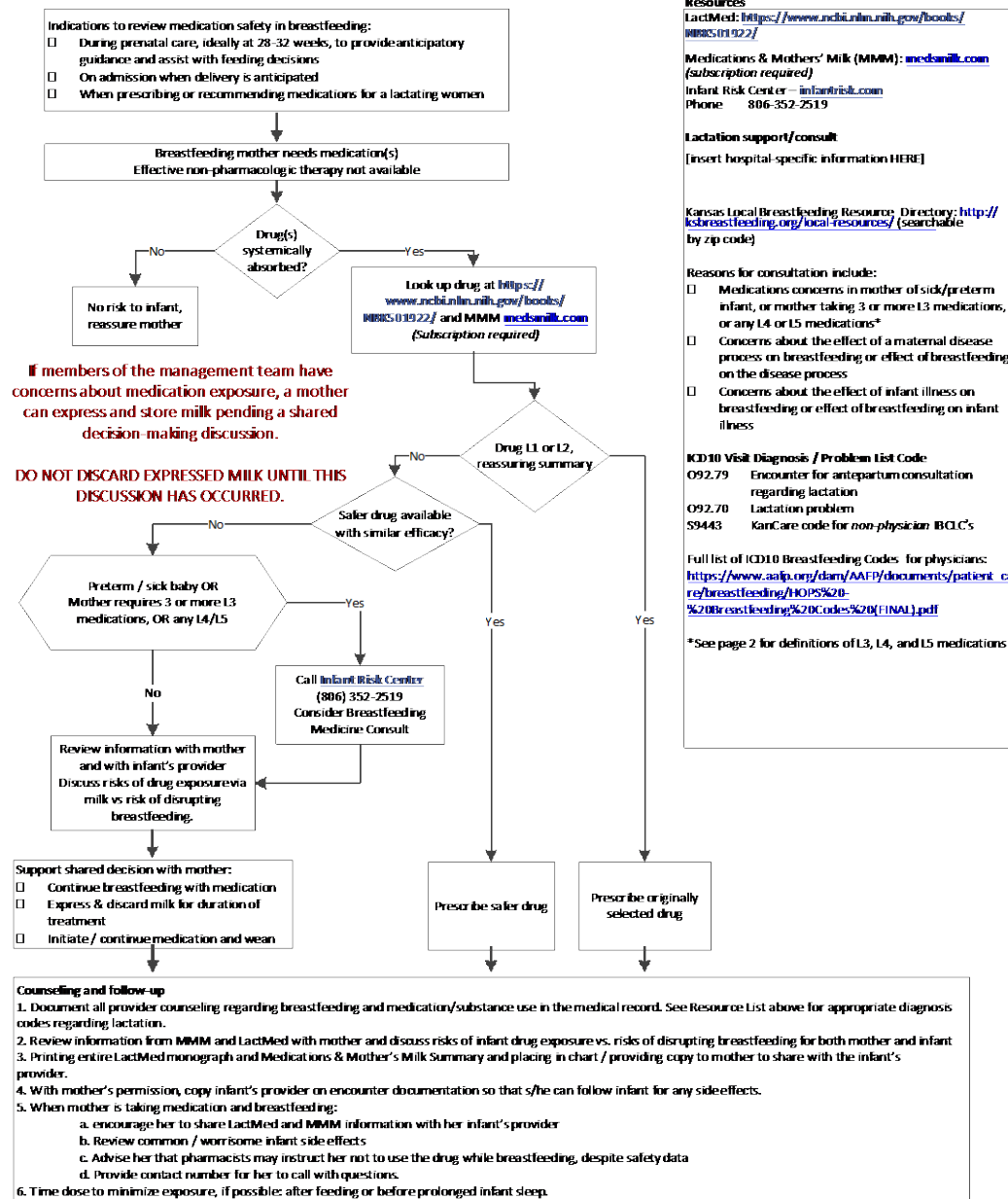
# Lactation Classifications

- L<sub>1</sub>: Compatible, studies have shown no risk to infant
- L<sub>2</sub>: Probably Compatible, studies have shown risk is very remote in infants of mothers taking these medications
- L<sub>3</sub>: Probably Compatible, should only be given if the potential benefit justifies the potential risk to the infant
- L<sub>4</sub>: Potentially Hazardous, benefits of use to the mother may be acceptable despite risk to infant
- L<sub>5</sub>: Hazardous (Contraindicated), The risk of using the drug in breastfeeding women clearly outweighs any possible benefit from breastfeeding.

# Using the Algorithm

- Concise and Simple
- Any provider can use it
- NIH Drugs and Lactation Database is free, updated regularly
- Medications and Mother's Milk app is an excellent and extensive resource, does require a subscription, and updated regularly
- Infant risk line - easy and quick to navigate, excellent when considering more risky medications

## Medication in Lactation





# Drugs and Lactation Database

- <https://www.ncbi.nlm.nih.gov/books/NBK501922/>
- Search by Drug Name or Drug Class
- Categories for Each Drug:
  - Summary of Use
  - Drug Levels
    - Infant
    - Maternal
  - Effects on Infant
  - Effects on Lactation
  - Alternate Drugs
  - Drug Class
  - References

# Medications and Mother's Milk App

- Search by Generic or Trade Name or Category and Lactation Classification (L1 – 5)
- Information on Each Drug:
  - Summary
  - Pharmacokinetics
  - Adult concerns and dosing
  - Pediatric concerns
  - Infant monitoring
  - Alternatives
  - References
- Complimentary drug entries
  - 11 prescription
  - 10 over the counter
  - 5 "other"



# Infant Risk Line

- It is important to consider the age of infant and longevity of breastfeeding along with risk to mom and baby.
- Long term maternal medications that pose conundrums, i.e. opioids for chronic pain, biologics or anti-inflammatory agents, or mental health meds. Consider especially a newborn's response to levels in milk in those meds that didn't cross placenta in utero.
- These are appropriate consults for the Infant Risk Line

# Case 1

- Molly is a G1P1 new mother bringing newborn Halle in for her first pediatrician visit. Molly was prescribed Naproxen and Hydrocodone by her physician for post-partum pain control and is concerned because she is breastfeeding and worries if she can take these medications while breastfeeding. What do you tell her?

# Case 1 discussion

- Hydrocodone is an analgesic, L3 class with limited data, probably compatible
  - $T_{1/2}$  – 3.8hr,  $T_{max}$  1.3hr, PB 19-45%, MW 299 (low), complete oral bioavailability, RID 2.21% - 3.7%
  - Limit dose to no more than 30mg/day
  - Monitor for sedation and apnea at higher doses
  - Alternative hydromorphone

# Case 1 Discussion (cont.)

- Naproxen is an NSAID, L3 class with limited data, probably compatible
  - $T_{1/2}$  12-15hr,  $T_{max}$  2-4hr, PB 99.7%, MW 230 (low), oral bioavailability 74 – 99%, RID 3.3%
  - Use with caution due to long half life
  - Safer alternatives Ibuprofen or acetaminophen

# Case 1 continued

- Molly comes back in 3 days later with a healthy, growing Halle who is nursing vigorously. Unfortunately, Molly has developed some post-partum depression and has been started on Lexapro for this. She is again, very concerned for the effects of this medication on her beautiful new baby. What do you tell her?





# Case 1 discussion continued

- Lexapro (escitalopram) is an SSRI antidepressant, L2 class, limited data, probably compatible
  - $T_{1/2}$  27-32 hrs,  $T_{max}$  5 hours, PB 56%, MW 414, oral bioavailability 80%, RID 5.2 – 7.9%
  - Watch for sedation or irritability in infant, not waking to feed or poor feeding and weight gain
  - Alternatives: setraline, fluoxetine

# Case 2

- Jill is an expectant mother with Crohn's disease who is coming in for a prenatal visit. She is currently well controlled on Humira (adalimumab), and has continued her regular dose throughout pregnancy without complication. She is wondering if she will be able to continue taking her current regimen and breastfeed her child regularly after he is born. What do you tell her?

# Case 2 Discussion

- Adalimumab is a IgG1 monoclonal antibody specific for human TNF, which is given to prevent pain and destruction in autoimmune syndromes
- Class L3 – limited data and probably compatible
- Large molecular weight, low oral availability
- Low protein binding, half life of 2 weeks
- Likely fine, but no long term data
- Infant monitoring – vomiting, weight gain, frequent infections
- Alternatives: Infliximab

# Case 3

- Sarah has just delivered her third child at 29 WGA. He is currently in the NICU receiving assisted ventilation and tube feeds. She has been pumping to provide breastmilk, and she recently disclosed (after mentioning that she does not have custody of her other children) that she is on medications for her ADHD (Focalin XR), and methadone as she is a recovering drug addict. She is hoping to restart taking Depakote for her Bipolar disorder, which she was told to stop during her pregnancy. The bedside nurse is concerned about using mom's milk to feed the infant. What do you tell her?



# Case 3 Discussion

- Depakote – L4, limited data, possibly hazardous
  - MW 144, 94% PB, RID 0.99-5.6%, complete oral bioavailability,  $\frac{1}{2}$  life 14hr
  - Thought to be safe due to low amount transferring into milk, but 1 report of infant with thrombocytopenic purpura
  - Attempt to find alternative: Quetiapine (L2), Olanzapine (L2)
- Focalin XR – L3, no data, probably compatible
  - $\frac{1}{2}$  life 2-4.5hr for immediate release, MW 270, oral bioavailability 22-25%
  - Observe infants for agitation and poor weight gain
- Methadone – L2 with significant data, compatible
  - $T_{1/2}$  13-55hr, PB 89%, MW 309, Oral bioavailability 50%, RID 1.9 – 6.5%

# When prescribing or counseling, remember:

- Communication!!
- Documentation!!
- Provide written information!!
- Follow up!!

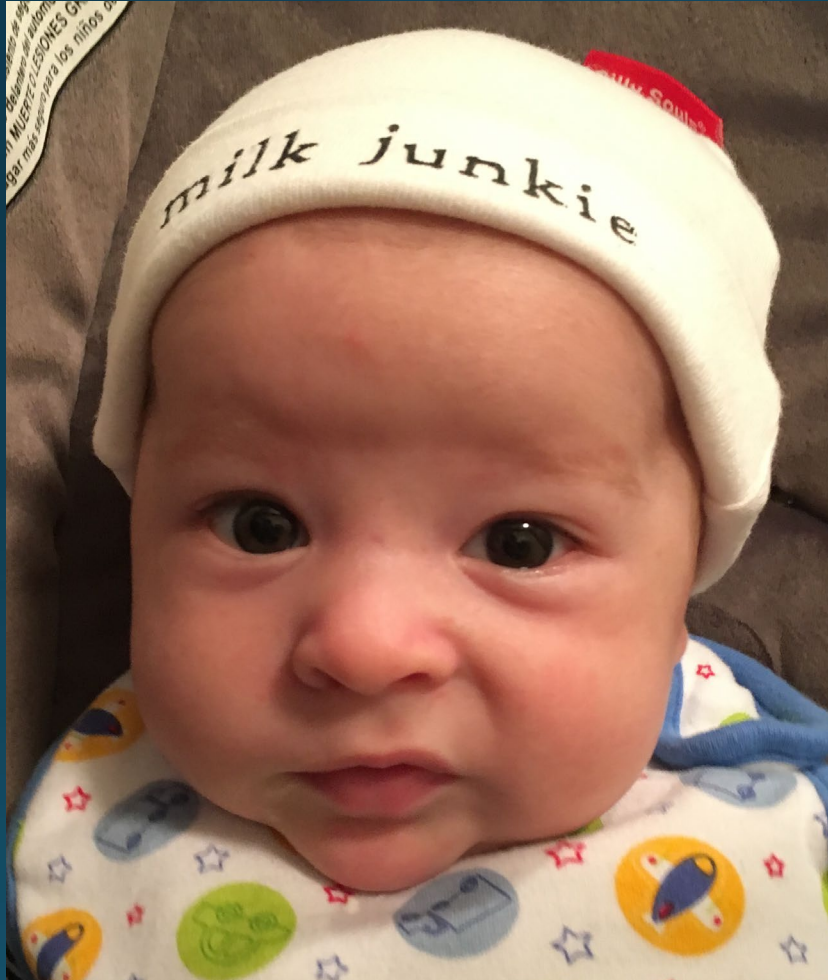


# References

- Hale, Thomas. Hale's Medications and Mother's Milk. Version 6.8.1, Springer Publishing Company, LLC, 2019. Apple App Store.
- Drugs and Lactation Database LactMed, National Library of Medicine. (March 28, 2011). Retrieved from <https://www.ncbi.nlm.nih.gov/books/NBK501922/>
- Pazdernik, Thomas and Kerecsen, Laszlo. (2007). *Rapid Review Pharmacology Second Edition*. Philadelphia, PA: Mosby an affiliate of Elsevier.
- Reece-Stremptan, S, Campos, M, Kokajko, L, and ABM. (2017). ABM Clinical Protocol #15: Analgesia and Anesthesia for the Breastfeeding Mother, Revised 2017. *Breastfeeding Medicine*, 12(9). DOI: 10.1089/bfm.2017.29054.srt.
- Amir, L, Grzeskowiak, L, and Kam, R. 2019. 'Ethical Issues in Use of Medications During Lactation' *Journal of Human Lactation* 1-6.



# Questions???



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