


# Medications and Mother's Milk

Baby Friendly Conference



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## Outline

- Medication use during lactation
- Evidence to support medication use
- Factors to consider when selecting medications for use during lactation
  - Drug, maternal, fetal
- Suggested references

Conflict of interests – none to declare

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## Medication Use

- In Canada ~85% of women initiate breastfeeding
- >90% of women take meds in the 1<sup>st</sup> week postpartum
- Treatment for:
  - Problems related to lactation
  - Acute conditions
  - Chronic medical conditions
    - depression, diabetes, seizure conditions, GI conditions

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## Medication Use

- Women concerned about effects on infant
  - Want to do what's best for infant
- Motherisk study
  - Recontacted 203 women who called about antibiotic use
    - 19 women did not take antibiotic
    - 7 weaned infant
- Cohort study of 34 women on antiepileptics vs controls not on meds
  - Breastfeeding 50% vs. 85%

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## Medication Advice

"When in doubt, don't breast feed"

- Not beneficial for women or infant
- Negative or conflicting information can lead to unnecessary interruption or discontinuation of breastfeeding
- Temporary interruptions increases likelihood of permanent weaning
- 1<sup>st</sup> source of information important

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## Lack of evidence

- Breastfeeding women excluded from clinical trials of new medications
  - "Gold standard" RCTs generally not available
- Manufacturers not required to study medication use in lactation
  - Product info from manufacturer usually insufficient (CPS, PDR, etc)

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## Evidence Sources

- Evidence comes from:
  - theoretical risks
  - case reports of ADRs
  - estimation of infant exposure
    - Milk/plasma ratio, relative infant dose
  - some epidemiologic studies (case-control, cohort)
  - expert opinion
    - Experts may not agree
- Difficult to develop consistent evidence based recommendations
  - HCP may provide conflicting advice / personal opinion
- Recommendations vary between references

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## Standard references do not agree on "safe" medication

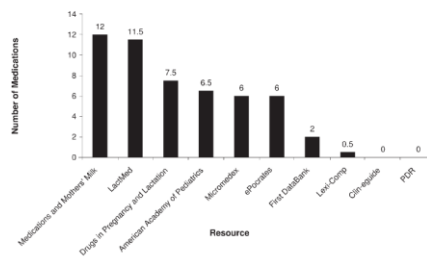


Figure 1. Number of safe medications (out of 14). Rating scale 0 = contraindicated; 1 = safe. Metronidazole was given 0.5 rating due to some sources recommending oral transfusions of breast-feeding in one setting.

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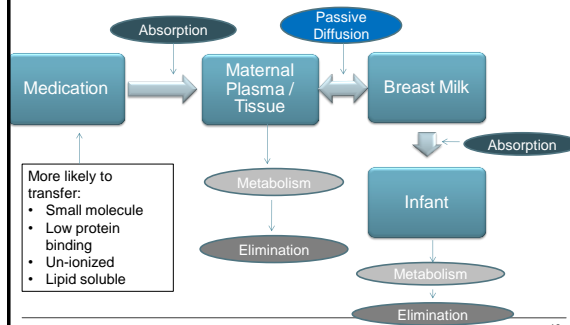


## Factors to consider

- Medication related
- Maternal considerations
- Infant factors

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## Principles of Drug Transfer into Breast Milk



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## Methods of estimating infant drug exposure – M/P ratio

### Maternal milk:plasma ratio

$$\frac{[\text{Drug in mother's milk}]}{[\text{Drug in mother's plasma}]}$$

- Index of the amount of maternal dose that will cross into the breast milk
  - Low transfer ratio <1
  - High transfer ratio >1
- Point estimate or AUC
- Dependent on timing of dose administration, sampling time of blood and breast milk
- Does not give any indication of effects on infant
- Little clinical utility

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## Methods of estimating infant drug exposure - RID

### Relative Infant Dose

$$\frac{\text{Infant dose (mg/kg/day)}}{\text{Maternal dose (mg/kg/day)}} \times 100\%$$

- Estimate infant dose
  - Drug concentration in milk x 150 mL/kg/day
  - Can compare this to peds dosing, if available
- By convention RID <10% RID considered safe
  - Most meds RID <1-2%
- Infant absorption and metabolism not considered

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### Maternal factors to consider

- Are there non-drug treatments?
- Duration of treatment?
- Can treatment be delayed?
- Is the drug absorbed? If it is how does the mom metabolize the drug?

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### Maternal factors to consider

- Timing
  - to minimize infant exposure breastfeed before dose is due, take at HS
  - colostrum in first 3 days of life more likely to contain meds but volume is low
- Will the drug affect milk supply?
  - ↓ dopamine agonists, high dose estrogens
  - ↑ dopamine antagonists – used therapeutically
    - domperidone, metoclopramide

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### Infant factors to consider

- Age of infant? Premature?
  - <6 months at highest risk of drug ADRs
  - 78% of ADRs reported in infants 2 months of age or younger
- Immature BBB in first year of life
  - Lipophilic drugs with CNS side effects are more likely to transfer into breastmilk and potentially cause CNS side effects in the infant
- Health status of the infant?
  - Premature? Major organ dysfunction?
- Exclusively breast fed? Formula or solid food?

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### Infant factors to consider

- Was the infant exposed in utero?
- Is the drug absorbed by the infant?
  - Still a risk of GI side effects if not absorbed
- Will the drug accumulate in the infant because of immature drug metabolic pathways?
  - Immature renal and hepatic function
    - Decreased drug clearance
    - t<sub>1/2</sub> caffeine >90 hrs in neonates vs 2.6 hrs in a 6 month old

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### Infant factors to consider

- Is the drug used therapeutically in peds?
  - Can extrapolate safety/harm from peds data
- Are potential infant side effect easy to monitor?
  - drowsiness, fussiness, diarrhea, etc
  - are adverse effects undetectable?
  - does the infant require blood work or monitoring by a health care professional?

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### Drugs of concern during lactation

- Some examples
- Chemotherapy
  - Radiopharmaceuticals
    - May need to temporarily withhold breastfeeding
  - Drugs of abuse – illicit and prescription
  - Drugs that can decrease milk supply
    - estrogens
    - pseudoephedrine, amphetamines
    - dopamine agonist (bromocriptine, cabergoline)

Consult specialized lactation references for complete list

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## Drugs reported to cause ADRs

- Cohort of 838 infants
  - 89% <4 months of age
- One or more maternal drugs
  - analgesics 23.4%; antibiotics 19.8%; antihistamines 10.1%; sedatives 5%
- 11.2% reports of minor ADRs in infant
  - Diarrhea - antibiotics
  - Sedation - analgesics, narcotics\*, sedatives, antidepressants
  - Irritability – antihistamines

\*Codeine – high risk ultra-fast CYP 2D6 metabolizers (codeine → morphine)

Ito S et al. Am J Obstet Gynecol. 1993 May;168(5):1393-9.

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## Evidence Based References

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## Drugs in Pregnancy and Lactation

### “Briggs”

- ++ use by pharmacists
- Not ideal for lactation
  - Better pregnancy resource
  - References retired AAP recommendations from 2001
  - Inconsistent pharmacodynamic info
    - Pantoprazole monograph – “unstable at acidic pH”
      - Not including in other PPI monographs
    - High molecular weight drugs (heparin, LMWH, mabs, protein based drugs)
      - Not all monographs mention “GI inactivation likely”



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## Medications and Mother’s Milk

### “Hale’s”

- Recommended by experts in lactation
- Rx, non-Rx, radioactive agents, drugs of abuse
- Lactation risk category system:
  - L1 (safest) to L5 (hazardous)
  - All new drugs automatically L3 (probably compatible)
- Book published q2yrs \$44.95
- Online \$39.95 / year (individual)



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## LactMed

- Free website & app from the National Library of Medicine
- Updated monthly
- Peer reviewed monographs
- Endorsed by the American Academy of Pediatrics



<http://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm>

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## Conclusions

- Medication use during breastfeeding is common
- Almost all meds transfer in to breast milk to some degree
- Weak evidence for the safety/harms of medication use in breastfeeding - despite this:
  - many medications can be recommended
  - stopping breastfeeding may not be necessary

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## Conclusions

- Risk versus benefit decision
    - taking into account maternal and infant considerations
      - Mom needing treatment for URTI with a healthy 8 month old on some solids
- VERSUS
- Mom with epilepsy and depression with a 1 month old infant born prematurely and exclusively breastfed
- Use LactMed or Hale's

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## Questions?

### Selected References:

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