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Just Say No...? Medications and Mother's Milk

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Disclosure

I have no financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this CME activity.

Agenda

- Benefits and barriers to providing maternal human milk
- Medications and human milk physiology
- Shared decision making regarding the use of medications during lactation
- Special considerations





Objectives

- Identify three common barriers to providing breastmilk.
- Calculate the relative infant dose of a medication.
- List three evidence-based resources that can guide clinicians when discussing safe medication use with breastfeeding mothers.
- Describe the health providers role in shared decision making about medication use and lactation.
- Describe two factors that affect maternal decision making about medication use and lactation.

Infant Benefits*

- **Decreases the risk of:**
 - Mortality
 - Otitis Media
 - Upper and Lower Respiratory Infections
 - RSV
 - Asthma and atopic dermatitis
 - Gastrointestinal infections
 - Inflammatory bowel disease
 - Food allergies
 - Celiac disease
 - Obesity
 - Type I and II Diabetes
 - Childhood leukemia
 - SIDS
- **Improves:**
 - Feeding intolerance
 - Intelligence scores
 - Adult cardiovascular health



Premature Infant Benefits*



- **Decreases the risk of:**
 - Necrotizing Enterocolitis
 - Neonatal sepsis
 - Retinopathy of prematurity
 - Bronchopulmonary dysplasia
 - Hospital readmission
- **Improves:**
 - Neurodevelopmental outcomes
 - Hospital length of stay

Maternal Benefits*

Decreases the risk of:

- Breast cancer
- Ovarian cancer
- Metabolic syndrome
- Type II diabetes
- Cardiovascular disease
- Postpartum blood loss
- Post-partum depression

Improves:

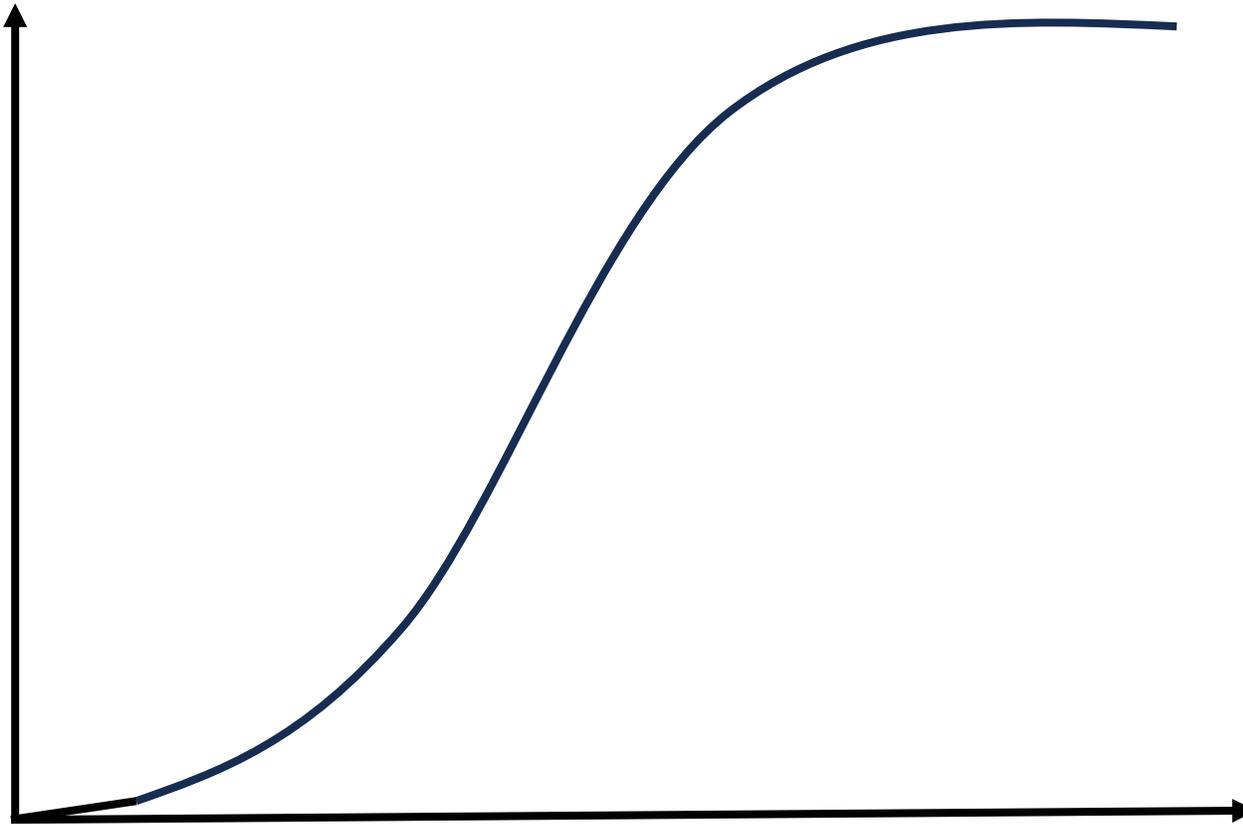
- Weight loss after pregnancy
- Maternal-infant bonding



* = Human Milk has dose dependent effects



Increasing
Effect



Increasing Dose

What is a common barrier to providing breastmilk?

Baby Friendly Hospital Practices

0%

Maternal concerns about taking medications while breastfeeding

0%

Paid Maternal Leave

0%

Term spontaneous vaginal delivery

0%



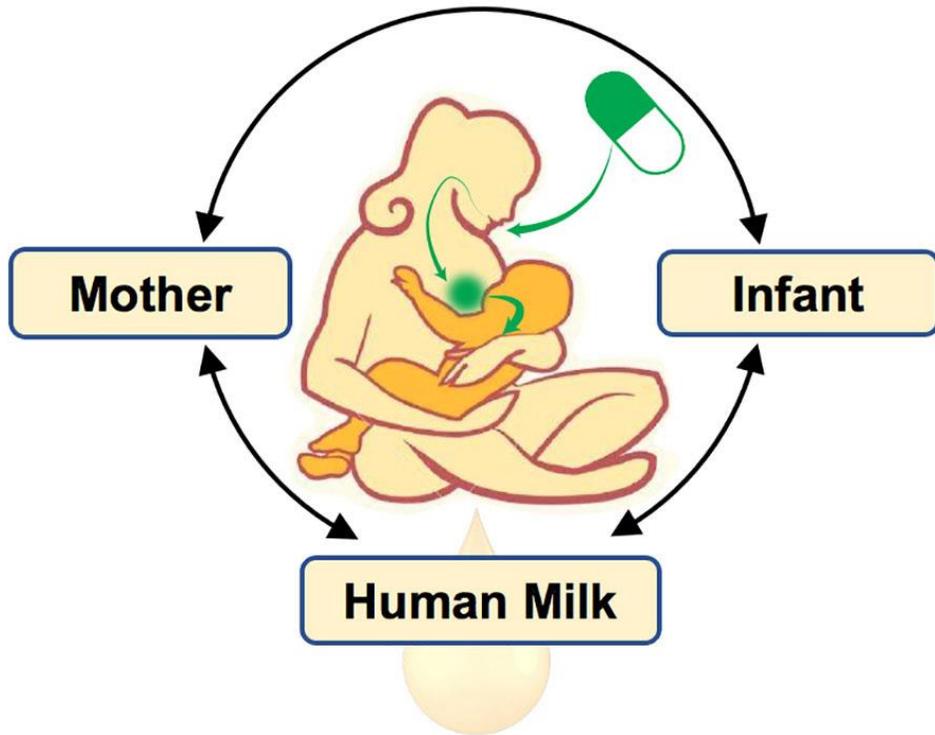
"Hold on, is this stuff certified organic?"

CartoonStock

Answer: B

Maternal concerns about taking medications while breastfeeding

- A. Issues with lactation and latching
- B. Concerns about infant nutrition and weight
- C. Maternal concerns about taking medications while breastfeeding
- D. Unsupportive work policies and lack of parental leave
- E. Cultural norms and lack of family support
- F. Unsupportive hospital practices and policies



Medications and Maternal Human Milk: General Principles

- Most medications transfer into human milk BUT are safe to use during lactation.
- Drug penetration into human milk is primarily determined by:
 - Maternal plasma level
 - Molecular weight
 - Protein binding
 - Lipid solubility
- Drug penetration into infant plasma is primarily determined by:
 - Infant oral bioavailability

“Safe” Medication Characteristics

- Short half life
- High protein binding (>90%)
- High molecular weight (>500)
- Lower pKa (<7.2)
- Low oral bioavailability
- Non-lipophilic





Infant Considerations

- Infants at higher risk for adverse effects:
 - Premature infants
 - Newborns
 - Unstable infants especially those with gastrointestinal instability or renal dysfunction
 - Genotypes known to affect drug metabolism (ie. Codeine)
- Pediatric approved drugs are generally less hazardous
- Avoid medications that alter maternal milk production

Relative infant dose

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

$$\text{Daily Infant Dose (mg/day)} = \frac{C_{\text{milk}}}{V_{\text{milk}}} = \frac{\text{Average drug concentration in milk (mg/ml)}}{\text{Volume of milk ingested in 24 hours (ml/day)*}}$$

* 150ml/kg/day

A 70 kg breastfeeding mother is taking a new pain medication for headaches. The dose is 350 mg po BID. Her 2-month-old infant weighs 6 kg. The daily infant dose is 0.3mg/day.

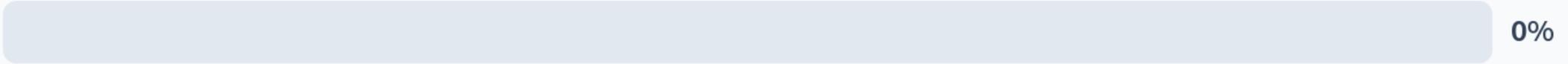
What is the relative infant dose?
(RID)

- A. 0.5%
- B. 1%
- C. 3%
- D. 5%



A 70 kg breastfeeding mother is taking a new pain medication for headaches. The dose is 350 mg po BID. Her 2-month-old infant weighs 6 kg. The daily infant dose is 0.3 mg/day. What is the relative infant dose? (RID)

0.5%



1%



3%



5%



Answer: A. 0.5%

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



Maternal dose = (350 mg X 2 doses) / 70 kg = 10 mg/kg/day



Infant dose = (0.3 mg/day) / 6kg = 0.05 mg/kg/day



RID = 0.05/10 X 100 = 0.5%

Dr. Hale's Lactation Risk Categories for Medications and Drugs

L1

Safest

- Extensive evidence demonstrating no adverse effects on the infant

L2

Safer

- Limited evidence without an increase in adverse effects on the infant

L3

Moderately
Safe

- Risk to the infant is possible, and further evaluation must be taken to consider individual situations.
- No studies, but expert opinion suggesting safety.

L4

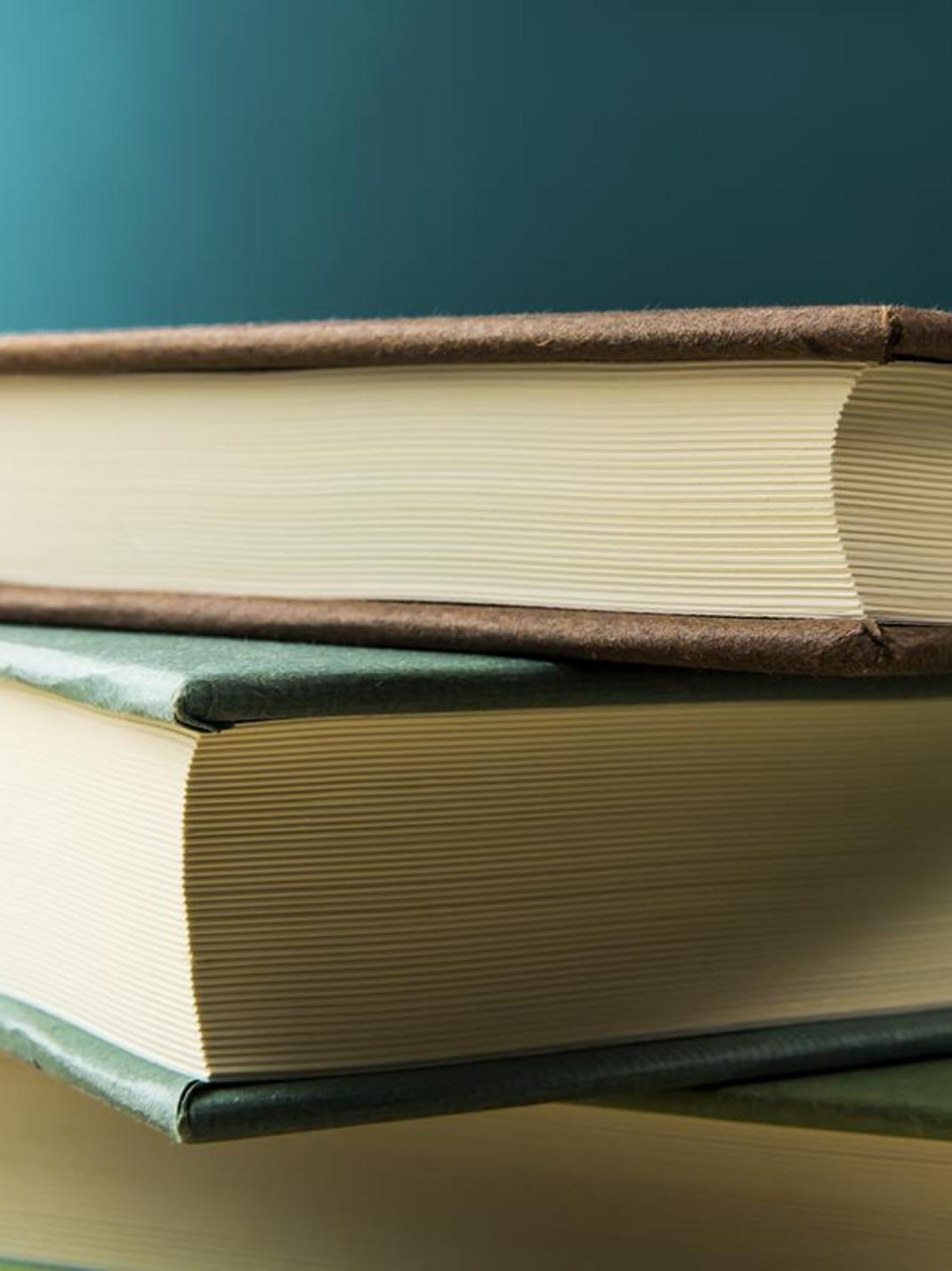
Possibly
Hazardous

- Positive evidence or expert opinion of risk to the infant or milk production
- Benefits from use in breastfeeding mothers may be acceptable despite risk to infant

L5

Hazardous

- Significant and documented risk to the infant and is contraindicated.
- Risk of using drug in breastfeeding women outweighs any benefit from breastfeeding



A hospitalized 8-day old term infant with a history of hypoxic respiratory failure and pulmonary hypertension is ready to begin oral feedings. The mother has been pumping and storing breastmilk since the infant's birth. She is taking escitalopram (Lexapro) for major depression and anxiety. She is concerned about exposing her infant to the medication through breastmilk.

Of the following, which resource is the best source for evidence-based information about medication use and lactation?

- A. Google
- B. Lexapro package insert
- C. NIH LactMed Database
- D. Physician Desk Reference (PDR)

Of the following, which resource is the best source for evidence-based information about medication use and lactation?

Google

0%

Lexapro package insert

0%

NIH LactMed Database

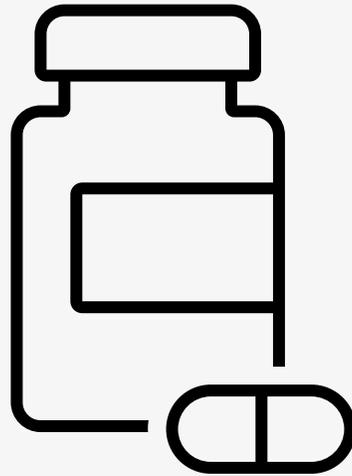
0%

Physician Desk Reference (PDR)

0%

Answer: C, NIH LactMed Database

Name	Description	Contact
LactMed National Institutes of Health	Medications and Lactation Database	https://www.ncbi.nlm.nih.gov/books/NBK501922/
Infant Risk Center Dr. Thomas Hale & Team	Research Center for medication safety during pregnancy and lactation	InfantRisk Center Hotline: 1-806-352-2519 Reference Guide: Medications and Mother's Milk
Human Lactation Center Division of Neonatology University of Rochester	Maintains a database of drugs in lactation, medical information, and programs around breastfeeding.	Human Lactation Center - Neonatology - Golisano Children's Hospital - University of Rochester Medical Center Contact number: (585) 275-0088
Mother to Baby Service Organization of Teratology Information Specialists (OTIS)	Provides information on medications during pregnancy and lactation.	Home Page – MotherToBaby Contact number: 866-626-6847 Free LactMed App
E-Lactancia	Medication and herbal medicine database in Spain (English and Spanish)	e-lactancia. Is this compatible with breastfeeding?



Risk vs. Benefit

- Drug Characteristics
- Infant Characteristics
- Duration of therapy (short-term vs. chronic)
- Timing of exposure (early vs. late post-partum)
- Compatible alternatives

Case: Amanda

History

Chief Complaint: 35-year-old G₁P₁ female presents with fever seven days after delivering a healthy baby girl.

HPI: Fever 103°F, chills, pelvic pain unrelieved with acetaminophen or ibuprofen

Past OB Hx: Cesarean section for failure to progress, healthy course

Past Medical Hx: Depression

Medications: *Sertraline (Zoloft), 50mg/day*

Exam

Vital signs: Temperature 101.6 °F, tachycardia

Breast exam: mildly engorged

Pelvic exam: cervical motion and uterine tenderness





Diagnosis: Postpartum endometritis

Admitted to Hospital:

- Medications: *IV Ampicillin, gentamicin and clindamycin*
- Daughter is rooming in to assist with breastfeeding goals
- Amanda is worried about adverse effects from medication exposure in breastmilk and asked “Is it safe?”.

Hospital Day 3:

- Remained febrile
- Abdominal and pelvic CT scan with *IV iodinated contrast*
 - Pelvic abscess
 - Septic pelvic thrombophlebitis
- Radiologist recommends “pump and dump” breastmilk for 24 hours
- Bedside Nurse recommends: Continue breastfeeding but will confirm with obstetrician who is in a delivery.

It is feeding time...what should Amanda do?

Breastfeed

0%

Pump and discard breastmilk and bottle feed formula

0%

Pump and discard breastmilk, followed by breastfeeding

0%

Wait until the obstetrician is available before feeding

0%



Amanda decides to bottle feed the baby formula.

After feeding:

- Several hours later, Obstetrician arrives and informs Amanda: “It is safe to breastfeed.”
- Amanda now feels safe breastfeeding but is frustrated by conflicting advice.

Hospital Day 5:

- CT scan is negative.
- Amanda is discharged home and continued breastfeeding.
- Due to time constraints, the obstetrician chooses not to inform the radiologist.
- The radiologist continued to give the same advice.



Amanda's medication review:

Antibiotics

- Most are safe and compatible with breastfeeding
- Avoid if possible:
 - Sulfa drugs, Nitrofurantoin: Early neonatal period and G6PD Deficiency
 - Tetracycline, Fluroquinolones

Analgesics

- Choose the lowest dose to achieve desired effect and alternate different types of medications to improve pain control
- Ibuprofen: short half-life and very low milk transfer
- Acetaminophen: milk levels < infant dose
- Narcotics:
 - Morphine, fentanyl, hydromorphone use in limited fashion as an adjunct to non-narcotic therapy
 - Codeine, oxycodone, hydrocodone and tramadol: excess sedation, breathing difficulties, metabolized by cytochrome P450 system, beware of ultra rapid metabolizers
 - Meperidine, pethidine: contraindicated due to neonatal sedation

Antidepressants

- If responds well to medication during pregnancy, don't change during lactation: infant exposure is less in lactation compared to pregnancy
- SSRI:
 - Sertraline: commonly prescribed for pregnancy and lactation, low to undetectable infant serum levels
 - Paroxetine: RID < 10%
 - Fluoxetine and citalopram can exceed RID >10%, Adverse effects: colic, fussiness, sedation, poor weight gain
- Tricyclic antidepressants
 - Nortriptyline: undetectable levels in serum with no adverse events reported
 - Doxepin: Avoid, associated with poor feeding, hypotonia, and sedation

ABM Clinical Protocol # 31:
Radiology and Nuclear Medicine Studies in Lactating Women

TABLE 1. COMMON NUCLEAR MEDICINE IMAGING AGENTS AND RECOMMENDATIONS FOR BREASTFEEDING

<i>Imaging agent</i>	<i>Breastfeeding interruption</i>
Noncontrast radiographs	No
Nonvascular administration of iodinated contrast	No
CT with iodinated intravenous contrast	No
MRI with gadolinium-based intravenous contrast	No
Nuclear medicine imaging	
PET	No
Bone scan	No
Thyroid imaging	
I-131	Cessation for this infant
I-123	Recommendations vary, up to 3 weeks
Technetium-99m pertechnetate	Up to 24 hours, depending on dose
Renal imaging	
Tc-99m DTPA	No ^a
Tc-99m MAG3	No ^a
Tc-99m DMSA	No ^a
Tc-99m glucoheptonate	No ^a
Cardiac imaging	
Tc-99m Sestamibi	No ^a
Tc-99m Tetrofosmin	No ^a
MUGA	
Tc-99m RBCs in vitro	No ^a
Tc-99m RBCs in vivo	Up to 12 hours, depending on dose
VQ scan	
Tc-99m MAA	12 hours
Breast imaging	
Screening or diagnostic mammography	No
Ultrasound	No
MRI with gadolinium-based intravenous contrast	No

^aThe International Atomic Energy Administration recommends withholding breastfeeding for 4 hours or one feeding to account for any external radiation and free Tc-99m pertechnetate in the product.

CT, computed tomography; MRI, magnetic resonance imaging; MUGA, multigated acquisition scan; Tc-99m MAA, technetium-99m macroaggregated albumin; PET, positron emission tomography; Tc-99m MAG3, technetium-99m mertiatide; Tc-99m DMSA, technetium-99m succimer; VQ, ventilation-perfusion.

The healthcare providers...

- Insufficient or inappropriate knowledge about medication use and lactation
- Guided by personal experience, beliefs and attitudes with breastfeeding
- Decision making guided by “potential risk” vs. breastmilk compatibility
- Paternalistic decision-making
- Provide contradictory advice



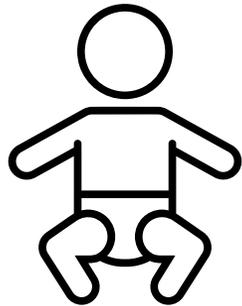


Don't “Just say No” ...

- Shared Decision Making
 1. Review breastfeeding goals
 2. Discuss risks and benefits to BOTH mother and child
 3. Present different options
 4. Empower the woman to make the best decision for BOTH mother and child
- *Exchange Information*

Balancing Benefits and Risks: Baby vs. Mom

Attain breastfeeding goals



Baby

Human Milk is the best food for my baby

I need to protect my baby

I am a good mother

My doctor says it's OK

Mother

I need this medication for my health

My medication could contaminate my milk

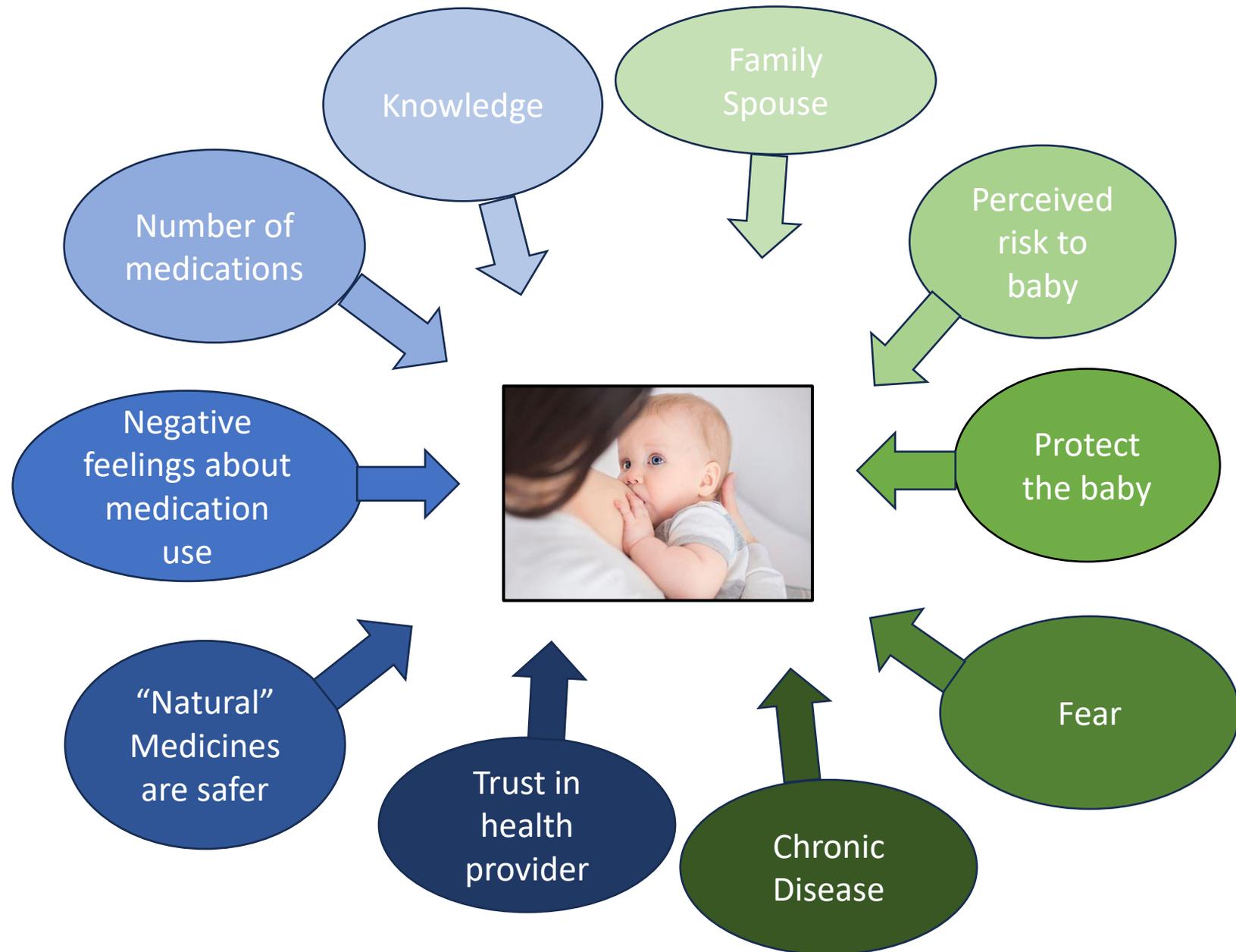
I am a bad mother

My doctor says it's not OK

Safely treat the medical condition



Factors associated with maternal decision making



A term infant is admitted to the NICU for management of NOWS. The primigravida mother has opioid use disorder. She is enrolled in an outpatient treatment program and has been taking buprenorphine for six months. Drug screening remained negative throughout pregnancy, and she does not use other substances.

Of the following, which statement is true regarding breastfeeding in this patient?

- A. Breastfeeding is contraindicated.
- B. Breastfeeding increases the need for pharmacological treatment for NOWS.
- C. Early cessation of breastfeeding is not associated with NICU admission.
- D. Supplementation of infant feedings may be required.



Of the following, which statement is true regarding breastfeeding in this patient?

Breastfeeding is contraindicated.

0%

Breastfeeding increases the need for pharmacological treatment for NOWS.

0%

Early cessation of breastfeeding is not associated with NICU admission.

0%

Supplementation of infant feedings may be required.

0%

Answer: D, Supplementation of infant feedings may be required.

Special Considerations for Health Providers

Opioid use disorder

Breastfeeding is safe and recommended unless contraindicated

Support with maintaining milk supply

Infants may require supplementation or fortification

It is safe to breastfeed with hepatitis C

Chronic disease

Consistent information across providers

Support for disease management while maintaining breastfeeding (ie. adaptive equipment)

Non-judgmental, non-pressured approach

Severe mental illness

Consistency, Collaboration, Clear Communication

Written information accompanied by discussion

Autonomy

Lithium and breastfeeding choice



Complimentary and alternative medicines

- Safety information is lacking
- Not subject to the same FDA standards for manufacturing, proven effectiveness and safety
- Maternal reasons for use:
 - Treat common conditions associated with lactation
 - Prepare for a natural birth and lactation experience
 - Support and maintain health and/or breastmilk production
 - Cultural/personal beliefs
 - Positive experiences with previous use
 - Perception that they may be safer than conventional medication
- Desire for and seek reliable information.
 - Desire holistic care from provider who has time, knowledge and is non-judgmental
 - Reliance on lay information sources and possible self-prescription
 - Complimentary medicines are “Natural” so therefore safe
- Decision making linked to psychological benefits associated with:
 - Perceived and actual increases in breastmilk production
 - Successful breastfeeding
 - Self-care in post-partum period

Summary

- Medication use is a common barrier to providing human milk.
- Most medications are safe to use during lactation with a RID < 10%.
- Using evidence-based resources such as LactMed can guide discussions regarding the risks and benefits of using specific medications while breastfeeding.
- The primary drivers that influence maternal decision making are infant safety and maternal health.
- Health providers have a responsibility to inform themselves about medication use and lactation.
- Shared decision making can assist mothers with making informed decisions about medication use that aligns with their breastfeeding goals



Questions?



“Do you ever serve *chocolate* milk?”

CDC Statistics

Breastfeeding Disparities Exist.

- Fewer non-Hispanic Black infants (77.3%) are ever breastfed compared with Asian infants (87.1%), non-Hispanic White infants (85.3%) and Hispanic infants (81.9%).³
- Infants eligible for and receiving the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) are less likely to ever be breastfed (74.0%) than infants eligible, but not receiving WIC (84.3%), and infants ineligible for WIC (91.5%).³
- Younger mothers aged 20 to 29 years are less likely to ever breastfeed (78.6%) than mothers aged 30 years or older (85.7%).³

Key Breastfeeding Indicators of Infants Born in 2020, National Immunization Survey – Child 2021-2022

Key Breastfeeding Indicators	Current Rates
Percentage of infants who are breastfed: Ever.*	83.1
Percentage of infants who are breastfed: At 6 months.*	58.2
Percentage of infants who are breastfed: At 1 year.*	37.6
Percentage of infants who are breastfed: Exclusively through 3 months.*	45.3
Percentage of infants who are breastfed: Exclusively through 6 months.*	25.4
Percentage of breastfed newborns who receive formula supplementation within the first 2 days of life.*	20.8

*Current rates represent infants born in 2020, [National Immunization Survey – Child 2021–2022](#).

Additional References:

- 1) Rowe H, Baker T, Hale TW. Maternal medication, drug use, and breastfeeding. *Child Adolesc Psychiatr Clin N Am*. 2015 Jan;24(1):1-20. doi: 10.1016/j.chc.2014.09.005. Epub 2014 Nov 14. PMID: 25455573.
- 2) Hari Cheryl Sachs, COMMITTEE ON DRUGS, Daniel A. C. Frattarelli, Jeffrey L. Galinkin, Thomas P. Green, Timothy Johnson, Kathleen Neville, Ian M. Paul, John Van den Anker; The Transfer of Drugs and Therapeutics Into Human Breast Milk: An Update on Selected Topics. *Pediatrics* September 2013; 132 (3): e796–e809. 10.1542/peds.2013-1985
- 3) Academy of Breastfeeding Medicine Protocols: [PROTOCOLS \(bfmed.org\)](http://bfmed.org)

Academy of Breastfeeding Medicine Clinical Protocol #21: Breastfeeding in the Setting of Substance Use and Substance Use Disorder (Revised 2023)

Miriam Harris,^{1,2} Davida M. Schiff,^{3,4} Kelley Saia,^{2,5} Serra Muftu,^{3,4}
Katherine R. Standish,⁶ and Elisha M. Wachman^{2,7}

TABLE 1. PRESCRIBED OPIOIDS, BENZODIAZEPINES, STIMULANTS, NON-PRESCRIBED STIMULANTS, ALCOHOL, NICOTINE, AND CANNABIS PHARMACOKINETIC CONSIDERATIONS TO INFORM BREASTFEEDING

<i>Opioids</i>	<i>Peak effect^a</i>	<i>Half-life^a</i>	<i>RID (%)</i>
Morphine	0.5–1 hour ²³⁷	2–4 hours ²³⁷	9.09–35 ⁹
Codeine	1–1.5 hours ²³⁷	3 hours ²³⁷	0.6–8.1 ⁹
Oxycodone	0.5–2 hours ²³⁷	3–4 hours ²³⁷	1.0–4.6 ⁹
Tramadol	2–3 hours ²³⁷	6–7.5 hours ²³⁷	2.9 ⁹
<i>Benzodiazepines</i>	<i>Peak effect</i>	<i>Half-life</i>	<i>RID (%)</i>
Diazepam	0.3–2.5 hours ²³⁷	44–48 hours ²³⁷	0.9–7.1 ⁹
Alprazolam	IR: 1–2 hours ER: 9 hours ²³⁷	IR: 11 hours ER: 10–16 hours ²³⁷	8.5 ⁹
Lorazepam	IR: 2 hours ER: 14 hours ²³⁷	IR: 12 hours ER: 20 hours ²³⁷	2.6–2.9 ⁹
Clonazepam	1–4 hours ²³⁷	17–60 hours ²³⁷	2.8 ⁹
Chlordiazepoxide	0.5–2 hours ²³⁷	24–48 hours ²³⁷	N/A
<i>Stimulants</i>	<i>Peak effect</i>	<i>Half-life</i>	<i>RID (%)</i>
Cocaine	0.5 hour ²³⁷	1.5 hours ²³⁸	N/A
Methamphetamine	2.5 hours ²³⁹	4–5 hours ²³⁷	N/A
MDMA	2–4 hours ²³⁷	4–6 hours ²³⁷	N/A
Cathinone	2.3 hours ²⁴⁰	1.5 hours ²⁴⁰	N/A
Amphetamine	IR: 3–4 hours ER: 5–7 hours ²³⁷	IR: 10–12 hours ER: 11–12 hours ²³⁷	1.9–2.1 ¹³²
Dexamphetamine	IR: 3 hours ER: 8 hours ²³⁷	IR: 3–4 hours ER: 5–7 hours ²³⁷	4.0–10.6 ¹³³
<i>Substance</i>	<i>Peak effect</i>	<i>Half-life</i>	<i>RID (%)</i>
Alcohol	0.5–1.5 hours ²³⁷	4–5 hours ²³⁷	16 ⁹
Nicotine	0.25 hours ²³⁷	1–2 hours ²³⁷	N/A
Cannabis (THC)	0.25–0.5 hours ²³⁷	25–36 hours ²³⁷	0.4–8.7 ⁹

^aPeak and half-life values reference adult pharmacokinetic data for a potential breastfeeding individual. The above prescribed opioid, benzodiazepine, and stimulant data are derived from oral route of administration. IV route of administration for equivalent IV medications have shorter peak effects, in the order of minutes. In intravenous route of administration, the half-lives for opioids may be shorter. For nicotine and cannabis, peak effect and half-lives are for inhalation route of administration.

ER, extended release; IR, immediate release; IV, intravenous; MDMA, 3,4-methylenedioxy methamphetamine; N/A, data not available; RID, relative infant dose; THC, delta-9-tetrahydrocannabinol.

