

Jenny Thomas, MD, MPH, IBCLC, FAAP, FABM



Dr. Jen 4 Kids

www.drjen4kids.com

1

Can I Take This While I am Breastfeeding?

Jenny Thomas, MD, MPH, IBCLC, FAAP, FABM



2

Hormones That May be Affected by Medications

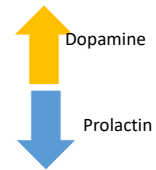
Prolactin: mediates CNS regulation of milk secretion. Influenced by rate of milk removal by infant
Oxytocin: neuroendocrine reflex that stimulates myoepithelial cells which then force milk into the ducts (MER)

3

Prolactin

Regulation

Dopamine constantly inhibits prolactin making prolactin the only hormone to be regulated in a such a way.



© 2011 Lippincott Williams & Wilkins. All rights reserved. This publication is protected by copyright. Any unauthorized use of this work may constitute a violation of applicable laws. For more information, contact the publisher.

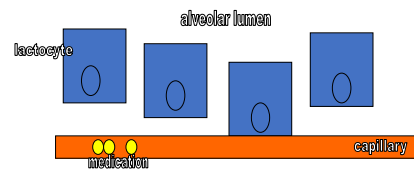
4

Timing of Medication delivery

- Birth to about day 4: medications can pass easily into breastmilk because gap junctions between cells are permeable.
- When gap junctions close, then medications would need to penetrate 2 lipid bilayers to get into milk
- Similar to blood-brain barrier

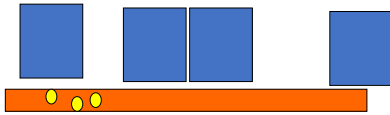


5



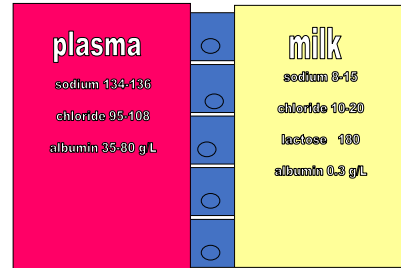
Day of delivery until day of life 4

6



Day 4- closure of gap junctions
Establishment of bloodmilk barrier

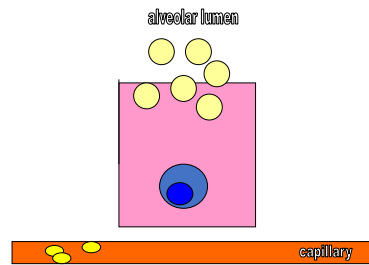
7



8

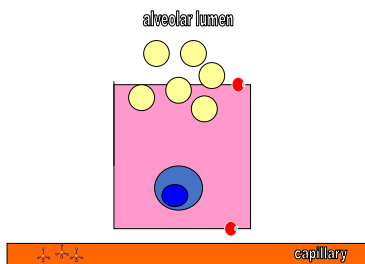
How Does
Medication Get into
Breastmilk....

9



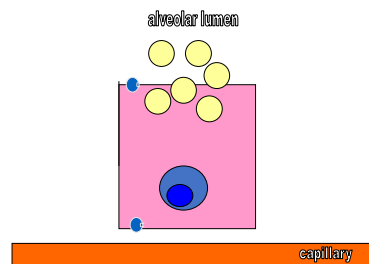
simple diffusion

10



influx transporters

11



protein transporter

12

Relative Infant Dose

Infant dose (mg/kg/day)

Maternal dose (mg/kg/day)



13

For a drug to make a difference

- Needs to be orally available
- Absorbed through GI tract
- Transferred into milk
- Orally available to infant
- Absorbed by infant GI tract
- Present in a clinically significant amount



14

Medication characteristics

Poor oral absorption

- Large molecular weight (800-1000 Daltons)
- Examples: Heparin, Aminoglycosides, 3rd generation cephalosporins, radiocontrast agents

Large Molecular Weight

- Insulin
- hGH
- Interferon
- Probably unstable in gastric pH

15

Medication characteristics

Poorly absorbed

- Gadolinium salts (MRI)
- Iodinated contrast agents (CT)
- Vancomycin
- 3rd generation cephalosporins

Bioavailability

- Poor with drugs sequestered in the liver
- Morphine
- Sumatriptan

16

General Guidelines

- Choose meds with:
- Short half-life
 - High protein binding
 - Large molecular weight
 - Low oral absorption
 - Low lipid solubility

17

General Guidelines

- Use topical therapy when possible
- Medications that we use for a newborn baby are generally safe to use in a nursing mom
- Pregnancy risk is not the same as breastfeeding risk

18

Substance Use Disorders

19

ABM Protocol 21

"Drugs of any type should be avoided in pregnant and breastfeeding women, unless prescribed for specific medical conditions. The casual use of drugs—legal, illegal, illicit, dose appropriate or not—still may have ramifications for the developing fetus and infant that we have yet to determine, and hence, in general, drugs of all types should be avoided unless medically necessary."

20

Opioid use

Legal and notsomuch

21

Challenges

Drug use often isn't the only problem

- HIV
- Hep B and Hep C
- Poor Nutrition
- Poor behavior choices
- Psychiatric disorders

Polydrug use is the norm for this population (includes tobacco and alcohol)

The drugs are often cut with dangerous substances

22

Challenges

- Lack of comprehensive care
- The choice to breastfeed seems as if the mother is less likely to abuse substance- not true
- Heavy alcohol, marijuana use, and moderate cocaine use did not significantly deter women from breastfeeding their infants (1988 US National Maternal and Infant Health Survey)
- Lack of evidence- based guidelines for this population

23

Challenges

- The substance use doesn't usually start with lactation.
- Makes it difficult to assess outcomes based on pregnancy *or* breastfeeding use.
- Much of what we know about substance use in lactation is based on care reports or studies with small numbers.

24

Challenges

Despite all this- all the risks, the benefits of human milk and breastfeeding need to factor into the risk: benefit analysis

25

Methadone

- Has been studied
- Concentration in human milk is low
- No documented long- or short-term effects of methadone in human milk on neurodevelopment
- Does cause Neonatal Abstinence Syndrome (NAS)- withdrawal symptoms in infants including CNS hyperirritability and autonomic nervous system dysfunction
- Infants who are not breastfed are more likely to have severe NAS
- Lactation is encouraged if the dose is stable, no matter the dose

26

Nature and nurture

- Environmental risk factors + prenatal exposures
- Results in epigenetic changes in gene expression and methylation patterns
- Creates immediate and long-term changes related to development
- That's a topic for later

27

Breastmilk and NAS

- Methadone and Buphenorphine are compatible with breastfeeding
- Infants of breastfeeding mothers had significantly reduced mean NAS scores, delayed onset of withdrawal, a decreased need for medication and shorter hospitalizations than formula fed infants.
- Breastmilk is unlikely to ameliorate all the symptoms of NAS

Abdel-Latif, Pediatrics, 2006

28

Creating barriers

- Lack of support from the healthcare community
- Misinformation about breastfeeding while on maintenance opioid therapy
- We need robust ongoing support

29

Subutex (Buphenorphine)

- Cases- all small numbers with conflicting data
- All suggest that the amounts in human milk are small and unlikely to have negative effects on the developing infant
- However, infants exposed during pregnancy required significantly less morphine for the treatment of NAS, a shorter period for NAS treatment and a significantly shorter hospital stay than those infants exposed to methadone (Jones, NEJM, 2010)

30

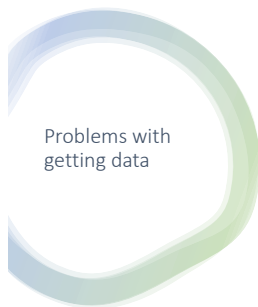
Other Opioids ABM protocol 15, FDA

- Codeine: case report of a death. Not recommended.
- Because most people do not know if they are ultra-rapid metabolizers, and because early signs of opioid overdose in an infant may be difficult to notice, **breastfeeding is not recommended** during treatment with codeine or tramadol.
- Short courses of other opioids can be used safely.

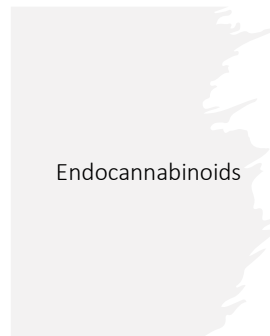


31

32



- No predictable pharmacokinetics
- Babies who are exposed to cannabis during lactation are likely to have been exposed during pregnancy too
- The marijuana is often combined with tobacco and therefore tobacco side effects need to be considered
- Other factors, like cannabis exposure during a passive smoke exposure, quality of the mother-infant relationship cloud the picture
- Recall and reporting bias



- Endocannabinoids are the endogenous marijuana-like substances found in animals and humans.
 - Made by the brain
 - Made by the breast as a component of breastmilk
- Cannabinoids are the constituents in marijuana and endocannabinoids which activate cannabinoid receptors.
- Endocannabinoid system contains:
 - Specific genes which code for cannabinoid receptors
 - The things those receptors bind (remember, endogenous)
 - Proteins that synthesize and degrade them

33

34



- The endocannabinoid system:
 - Interacts with molecules which regulate appetite and weight
 - Regulation of energy and food intake
 - Involved in the expression of key genes involved in neural development

Endocannabinoid receptors

CB1 is predominantly expressed in the central nervous system

- Leads to typical cannabis psychoactivity
- Plays a role in appetite and food intake by when activated
- Binds anandamide and arachidonoyl glycerol (AG)

CB2 is primarily expressed in various immune cells

- Does not lead to psychoactivity
- Generally involved in protective biological actions

35

36

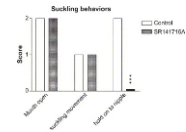
Cannabinoid Physiology

- In animal models, prenatal manipulation the CB1 receptor system produces long-term effects in the offspring.
 - Disruptions of memory
 - Addictive behaviors
 - Disorders of higher cognitive 'executive' functioning of the prefrontal cortex
 - This was found to be true in 4 year olds exposed prenatally to exogenous cannabis

37

CB1 receptors and Milk intake

- Pups were manually brought in proximity of the nipple and scored them for components of behavior which are required for successful milk ingestion



Fride, E. (2004)

38

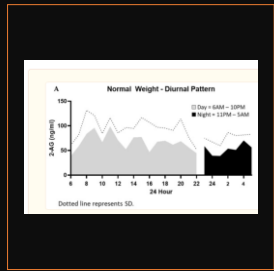
Cannabinoid Physiology

- CB2 receptors
 - Are inducible
 - Anti-inflammatory effects
 - May be involved the regulation of emotions
 - Agonists are anxiolytics
 - Antagonists or disruption of the receptor: possible role in drug addiction, eating disorders, psychosis, depression, and autism spectrum disorders

39

2-AG

Human milk 2-AG may also help support infants' circadian rhythm



Datta *Nutrients* 2021

40

Cannabis sativa

- Most commonly smoked, ingested orally or inhaled
- Delta-9 tetrahydrocannabinol (Δ^9 THC) is the most psychoactive of the phytocannabinoids
- Δ^9 THC is highly lipophilic and is stored in adipose tissues for weeks to months
- Once inhaled, it enters plasma and is distributed to brain and liver primarily
- Plasma concentration is brief (minutes) and CNS concentrations are longer (hours)

Baker Ob&Gyn 2018

41

Cannabis Pharmacology

- Frequent cannabis use:
 - in teenage girls predicts later depression and anxiety
 - Increased risk of schizophrenia: the relative risk for schizophrenia among high consumers of cannabis is 6 compared with non- users.
 - In those with schizophrenia, frequent cannabis use worsens prognosis.

42

Cannabis Pharmacology

- Combined frequently with tobacco
- Has more than 450 compounds
- Active metabolite is TetraHydroCannabinol (THC)
- Half-life is 1-2.3 days
- Traces can persist for more up to 4 to 6 weeks
- Rapidly distributed to brain and adipose tissue
- Stored in adipose tissue for long periods (weeks to months)

43

Marijuana Pharmacology

- Absorption
 - Inhaled ~ 25% (varies with topography; range of 2-56%)
 - Oral ~ 10-20%
- Distribution
 - High lipid solubility: fat, high perfusion organs
 - Protein binding: 97% or higher
- Cannabinoids obtained from Cannabis plant
 - 400 different types of cannabinoids
- Maternal Transfer
 - Breastmilk: 0.8% per joint (highly variable)
 - 10% to 30% excretion in high milk: 0.2 to 0.4 hours excretion

Perez-Reyes, NEJM

44

Hale et al

- Found that Δ9 THC peaked at one hour and receded slowly over the next 4 hours
- Δ9 THC transferred into human milk was 2.5% of the maternal dose
- Unanswered:
 - What is the plasma level in the infant?
 - What effect would repeated and continuous doses be on the concentration in human milk?
 - Doses after ingestion of oral cannabis products?
 - What does exogenous cannabis due to endogenous signaling systems?

Baker Ob&Gyn 2018

45

Marijuana Effects

- Decreases milk production
 - Suppression of prolactin production
 - Through a direct effect of mammary gland (animal studies)
- Effects on Infant
 - Observational reports: lethargy, less frequent feedings.
 - Shorter feeding times, poor suck, reduced muscle tone (Liston, 1998)
 - Effect on brain development unknowns; theoretically could impact brain development
- Effect on Parenting
 - Ability to nurse and care for a child may be compromised

46

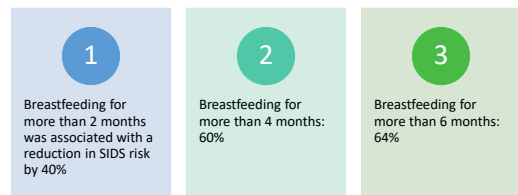
Outcomes

- THC is absorbed and metabolized by the infant
- Cannabinoid
- Exposure during critical windows of development can induce subtle and long-lasting developmental outcomes.
- Exposure to second-hand marijuana smoke is associated with a two-times risk of SIDS

Klonoff-Cohen 2001

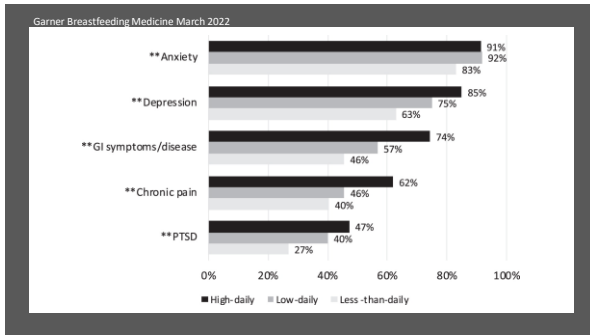
47

SIDS reduction

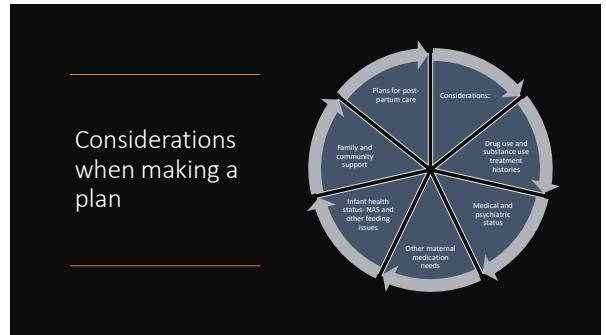


Meek, Noble 2022

48



49



50

Guidelines for screening

- There are no specific guidelines for drug screening in pregnancy, and when combined with unreliable self-reporting, the true numbers of affected births are unknown.
- Approximately 5% of women will admit to taking illicit drugs while pregnant (Substance Abuse and Mental Health Services Administration, 2014).
- However, self-reported studies regarding maternal substance use disorders have a high incidence of underreporting, due to fear and associated stigma (Stone, 2015).

51

Who to screen

- Consuming drugs in pregnancy is considered child abuse in at least 19 states in the United States, and women can lose custody of their children based on a positive screening test, even without confirmation (Young et al., 2007; Stone, 2015).
- While these laws were originally designed to protect the fetus, the fear instilled in women can prevent them from enrolling in treatment programs and accessing medical care throughout pregnancy.

Price, Frontiers in Pharmacology 2018

52

Considerations

- General misunderstanding of addiction and substance use/misuse within the medical profession that is further complicated with respect to pregnant women and children.
- This misunderstanding is based on a lack of addiction knowledge in primary healthcare providers as well as a lack of evidence-based knowledge of drugs in pregnancy and the neonate.

Price, Frontiers in Pharmacology 2018

53

Considerations

- Local, state and federal policies tend to focus on the (generally unproven) risks of illicit drugs, while ignoring the real need for medication and medical care for pregnant women.
- Drug use and misuse is then not treated as a medical issue and becomes increasingly politicized, legalized and stigmatized in these pregnant women and for their children.

Price, Frontiers in Pharmacology 2018

54

Social Justice

- All women should be screened using a validated screening test, and not biochemical measures.
- Decisions regarding the type of screens being performed, and the results of screening, need to be made based on a balance between scientific, medical, public health, legal, and ethical considerations around drug testing.

ACOG Committee on Health Care for Underserved Women and American Society of Addiction Medicine, 2012; American Society of Addiction Medicine, 2017