IMPROVING CARE FOR THE OPIOID-EXPOSED NEWBORN

Bonny Whalen, MD

West Virginia Perinatal Summit
November 14, 2016
DISCLOSURE

- No financial arrangements or affiliations with a commercial entity to disclose
- All of the drugs used in the treatment of NAS are used “off label”
LEARNING OBJECTIVES

- Describe 3 baby-centered care techniques that help foster neurobehavioral organization in infants with NAS
- Discuss how rooming-in couplet care can help decrease need for pharmacologic Rx in opioid-exposed newborns
- Discuss varied pharmacokinetic factors and 2 evidence-based resources to consider when determining safety of medications in lactation when caring for infants born to mothers with substance use disorders
U.S. NAS STATISTICS

- **Incidence**
  - 1.2 → 3.9 → 5.8/1000 live births over a 12 yr period
  - ~ Twice as many at risk

- **Cost (charges)**
  - $39,400 → $53,400 → $75,700 → $93,400/patient
  - 80% Medicaid (vs 45.5 % all others)
  - $730 million annually in 2009 → $1.5 billion in 2012

NAS in West Virginia: 2007-2013

- 5.7% maternal substance use in pregnancy (2014 birth certificate data) vs 19.2% licit / illicit drugs & alcohol in utero (2009 umbilical cord study in 8 birthing hospitals)
  

- 3rd highest prescribing rate of opioid analgesics

- NAS in 2013: ~ 32/1,000 births (SE region = ~ 49/1,000 births)
  
  - Total hospital rates:
    0 to ~56/1,000 live births
  

  Global NAS, 1997-2013

  Ko et al. MMWR. 2016.
IN-UTERO OPIOID EXPOSURE AND THE NEONATE

- Growth restriction
- Prematurity

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Heroin</th>
<th>MTD</th>
<th>BUP</th>
<th>MTD vs BUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birthweight</td>
<td>2601 g</td>
<td>3050 g*</td>
<td>2900 g*</td>
<td>NS</td>
</tr>
<tr>
<td>IUGR</td>
<td>27.7%</td>
<td>10.5%*</td>
<td>9.3%*</td>
<td>NS</td>
</tr>
<tr>
<td>Delivery &lt; 37 wk</td>
<td>29.8%</td>
<td>26.3%</td>
<td>21.8%*</td>
<td>NS</td>
</tr>
</tbody>
</table>

* P < 0.05 for heroin vs. substitution agent


<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MTD</th>
<th>BUP</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birthweight</td>
<td>2878.5 g</td>
<td>3093 g</td>
<td>0.03*</td>
</tr>
<tr>
<td>Delivery &lt; 37 wk</td>
<td>14%</td>
<td>7%</td>
<td>0.07</td>
</tr>
<tr>
<td>Gestational age at delivery</td>
<td>37.9 wk</td>
<td>39.1 wk</td>
<td>0.007*</td>
</tr>
</tbody>
</table>

~25% pregnant women smoke in West Virginia: #1 in nation

https://www.cdc.gov/nchs/data/nvsr/nvsr65/nvsr65_01.pdf
http://www.dhhr.wv.gov/wvdtp/cessation/tobaccofreepregnanc/Pages/default.aspx
NEONATAL CO-MORBIDITIES

Nicotine exposure & it’s effects

- Tobacco use in pregnancy ~85%

- Increased risk for IUGR / prematurity / low birth weight

- Increased risk for SIDS / respiratory distress

- Increased NAS sx, need for & dosing of Pharm Rx
NEONATAL CO-MORBIDITIES

SSRI exposure / behavioral effects
- 13% maternal SSRI Rx in pregnancy
- Increased SSRI toxicity / withdrawal
- Increased NAS sx … need for Rx
# Neonatal Abstinence Syndrome (NAS)

<table>
<thead>
<tr>
<th>CNS Hyperexcitability</th>
<th>Autonomic Dysregulation</th>
<th>Gastrointestinal Disturbances</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-pitched crying</td>
<td>Fever</td>
<td>Excessive sucking</td>
</tr>
<tr>
<td>Sleeplessness</td>
<td>Sweating</td>
<td>Poor / disorganized feeding</td>
</tr>
<tr>
<td>Hyperactive moro reflex</td>
<td>Yawning</td>
<td>Regurgitation</td>
</tr>
<tr>
<td>Tremors</td>
<td>Mottling</td>
<td>Projectile vomiting</td>
</tr>
<tr>
<td>Increased muscle tone</td>
<td>Nasal stuffiness</td>
<td>Loose stools</td>
</tr>
<tr>
<td>Myoclonic jerks</td>
<td>Sneezing</td>
<td>Watery stools</td>
</tr>
<tr>
<td>Seizures</td>
<td>Respiratory distress</td>
<td></td>
</tr>
</tbody>
</table>
### In-utero Opioid Exposure and the Neonate

<table>
<thead>
<tr>
<th>Condition</th>
<th>US Children’s Hospitals</th>
<th>Tennessee</th>
<th>West Virginia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low birthweight</td>
<td>16.7%</td>
<td>21.2%</td>
<td>? (&gt;&gt; 9.5%)</td>
</tr>
<tr>
<td>Respiratory complications</td>
<td>29.5%</td>
<td>28.7%</td>
<td>20.3%</td>
</tr>
<tr>
<td>Feeding difficulties</td>
<td>17.6%</td>
<td>13.1%</td>
<td>2.6%</td>
</tr>
<tr>
<td>Seizures</td>
<td>4.4%</td>
<td>3.7%</td>
<td>0.9%</td>
</tr>
</tbody>
</table>

WHY ELSE IS NAS CARE SO COSTLY?
NAS due to In-utero Opioid Exposure

- $\geq 3/4$ infants develop some degree of NAS
- Symptoms start on DOL 2, peak $\sim$ DOL 3-4
  - No rel’p b/w dose of opioid-substitution agent and NAS severity or duration of Rx
- AAP recommendation: Observe for 4-7 days minimum
- In most studies, $\geq 1/2$ infants require Rx for NAS

NAS AND LOS

- If Rx required, LOS can be lengthy

- Length of Treatment (LOT): Days to months depending on severity of NAS, poly-substance exposure, hospital setting / center, medication used

<table>
<thead>
<tr>
<th>Medication</th>
<th>length of stay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>12 to 34 days</td>
</tr>
<tr>
<td>Methadone</td>
<td>14 to 52 days</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>34 to 93 days</td>
</tr>
</tbody>
</table>

- Average LOS: 23 days nationally; variation: 2-12 weeks
  - W.VA: 12.7 days (median 8d) vs 2.9 days (median 2d) for non-NAS babies - Stabler et al. J. Rural Health. 2016.

# NAS and Site of Care

<table>
<thead>
<tr>
<th>Hospital Location</th>
<th>Observation</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1 Nursery</td>
<td>86%</td>
<td>12%</td>
</tr>
<tr>
<td>Level 2 NICU</td>
<td>6%</td>
<td>33%</td>
</tr>
<tr>
<td>Level 3 NICU</td>
<td>7%</td>
<td>54%</td>
</tr>
<tr>
<td>Pediatric Unit</td>
<td>---</td>
<td>16%</td>
</tr>
<tr>
<td>Other</td>
<td>1%</td>
<td>1%</td>
</tr>
</tbody>
</table>

4% of NICU beds occupied by babies with NAS

Proportion of NICU days, by NICU

>20% of US NICU days attributed to NAS care


(N=299)
# Need for Improvement in NAS Care

- **Variation in NAS care common & standardization lacking**
  
  
  
  

## Variation in Care in VON Nurseries:

*Many hospitals without policies*

<table>
<thead>
<tr>
<th>Service</th>
<th>Feb ‘14 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal substance use screen</td>
<td>75</td>
</tr>
<tr>
<td>Evaluation and treatment</td>
<td>76</td>
</tr>
<tr>
<td>Pharmacologic treatment</td>
<td>68</td>
</tr>
<tr>
<td><strong>Non-pharmacologic treatment</strong></td>
<td><strong>59</strong></td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>49</td>
</tr>
<tr>
<td>Standardization scoring</td>
<td>45</td>
</tr>
</tbody>
</table>

## Need for Improvement in NAS Care

<table>
<thead>
<tr>
<th>Variation in Care in BORN Nurseries: Parental Care Decreased during Rx</th>
<th>Observation %</th>
<th>Treatment %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Environment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low level lighting</td>
<td>63</td>
<td>74</td>
</tr>
<tr>
<td>Quiet environment</td>
<td>79</td>
<td>84</td>
</tr>
<tr>
<td>Vibrating or moving seat/bed</td>
<td>30</td>
<td>42</td>
</tr>
<tr>
<td>Non-nutritive sucking (pacifier)</td>
<td>76</td>
<td>82</td>
</tr>
<tr>
<td><strong>Parental care</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin to skin</td>
<td>75</td>
<td>59</td>
</tr>
<tr>
<td>Breastfeeding when appropriate</td>
<td>86</td>
<td>76</td>
</tr>
<tr>
<td>Rooming-in</td>
<td>71</td>
<td>40</td>
</tr>
<tr>
<td>Holding</td>
<td>82</td>
<td>74</td>
</tr>
</tbody>
</table>

## Need for Improvement in NAS Care

<table>
<thead>
<tr>
<th>Rooming-In Care</th>
<th>Observation %</th>
<th>Treatment %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>1</td>
<td>41</td>
</tr>
<tr>
<td>Rarely</td>
<td>9</td>
<td>17</td>
</tr>
<tr>
<td>Occasionally</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Sometimes</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Usually</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Almost always</td>
<td>73</td>
<td>11</td>
</tr>
<tr>
<td>Unsure</td>
<td></td>
<td>4</td>
</tr>
</tbody>
</table>

Bogen et al. *Acad Pediatr.* 2016. (pending publication)
BENEFITS OF ROOMING-IN / COUPLET CARE

- Rooming-in facilitates privacy for mothers to provide frequent skin-to-skin & intimate contact with infant, and fosters breastfeeding
  - Practices known to help infants with neurologic symptoms of NAS and likely to shorten LOS
    McQueen et al. *Advances in Neonatal Care.* 2011.
  - Skin-to-skin and breastfeeding linked with significant improvements in health and neurodevelopmental outcomes of infants - especially important for this population of infants who are at significant medical and psychosocial risk
IMPROVED CARE & OUTCOMES WITH ROOMING-IN & MATERNAL PRESENCE

- **Decreased need for pharm Rx:**

- **Decreased LOT by:**

- **Decreased LOS by:**
SUPPORTIVE “NON-PHARMACOLOGIC” CARE FOR NEWBORNS

Goal: Minimize stimulation & promote adequate rest and nutrition

- Room-in / stay with infant at all times
  - Decreased need for NAS Rx
  - Shorter length of stay / treatment
  - More likely to be dc into custody of mother

- Decrease stimulation
  - Low lights
  - Quiet / calm room
  - Slow movements
  - Limit visitors
  - Avoid “excessive handling” of baby

- Feed baby when hungry, at early feeding cues, until content
SUPPORTIVE CARE FOR NEWBORNS

- Cluster Care: Provide uninterrupted periods of sleep / rest
  - Synchronize parental & staff care / behaviors with infant’s
  - Organize care & handling so infant not overwhelmed w/ multiple stimuli

- Use calming techniques
  - Hold infant skin-to-skin (or swaddled in blanket)
  - Position hands-to-face with flexed extremities
  - Gentle rocking / swinging / swaying in head-to-toe direction
  - Sucking on finger / pacifier
  - Shooshing noises
NAS CARE IMPROVEMENT VIA STANDARDIZATION

- AAP recommends that all Nurseries develop and adhere to standardized plan for evaluation and comprehensive treatment of infants at risk

- Standardized weaning protocols (at state-level) effective
  - ↓ pharm Rx by ~14 days and LOS by ~10 days
  - ↓ pharm Rx by 11 days and LOS by ~8 days
NAS Care Improvement via Standardization

VON’s NAS iNICQ Initiative

- **Aim:** Engage centers in multi-center QI collaborative focused on improving quality, safety and value of care for substance-exposed infants and families through rapid-cycle adoption of AAP NAS guidelines, standardizing NAS-relevant policies and practices.
VON’s NICQ Intervention’s Components

- NAS QI Toolkit
- 8 Potentially Better Practices (PBPs)
- Virtual Video Visit to Center of Excellence
  - Trauma-informed, family-centered care
- Structured educational curriculum
  - Expert-led Webinar Series
  - List-Serve coaching
- Data-driven improvement stories
- Data audits and feedback
8 POTENTIALLY BETTER PRACTICES (PBPs)

- **PBP 1:** Develop and implement a standardized process for the Identification; Evaluation, Treatment; Discharge management for infants with NAS.
- **PBP 2:** Develop and implement a standardized process for measuring and reporting rates of NAS and drug exposure.
- **PBP 3:** Create a culture of compassion, understanding and healing for the mother-infant dyad.
- **PBP 4:** Provide care for infants and families in sites that promote parental engagement in care and avoid separation of mothers and infants.
VON’S POTENTIALLY BETTER PRACTICES

- **PBP 5:** Engage mothers / family members in providing non-pharmacologic interventions as “first-line” therapy for all substance-exposed infants.

- **PBP 6:** Develop clear eligibility criteria for breastfeeding and actively promote and support breastfeeding by eligible mothers.

- **PBP 7:** Develop a standardized process to ensure safe discharge into the community.

- **PBP 8:** Provide Interdisciplinary Universal Education / Training to all caregivers who may encounter substance-exposed infants and families.
• Increasing % of substance-exposed infants in our region

• In 2006, implemented comprehensive substance-exposed policy:
  • Multi-disciplinary but small core committee
  • Evidence-based & comprehensive
  • Inconsistently implemented
Higher rates by 2012: 1.5% vs 0.6% nationally

Source: NH Department of Health and Human Services, Maternal and Child Health
• Rural children’s hospital in academic tertiary care center in Lebanon, NH
  • 18-basinette mother-baby LDRP unit: ~ 1200 births/year
  • 30-bed Level II and III NICU: ~450 admissions/year
  • 23-bed pediatric inpatient unit: ~ 2500 admissions/year

• 2012: Joined VON iNICQ collaborative
  • Increased multidisciplinary team to > 40 & implemented formal QI methods
    • OB, Psychiatry, Newborn Nursery, NICU, Inpatient Pediatrics, Social Work, Lactation
A NEED TO IMPROVE FURTHER

<table>
<thead>
<tr>
<th></th>
<th>Pre-intervention 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>% infants at-risk</td>
<td>4%</td>
</tr>
<tr>
<td>% infants treated</td>
<td>46%</td>
</tr>
<tr>
<td>Ave LOS</td>
<td>16.9 days</td>
</tr>
<tr>
<td>Cumulative morphine dose</td>
<td>13.7 mg</td>
</tr>
<tr>
<td>Mean hospital costs/treated infant</td>
<td>$19,737</td>
</tr>
<tr>
<td>Mean hospital costs/at-risk infant</td>
<td>$11,000</td>
</tr>
</tbody>
</table>
Pre-QI NAS Care

- **BP Rooming-in observation**
  - Scored in bassinette
  - Q 4hr → q 2hr if score ≥ 8

- **Transfer to ICN for 3 scores of ≥ 8 or 2 of ≥ 12**
  - No rooming-in
  - No privacy
  - Stimulating environment

- **Pediatrics for wean**
  - Scoring as per BP
  - Rooming-in
WHY IS THIS A NICU ISSUE?
THIS SHOULD NOT BE AN NICU ISSUE

- Babies are not critically ill or medically complex
- Most babies born outside facilities w/ L3 NICUs
- NICU beds cost a lot

In the NICU:
- Excessive stimulation present
- Barriers to skin-to-skin & breastfeeding
- Interference with mother-infant bonding
- Rooming-in difficult
CHaD’S QI WORK

1. RN scoring training/reliability
2. Family interviews
3. Baby-centered scoring & care
4. Prenatal education
5. Parent symptom diary
6. Standardize score interpretation
7. Rooming-in pilot
8. “Cuddlers”
9. Full rooming-in
10. Addiction training
11. Transfers

Jan 2013: Formed Multi-D VON NAS QI team
April 2013 - Oct 2014: 11 PDSA cycles
NAS Care Now

- Provide NAS parent education
- Rooming-in through entire stay
- Family involvement in scoring
- Encourage STS and (breast)feeding pre-scoring
- Score baby STS in mom’s arms
- Score on baby’s schedule – encourage feeding at least q 3 hr
- Evaluate at bedside for 3 scores of ≥ 8 or 2 of ≥ 12
  - Assess & interpret score
  - Determine Rx criteria (e.g. not feeding/sleeping/consoling well)
Decreased Need for Pharm Rx

% Opioid-exposed Newborns Receiving Morphine

Baseline: 46% 51% 27%
Intervention Year 1: 51%
Intervention Year 2: 27%

% Opioid-exposed Newborns Receiving Adjunctive Agents

Baseline: 13% 7% 2%
Intervention Year 1: 7%
Intervention Year 2: 2%

N = opioid-exposed infants per year

Decreased Length of Stay

Decreased Hospital Costs

# Rooming-In to Treat NAS: Improved Family-Centered Care at Lower Cost

<table>
<thead>
<tr>
<th></th>
<th>Pre-intervention 2012</th>
<th>Post-intervention 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>% infants at-risk</td>
<td>4%</td>
<td>5%</td>
</tr>
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<td>27%</td>
</tr>
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<tr>
<td>Mean hospital costs/treated infant</td>
<td>$19,737</td>
<td>$8,755</td>
</tr>
<tr>
<td>Mean hospital costs/at-risk infant</td>
<td>$11,000</td>
<td>$5,300</td>
</tr>
</tbody>
</table>

## VON’S INICQ NAS IMPACT

<table>
<thead>
<tr>
<th>Presence of Hospital NAS Policies</th>
<th>February 2013</th>
<th>August 2014</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal substance use screen</td>
<td>75</td>
<td>90</td>
<td>0.002</td>
</tr>
<tr>
<td>Evaluation and treatment</td>
<td>76</td>
<td>95</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Standardization scoring</td>
<td>45</td>
<td>77</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-pharmacologic treatment</td>
<td>59</td>
<td>84</td>
<td>&lt;0.001</td>
</tr>
<tr>
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<td>92</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>49</td>
<td>72</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

# Improved Neonatal Outcomes

<table>
<thead>
<tr>
<th>Neonatal Outcomes</th>
<th>February 2013</th>
<th>August 2014</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOT (days)</td>
<td>16 (10, 27)</td>
<td>15 (10, 24)</td>
<td>0.008</td>
</tr>
<tr>
<td>LOS (days)</td>
<td>21 (14, 33)</td>
<td>19 (15, 28)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

N=3458

POTENTIAL TO SCALE-UP?

- Reducing LOS by 2 days could result in an estimated savings of $170 million dollars in U.S. hospital charges
  

- Standardized weaning protocols (at state-level) may prove even more (cost)effective
PHARMACOLOGIC TREATMENT FOR NAS

“There is insufficient data to determine safety or efficacy of any specific opiate compared to another opiate.”


Methadone w/ decreased LOT and LOS compared with morphine in 14 US Children’s Hospitals – 2004-2011

<table>
<thead>
<tr>
<th></th>
<th>Bivariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LOT mean</td>
<td>LOS mean</td>
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<tr>
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</tbody>
</table>

No significant difference in hospital charges
ROOMING-IN & MATERNAL PRESENCE
BEST FOR BABIES …

- **Decreased need for pharm Rx:**
  

- **Decreased LOT by:**
  

- **Decreased LOS by:**
  
SUPPORTING THE BREASTFEEDING NEWBORN WITH IN-UTERO OPIOID EXPOSURE
BREASTFEEDING AND THE OPIOID-EXPOSED NEWBORN

- Breastfed infants may experience decreased NAS severity

- Anticipate potential problems re: in-utero opioid exposure & support as needed
  - Prematurity
  - Growth restriction
  - NAS
    - CNS hyperirritability
    - Autonomic hyperfunction
    - GI dysfunction
  - Feeding difficulties
  - Increased weight loss
TRICKS & TIPS FOR BREASTFEEDING

- Breastfeed:
  - in a calm environment
  - at early feeding cues
  - till content

- Skin-to-skin before & during feeding

- Breastfeed in “C-hold”

- Hand expression & breast massage before & during feeding

- If baby having problems:
  - Give drops of colostrum first
  - Have baby suck on finger to organize suck
  - Use supplemental nurser system at breast

- Provide emotional support

- Formal Lactation Consultation
BREASTFEEDING AND COMORBIDITIES

- Anticipate other potential comorbid exposures & evaluate safety in breastfeeding

YOU CAN GET HIV VIA...

- Unprotected sex
- Pregnancy, childbirth & breastfeeding
- Injecting drugs
- Working in healthcare
- Blood transfusions & organ/tissue transplants
POTENTIAL COMORBID EXPOSURE RECS

- **HIV/HTLV**
  - Breastfeeding contraindicated; advise breastmilk alternative

- **Active, untreated tuberculosis**
  - May BF after 2 wk of Rx

- **Active herpes simplex virus with breast lesions**
  - May BF from unaffected breast

- **Hepatitis C**
  - Pump / dump if nipples bleeding; offer stored breastmilk

- **Cigarette smoking / nicotine patch**
  - Advise BF with no passive smoke exposure
  - Discuss benefits of BF related to decreased risk of SIDS, OM, resp. tract infections, asthma
  - Patch helps prevent rapid entry of nicotine into BM & decreases exposure to direct pharm actions of nicotine

- **Medication Rx for psychiatric conditions**

EVALUATING SAFETY OF MEDICATIONS IN LACTATION
MEDICATIONS IN LACTATION

- AAP’s Committee on Drugs

- Thomas Hale’s Medications and Mothers’ Milk
  - Lactation Risk Categories
    - L1: Safest
    - L2: Safer
    - L3: Moderately safe
    - L4: Possibly hazardous
    - L5: Contraindicated

- NIH’s LactMed
KEY FACTORS IN DETERMINING MED SAFETY

- **V_d: Volume of distribution**
  - Drugs w/ high V_d may enter diff body compartments → lower conc. in blood, though may take longer to clear from body, may also have lower milk levels
  - V_d of 1-20 L/kg generally c/w breastfeeding

- **PB: Maternal protein binding**
  - High PB reduces infant’s exposure to med
  - PB > 90% usually c/w breastfeeding

- **MW: Molecular weight**
  - Drugs w/ high MW actively transported or dissolved in cells’ lipid membranes → less likely to pass into milk
  - MW > 800 Da less likely to pass into milk compartment

# Key Factors in Determining Med Safety

<table>
<thead>
<tr>
<th>More/generally compatible w/ BF</th>
<th>Less compatible w/ BF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vd 1-20 L/kg</td>
<td>Vd &gt; 20 L/kg</td>
</tr>
<tr>
<td>PB &gt; 90%</td>
<td>PB &lt; 90%</td>
</tr>
<tr>
<td>MW &gt; 800 Da</td>
<td>MW &lt; 800 Da</td>
</tr>
<tr>
<td>Low pH</td>
<td>High pH</td>
</tr>
<tr>
<td>Water soluble</td>
<td>Lipid soluble</td>
</tr>
<tr>
<td>Milk-to-plasma (M/P) ratio &lt; 1</td>
<td>Milk-to-plasma (M/P) ratio &gt; 1</td>
</tr>
<tr>
<td>Relative Infant Dose (RID) &lt; 10% maternal dose</td>
<td>Relative Infant Dose (RID) &gt; 10% maternal dose</td>
</tr>
</tbody>
</table>

Also consider infant’s age, frequency of BF, volume of intake, etc.

METHADONE AND LACTATION

- Very long acting opiate analgesic
- Introduced into clinical use 1965
- No RCTs in Lactation
  - Case studies only
- Lactation Risk Category: L3
  - Small amounts transfer into breastmilk
  - Theoretic Infant Dose: 38 mcg/kg/day
  - Relative Infant Dose (RID): 2.8%

L3: MODERATELY SAFE
- No controlled studies in breastfeeding women
- Risk of untoward effects to infant is possible
- Controlled studies show minimal non-threatening effects
- New medications with no published data

Hale T. Medications and Mother’s Milk. 2014.
BUPRENORPHINE AND LACTATION

- Potent long acting narcotic agonist and antagonist
- No RCTs in Lactation
  - Case studies only w/ limited #s
- Lactation Risk Category: L2
  - No documented increase in adverse effects for infants
  - Oral bioavailability = 31%
  - Theoretic Infant Dose: 2.2 mcg/kg/day
  - Relative Infant dose (RID): 1.93%
NALOXONE AND LACTATION

- Narcotic antagonist – used in combination with buprenorphine
  - Suboxone: 4:1 ratio of buprenorphine/naloxone
- No studies available in Lactation
- Lactation Risk Category: L3
  - Poor oral absorption = “Nil”
USING LACTMED: BUSPAR

Buspirone
CASRN: 36505-84-7

FULL RECORD DISPLAY
Displays all fields in the record.
For other data, click on the Table of Contents

Drug Levels and Effects:

Summary of Use during Lactation:

Limited information indicates that maternal doses of buspirone up to 45 mg daily produce low levels in milk. Because no information is available on the long-term use of buspirone during breastfeeding, an alternate drug may be preferred, especially while nursing a newborn or preterm infant.
Drug Levels:

Maternal Levels. A woman was taking buspirone 15 mg 3 times daily during pregnancy and postpartum. On day 13 postpartum, buspirone was undetectable in breastmilk by HPLC assay (limit of detection and time of sample not stated).[1]

Infant Levels. In the exclusively breastfed infant of a mother who was taking buspirone 15 mg 3 times daily, buspirone was undetectable in the infant's serum by HPLC assay (limit of detection and time of sample not stated) on days 13 and 21 postpartum.[1]

Effects in Breastfed Infants:

Possible drug-induced seizure-like activity and cyanosis occurred in a breastfed 3-week-old whose mother was taking buspirone 15 mg 3 times daily as well as fluoxetine and carbamazepine during pregnancy and breastfeeding. The authors thought that this reaction, if drug induced, was most likely caused by fluoxetine.[1]

One exclusively breastfed 11-week-old infant was breastfed during maternal therapy with buspirone 10 mg daily and venlafaxine 300 mg daily. No adverse reactions were reported by the mother or in the medical records.[2]

Effects on Lactation and Breastmilk:

Buspirone increases serum prolactin.[3][4][5][6] Galactorrhea was reported in a woman taking venlafaxine after buspirone was added to her regimen. However, when buspirone was discontinued, galactorrhea persisted.[7] The prolactin level in a mother with established lactation may not affect her ability to breastfeed.

Alternate Drugs to Consider:

Lorazepam, Oxazepam
USING HALE: BUSPAR

More/generally compatible w/ BF

- Vd 1-20 L/kg
- PB > 90%
- MW > 800 Da
- Low pH
- Water soluble
- M/P < 1
- RID < 10%

**BUSPIRONE**

**LRC: L3 - No Data-Probably Compatible**

**Trade**: BuSpar

**Category**: Antianxiety

Buspirone is an antianxiety agent used in the treatment of generalised anxiety disorder. No data exists on excretion into human milk. It is secreted into animal milk, so the same would be expected in human milk. It is not known if this product is safe for breastfeeding women or the levels the infant would ingest daily. The brief half-life of this product and its metabolite would not likely lead to buildup in the infants plasma.

- **T ½** = 2-3 hours
- **Vd** = 5.3 L/kg
- **Tmax** = 60-90 minutes
- **MW** = 386

<table>
<thead>
<tr>
<th>M/P</th>
<th>PB</th>
<th>Oral</th>
<th>pKa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>86%</td>
<td>90%</td>
<td>1.22, 7.32</td>
</tr>
</tbody>
</table>

**Adult Concerns**: Dizziness, nausea, drowsiness, fatigue, excitement, euphoria.

**Pediatric Concerns**: None reported.

**Infant Monitoring**: Sedation, not waking to feed/poor feeding and weight gain.

**Drug Interactions**: Cimetidine may increase the effect of buspirone. Increased toxicity may occur when used with MAO inhibitors, phenothiazines, CNS depressants, digoxin and haloperidol.

**Relative Infant Dose**: 5 mg TID

**Alternatives**:

**References**:
1. Pharmaceutical manufacturer prescribing information, 1996.
TRIAL LACTMED AT THE BREAK TO LOOK UP MEDS YOU ARE CONCERNED ABOUT …

GENERAL RECOMMENDATIONS

- Most medications are safe & in most cases, benefits of breastfeeding outweigh potential risks (excluding meds that are absolutely contraindicated)

- Aim for medication safest in breastfeeding for maternal condition being treated
  - e.g., Paxil and Zoloft as SSRIs for depression vs. Prozac

- Use meds w/ shorter half lives (w/ shorter peak intervals)
  - After 5 half-lives, ~ 97% med is eliminated from breastmilk

- Attempt to minimize exposure to infant
  - Take med at time of breastfeeding or just after
    - Try to avoid feeding infant when med reaches max plasma concentration
  - Take med before infant’s longest sleep stretch
  - Pump/dump feeding(s) if needed if concerns re: any potential exposure (or for recommended duration per Hale or Lactmed)
# Ensure no active substance / alcohol use

## Drugs of Abuse for Which Adverse Effects on Breastfeeding Infants Have Been Reported*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Reported Effect or Reason for Concern</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alcohol</strong></td>
<td>Impaired motor development or postnatal growth, decreased milk consumption, sleep disturbances. Note: Although binge drinking should be avoided, occasional, limited ingestion (0.5 g alcohol/kg/d; equivalent to 8 oz wine or 2 cans of beer per day) may be acceptable.</td>
<td>Koren 2002, Backstrand 2004, Mennella 2007 National Academy of Sciences 1991</td>
</tr>
<tr>
<td><strong>Amphetamines</strong></td>
<td>Hypertension, tachycardia, and seizures. In animal studies of postnatal exposure, long term behavioral effects, including learning and memory deficits and altered locomotor activity, were observed.</td>
<td>Product labeling</td>
</tr>
<tr>
<td><strong>Benzodiazepines</strong></td>
<td>Accumulation of metabolite, prolonged half-life in neonate or preterm infant is noted; chronic use not recommended.</td>
<td>Jain 2005, Malone 2004</td>
</tr>
<tr>
<td><strong>Cocaine</strong></td>
<td>Intoxication, seizures, irritability, vomiting, diarrhea, tremulousness.</td>
<td>Chasnoff 1987, Winecker 2001</td>
</tr>
<tr>
<td><strong>Heroin</strong></td>
<td>Withdrawal symptoms, tremors, restlessness, vomiting, poor feeding.</td>
<td>vandeVelde007</td>
</tr>
<tr>
<td><strong>LSD</strong></td>
<td>Potent hallucinogen.</td>
<td></td>
</tr>
<tr>
<td><strong>Methamphetamine</strong></td>
<td>Fatality, persists in breast milk for 48 h.</td>
<td>Ariagno 1995, Bartu 2009</td>
</tr>
<tr>
<td><strong>Methylene dioxy-methamphetamine (ecstasy)</strong></td>
<td>Closely related products (amphetamines) are concentrated in human milk.</td>
<td></td>
</tr>
<tr>
<td><strong>Marijuana (cannabis)</strong></td>
<td>Neurodevelopmental effects, delayed motor development at 1 y, lethargy, less frequent and shorter feedings, high milk-plasma ratios in heavy users.</td>
<td>Djulus 2005, Campolongo 2009, Garry 2010</td>
</tr>
<tr>
<td><strong>Phencyclidine (PCP)</strong></td>
<td>Potent hallucinogen, infant intoxication.</td>
<td>AAP 2001, Academy of Breastfeeding Medicine</td>
</tr>
</tbody>
</table>

*Effect on maternal judgment or mood may affect ability to care for infant.

Adapted from AAP COMMITTEE ON DRUGS. *Pediatrics.* 2013.
QUESTIONS AND OTHER CHALLENGES?
KEY REFERENCES


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