Opioid Use During Pregnancy: Treatment Strategies for Women, Babies, and Children

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- Marylou Behnke, MD, FAAP, Professor
  Department of Pediatrics, Division of Neonatology

- Tamara D. Warner, PhD, Research Assistant Professor
  Department of Pediatrics, Division of Neonatology

University of Florida College of Medicine
Learning Objectives

1. Discuss issues related to the management of opioid dependency during pregnancy

2. Define Neonatal Abstinence Syndrome (NAS) and discuss treatment strategies

3. Present what is known about the short- and long-term effects of prenatal opioid exposure, including intervention strategies.
Disclosure Statement

- All presenters, Dr. Kay Roussos-Ross, Dr. Marylou Behnke, and Dr. Tamara Warner, have disclosed no relevant, real or apparent personal or professional financial relationships.
Opiate Use In Pregnancy... An Alarming Trend

Kay Roussos-Ross, MD
Assistant Professor
Departments of Ob/Gyn and Psychiatry
Drug Use in Pregnancy

- Nicotine
- Alcohol
- Benzodiazepines
- Marijuana
- Stimulants
- Cocaine
- Opiates
Current Substance Use Among Pregnant Women
Aged 15-44, by Age, 2008-2009 Combined

Source: SAMHSA, NSDUH, 2010
TOURISTS!!
THANK GOD!
MAY I SUGGEST
RESTAURANTS,
HOTELS,
DESTINATIONS?

WE'RE JUST HERE
TO BUY SOME
PAIN PILLS.
Oxycodone counties
Among the top 50 dispensing practitioners in the U.S., 49 are in Florida and are concentrated in nine counties, ranked by Oxycodone units dispensed:

<table>
<thead>
<tr>
<th>County</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Broward</td>
<td>5.2 million</td>
</tr>
<tr>
<td>2. Palm Beach</td>
<td>2.4 million</td>
</tr>
<tr>
<td>3. Miami-Dade</td>
<td>646,500</td>
</tr>
<tr>
<td>4. Pinellas</td>
<td>192,400</td>
</tr>
<tr>
<td>5. Hillsborough</td>
<td>184,330</td>
</tr>
<tr>
<td>6. Lake</td>
<td>169,200</td>
</tr>
<tr>
<td>7. Seminole</td>
<td>164,686</td>
</tr>
<tr>
<td>8. Orange</td>
<td>133,800</td>
</tr>
<tr>
<td>9. Lee</td>
<td>108,600</td>
</tr>
</tbody>
</table>

SOURCE: United Way of Broward County and U.S. Drug Enforcement Administration

ROB MACK/Staff graphic
In 2007, the number of overdose deaths from prescription opioids outnumbered deaths from heroin and cocaine combined...

Source: NIDA
Unintentional Overdose Deaths Involving Opioid Analgesics, Cocaine and Heroin
United States, 1999–2007

[Graph showing the trend of deaths from opioid analgesics, cocaine, and heroin from 1999 to 2007.]

Number of Opioid Prescriptions Dispensed by U.S. Retail Pharmacies, Years 1991-2011

Prescriptions (millions)

IMS’s Source Prescription Audit (SPA) & Vector One®: National

Opioids  Hydrocodone  Oxycodone
Hospital Discharge Rate of Newborns with Drug Withdrawal Syndrome, Florida, 1995-2009

Discharges per 1,000 Live Births

0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.4 0.4

Data Source: Hospital Discharge Records
Why are women using opiates?

• Prior injury
• Chronic pain
• Medical: Sickle cell disease/crisis
• Opiate dependence
• Methadone maintenance programs
Why do we allow women to continue using opiates in pregnancy?

• **Withdrawal syndromes**
  - Withdrawal from opioids in pregnancy may not be fatal to the mother but can lead to intrauterine demise of the fetus

• **“Lesser of two evils”**
  - Prevent cravings which decreases risks to mother and fetus
    - Prostitution
    - IV drug use
Opiates

**Short Acting**
- Percocet
- Vicodin
- Lortab
- Dilaudid
- Etc.

**Long Acting**
- Methadone
- Suboxone/Subutex
Mechanism of Action of Opiates

4 main receptors are involved:

- Mu, kappa, delta, sigma
- Mu receptors mediate the most profound analgesic effects
  - Most found in midbrain and the dorsal horn of the spinal cord
## Properties of opioid receptors

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mu</strong></td>
<td></td>
</tr>
<tr>
<td>Mu1</td>
<td>Supraspinal analgesia</td>
</tr>
<tr>
<td></td>
<td>Bradycardia</td>
</tr>
<tr>
<td></td>
<td>Sedation</td>
</tr>
<tr>
<td>Mu2</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td></td>
<td>Euphoria</td>
</tr>
<tr>
<td></td>
<td>Physical dependence</td>
</tr>
<tr>
<td><strong>Delta</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spinal analgesia</td>
</tr>
<tr>
<td></td>
<td>Respiratory depression</td>
</tr>
<tr>
<td><strong>Kappa</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spinal Analgesia</td>
</tr>
<tr>
<td></td>
<td>Respiratory depression</td>
</tr>
<tr>
<td></td>
<td>Sedation</td>
</tr>
<tr>
<td><strong>Sigma</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dysphoria, delirium</td>
</tr>
<tr>
<td></td>
<td>Hallucinations</td>
</tr>
<tr>
<td></td>
<td>Tachycardia, hypertension</td>
</tr>
</tbody>
</table>
Methadone

- Long half-life (>24 hrs)
- Peak dose 2-4 hrs
- Pure mu agonist
- 80-90% bioavailability; highly lipophilic
- Accumulation with repeated dosing for pain may result in sedation and respiratory depression in the non-tolerant patient
Buprenorphine

- Long half life (>24hrs)
- Peak dose 90 min
- Partial mu receptor agonist (but has high affinity for receptor and displaces other full opiate agonists)
- Kappa receptor antagonist
- Less risk of respiratory depression in overdose
Mean Total Dose of Morphine (mg)

Mean Hospital Stay (days)

Mean Duration of NAS Treatment (days)

Methadone | Buprenorphine
Mean Total Dose of Morphine (mg)

Mean Hospital Stay (days)

Mean Duration of NAS Treatment (days)

Methadone | Buprenorphine

Complications of Chronic Opiate Use

Fetal
- Neonatal abstinence syndrome
- IUGR
- Decreased head circumference
- PTD
- Stillbirth
- Chorioamnionitis

Maternal
- Hyperalgesia
- GI side effects
- Decreased libido
- Sweating
- Withdrawal
Methadone Maintenance

Goal

• Administer methadone in doses sufficient to prevent withdrawal and reduce/eliminate cravings
Methadone Maintenance

- **Treatment of choice** for opiate-dependent pregnant women
- Reduces fluctuations in maternal opioid levels, which reduces stress on the fetus
- Reduces drug-seeking behaviors
- Illicitly purchased heroin is adulterated with other compounds that may be harmful to the fetus
- Enhances the ability of the woman to participate in prenatal care and addiction treatment
ASAM Policy Statement
Recommendations

• Perinatal education about alcohol and other drugs for all pregnant women, public prevention programs, warning posters

• Professional education for all physicians and health care providers of women of reproductive age in the care and management of drug use

• Professional education for all providers of newborn and infant care regarding the identification and management of infants exposed to drugs and alcohol in utero
ASAM Policy Statement
Recommendations

• **Universal screening** in all settings including OB/GYN
  • Repeated follow up assessments

• **Opiate agonist treatment is the treatment of choice**
  for pregnant women dependent on illicit opioids or
  women who are already in opiate treatment
  (methadone, subutex)

• If a pregnant woman desires discontinuation of opiate
  use, she should be **advised to undergo a medically
  supervised withdrawal** during the second trimester
  when the risk of complications is the lowest.
ASAM Policy Statement

Recommendations

• Pregnant women should be given highest priority for admission to available treatment slots

• Keeping women and their children together during treatment leads to better outcomes for the children and increased likelihood of success in treatment
Recommendations

• Screen all women of reproductive age for drug use
• Encourage contraception among opiate users
• Encourage substance abuse treatment
• Florida’s Prescription Drug Monitoring Program
  • [http://www.doh.state.fl.us/mqa/pdmp/home.html](http://www.doh.state.fl.us/mqa/pdmp/home.html)
Recognizing and Treating Neonatal Withdrawal in the 21st Century

Marylou Behnke, MD, FAAP
Professor
Department of Pediatrics
Division of Neonatology
Common Drugs Associated with Neonatal Withdrawal

- Barbiturates
- Caffeine
- Benzodiazepines
- Clomipramine
- Alcohol
- Nicotine
- SSRIs
- Opiates
Clinical Presentation

- Type of drug
- Timing/amount last maternal use
- Maternal/infant metabolism
- Drug half-life
- Polydrug use
Differential Diagnosis

• Infection
• Metabolic problems
• Endocrine problems
• Anoxia
• CNS hemorrhage
• Colic
Suggested Evaluation

- Detailed maternal history
- Detailed physical examination of infant
- Abstinence scoring
- Serum glucose, calcium, magnesium
- CBC with differential and platelets
- Blood and other cultures as indicated
- Urine toxicology screen
Opiates

- ~50% of exposed infants develop NAS
- Maternal doses do not correlate with NAS
- Opiates should be used for treatment
- Few good RCTs of treatment
  - Variation in doses, timing, scoring tools, agents used, supportive care
- Withdrawal onset/duration
Scoring Tools

• Finnegan
  – 31 weighted items
  – Complex

• Lipsitz
  – 11 signs with scoring 0-3
  – Simple to use

• Ostrea
  – 6 criteria
  – No numeric scale, only a ranking
### Neonatal Abstinence Scoring (See instructions on back)

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Date/Time</th>
<th>Date/Time</th>
<th>Date/Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pacifier</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swaddle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hold</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rocked</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walked</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Snore</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parent</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Excessive Cry**

2

**Continuous Cry**

3

**Sleeps less than one hour after feed**

3

**Sleeps less than two hours after feed**

2

**Sleeps less than three hours after feed**

1

**Overactive Moro reflex**

2

**Very overactive Moro reflex**

3

**Moro not scored**

NS

**Mild tremors disturbed**

1

**Moderate / severe tremors disturbed**

2

**Mild tremors undisturbed**

3

**Moderate / severe tremors undisturbed**

4

**Increased muscle tone**

2

**Excitement**

1

**Myoclonic jerks**

3

**Generalized convulsions**

5

**Excessive sucking**

1

**Poor feeding**

2

**Regurgitation**

2

**Projectile vomiting**

2

**Loose stools**

2

**Watery stools**

3

**Sweating**

1

**Temperature 37.3°C - 38.3°C**

1

**Temperature 38.4°C and above**

2

**Yawning (greater than 3 - 4 in 1/2 hour)**

1

**Mottling**

1

**Nasal stuffiness**

1

**Sneezing (greater than 3 - 4 in 1/2 hour)**

2

**Nasal flaring**

1

**Resp rate greater than 60/min**

1

**Resp rate greater than 60/min & retractions**

2

**TOTAL SCORE**


### INITIALS

<table>
<thead>
<tr>
<th>Print RN Name</th>
<th>RN Signature</th>
<th>Initials</th>
<th>Print RN Name</th>
<th>RN Signature</th>
<th>Initials</th>
<th>Patient Name:</th>
<th>Patient Identification #:</th>
</tr>
</thead>
</table>

If printed electronically, pages 1 & 2 must be stapled.
## Scoring Tools

### Neonatal Abstinence Scoring Instructions (page 2 of 2)

| General | • Score infant 1/2 to one hour after feeding. The score is NOT a snapshot at the scoring time. Rather, score based on the total behavior of the infant during the hours between scoring times. Use the vital signs / Moro obtained before the feeding in scoring unless the infant is too fussy to obtain quiet measurements at that time.  
• Increase the frequency of scoring to every two hours and notify the medical team if the total score is 8 or greater, or the average of three consecutive scores is 8 or greater (ex: 9, 7, 8).  
• Choose only one score for each category. Score 0 if infant does not meet any of the criteria.  
• If the infant is NPO, score every four hours.  
• Chart detailed information on flowsheet. |
|---|---|
| Cry | • If the infant cries more than you would expect but is consolable, score as excessive.  
• If the infant cries continuously and is not consolable, score as continuous. |
| Sleep | • Score the total amount of sleep between scorings. Be aware of increasing sleep if on drug therapy and report to medical team. |
| Moro Reflex | • Based on judgement and experience. Be aware of decreased or absent reflex if on drug therapy. Report asymmetry to medical team. |
| Tremors | • Note if tremors present when infant is touched (disturbed) or if present even when not touched (undisturbed).  
• Comment on location of tremors (upper / lower extremities, generalized) and severity.  
• Be aware that increased temperature may indicate tremors / hypertonicity not observed. |
| Muscle Tone | • Score if unable to straighten arms / legs or if infant has body rigidity when held in standing position. Comment on degree of hypertonicity (mild, moderate, or severe). |
| Myoclonic Jerks | • Brief jerks of the extremities that last one or two seconds. |
| Convulsions | • Score if present since last scoring. |
| Excoriation | • Refers to skin over nose, elbows, fingers, toes, knees, and heels from rubbing on linen. Score at onset and if increasing. Do not score if unchanged. |
| Excessive Sucking | • Score if more than expected for a normal newborn. May have blisters on fingertips and knuckles. Be careful not to overfeed as a result of excessive sucking. |
| Poor Feeding | • May include uncoordinated suck / swallow / breathe or have decreased intake. |
| Regurgitation / Vomiting | • Note if there is a precipitating factor (handling, meds). Score if occurs more than expected for a newborn. Be aware of overfeeding. |
| Stools | • If there is a water ring around stool, score as Watery. |
| Sweating | • Do not score if sweating is the result of tight swaddling. |
| Fever | • Increased temperature may be an early sign of increased heat production from tremors or increased muscle tone. |
| Respiratory Rate | • Take respirations for a full minute. |
| Total Score | • Used to determine need for drug therapy. Notify medical team for score (or average of three continuous scores) above 8 or generally increasing scores. |

Treatment

Supportive
• First line of therapy
• ↓ Sensory stimulation
• Frequent, small feeds
• Hypercaloric formula
• Close observation

Pharmacologic
• Short-term amelioration of signs
• Use abstinence scoring
• Treat with similar drug
• Treat for:
  – Seizures
  – Excessive weight loss or dehydration
  – Inability to sleep
  – Fever unrelated to infection
Supportive Treatment

**Neonatal Abstinence Scoring** *(See instructions on back)*

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Date/Time</th>
<th>Date/Time</th>
<th>Date/Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Check all that apply and note</td>
<td>□ Medication</td>
<td>□ Medication</td>
<td>□ Medication</td>
</tr>
<tr>
<td>approximate amount of time</td>
<td>□ Pacifier</td>
<td>□ Pacifier</td>
<td>□ Pacifier</td>
</tr>
<tr>
<td>used during scoring period.</td>
<td>□ Swaddle</td>
<td>□ Swaddle</td>
<td>□ Swaddle</td>
</tr>
<tr>
<td>Put a * after parent if the</td>
<td>□ Bed</td>
<td>□ Bed</td>
<td>□ Bed</td>
</tr>
<tr>
<td>parent helped with scoring.</td>
<td>□ Held</td>
<td>□ Held</td>
<td>□ Held</td>
</tr>
<tr>
<td></td>
<td>□ Rocked</td>
<td>□ Rocked</td>
<td>□ Rocked</td>
</tr>
<tr>
<td></td>
<td>□ Walked</td>
<td>□ Walked</td>
<td>□ Walked</td>
</tr>
<tr>
<td></td>
<td>□ Snooze</td>
<td>□ Snooze</td>
<td>□ Snooze</td>
</tr>
<tr>
<td></td>
<td>□ Patting</td>
<td>□ Patting</td>
<td>□ Patting</td>
</tr>
<tr>
<td></td>
<td>□ Swing</td>
<td>□ Swing</td>
<td>□ Swing</td>
</tr>
<tr>
<td></td>
<td>□ Parent</td>
<td>□ Parent</td>
<td>□ Parent</td>
</tr>
</tbody>
</table>
Pharmacologic Treatment

- **Diazepam**
  - Multiple side effects
  - Toxicity concerns
- **Clonidine**
- **Chlorpromazine**
  - Long half-life
  - Multiple side effects
- **Phenobarbital**
  - Treats hyperactivity
  - Does not treat GI signs
- **Paragoric**
  - Multiple toxic additives
- **Tincture of opium**
  - Highly concentrated
- **Methadone**
  - Long half-life
  - Difficult to wean
- **Morphine**
- **Buprenorphine**
  - Can be given sub-lingual
Drug Dosing

Morphine

• Starting dose (Neofax): 0.03-0.1 mg/kg/dose PO q3-4h with feeds
• Increase dose by 0.02 mg/kg/dose
• After signs controlled, maintain dose for 3-5 days
• Taper by 10% of peak dose q 2-3 days
Other Aspects of Care

• OT/PT/Social work consults

• Monitoring
  – General monitoring
  – Monitoring when on drug therapy

• Diet
  – Breastfeeding
  – Formula
  – IV fluids

• Skin care
  – Diaper area
  – Knees/elbows
Developmental Outcomes of Prenatal Opioid Exposure: 
What We Know and What We Don’t Yet Know

Tamara D. Warner, Ph.D.
Research Assistant Professor
Department of Pediatrics
Division of Neonatology
Outline

• Background on teratology and conducting research in this area
• State of the research – animal models and humans
• What we know now
• What we don’t yet know – areas for further research
• Intervention
Prenatal Drug Exposures

**Teratogen**

- Any agent that can *disturb the development of an embryo or fetus*

- Classes of teratogens include:
  - Radiation
  - Maternal infections
  - Chemicals
  - Medications/Drugs
Principles of Teratology

Four primary teratogenic outcomes:

1. Death
2. Physical malformation
3. Growth retardation
4. Abnormal function

Vorhees, 1989
Principles of Teratology

The harm caused by a toxic agent is a **function of several factors**, including:

- Individual’s genetic makeup
- Fetal environment
- Postnatal environment
- Dose of the agent
- Developmental stage of the fetus at the time of exposure
Neurobehavioral Teratology

Focuses on the impact of prenatal exposure on a child’s central nervous system (CNS) and behavior

- Prenatal CNS injuries have effects that extend beyond the fetal and neonatal periods into infancy and beyond
- Most injuries to the developing nervous system do not result in CNS malformation, but rather in functional abnormalities, which are often not detectable at birth
Are Opioids Teratogenic?

• Methadone & buprenorphine **cross the placenta** and directly enter bloodstream of fetus

• **May affect brain development** by:
  – Increasing the release of dopamine
  – Interfering with opioid growth factor, which regulates tissue growth
FIGURE 1. Model to Study Effects of Prenatal Drug Exposure on Developmental Outcomes

Model for Prenatal Drug Exposure Research

Minnes, Lang & Singer 2011

Adapted from Mayes, 2002.
State of the Research

• Overwhelming majority of research on prenatal opioid exposure has **focused on methadone, not Rx drugs.**

• Animal models are POE are important **but do not always correlate with human results**
  • Dose of drugs and method of administration
  • Lack of polydrug exposure
## What Has Been Studied

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Type of Study</th>
<th>Approximate Number of Studies</th>
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</thead>
<tbody>
<tr>
<td>Cognitive development/intelligence</td>
<td>Humans</td>
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</tr>
<tr>
<td>Factors that may affect cognitive development</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General growth and development</td>
<td>Humans</td>
<td>14</td>
</tr>
<tr>
<td>Brain development</td>
<td>Both</td>
<td>1 human 2 animal</td>
</tr>
<tr>
<td>Brain neurotransmitters</td>
<td>Animal</td>
<td>7</td>
</tr>
<tr>
<td>Endocrine function (hormones)</td>
<td>Both</td>
<td>1 human 2 animal</td>
</tr>
</tbody>
</table>

Konijenberg & Melinder, 2012
Birth and Pregnancy Outcomes

- Stillbirth
- Prematurity
- Decreased birth weight
- Decreased birth length
- Decreased birth head circumference
- Fetal and neonatal abstinence syndrome
- Sudden infant death syndrome (SIDS)
- Congenital malformations? (1 study)

These effects are very similar to those for prenatal tobacco exposure and worse than prenatal cocaine exposure.
Cognitive Development

Little is known about long-term outcomes

• Ages studied range from 0 to 13 years; most are age 3 or younger

• Only one has followed the same children over time (longitudinal design)

• All but one have studied methadone exposure

• Most have used Bayley Scales of Infant Development
Cognitive Development

**Bottom line: Conflicting results**

- Virtually all children had polydrug exposure
- Assessed at different ages using different tests
- Poorer children may be at higher risk for problems
- Language skills may be more affected than non-language skills
General Growth & Development

- Increased chance of premature birth (≤ 37 weeks gestation)

<table>
<thead>
<tr>
<th>Study</th>
<th>Methadone</th>
<th>Buprenorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fajemirokum-Odudeyi et al., 2006</td>
<td>30% premature (23% heroin or polydrug)</td>
<td>NA</td>
</tr>
<tr>
<td>Lejeune et al., 2006</td>
<td>16% ≤ 37 weeks 3% born &lt; 33 weeks</td>
<td>10% ≤ 37 weeks 1.9% &lt; 33 weeks</td>
</tr>
</tbody>
</table>
General Growth & Development

- **Decreased somatic growth**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Methadone</th>
<th>Buprenorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smaller body weight</td>
<td>Yes at birth (4) No at birth (1) Yes at 5 years (1)</td>
<td>No at birth (1)</td>
</tr>
<tr>
<td>Smaller body length</td>
<td>Yes at birth (1) Yes at 2 years (1) Yes at 5 years (1)</td>
<td>No studies</td>
</tr>
<tr>
<td>Smaller head circumference</td>
<td>Yes at birth (2) Yes at 2 years (1) Yes at 3 years (1) Yes at 5 years (1)</td>
<td>No studies</td>
</tr>
</tbody>
</table>
Brain Development

Brain Volume

- Not a single study of methadone or buprenorphine in humans
- Heroin exposure is associated with decreased brain volume
- Decreased brain volume has been found in methadone-exposed animals (rats)
- More research is needed in this area
Brain Development

**Myelination**

- Formation of the fatty myelin sheath around neurons needed for efficient conduction of nerve impulses

- One study showing a negative effect in the developing rat brain at levels comparable to human use (Sanchez et al., 2008)
Endocrine Function

• Does POE affect the hypothalamic-pituitary-adrenal (HPA) axis?

• Cortisol/corticosterone production → response to stress
  • One study of methadone-maintained adults found elevated cortisol levels but may not apply to fetal exposure
  • One animal study using buprenorphine did not find elevated corticosterone levels

• Jury is still out
Brain Neurotransmitters

• All animal studies
• All but one study involved methadone
  • Norepinephrine
    – Reduced in the hippocampus
  • Serotonin
    – Irregularities in transport system in the cortex and hippocampus
    – Increased levels in the parietal cortex
Brain Neurotransmitters

- **Acetylcholine**
  - Disrupted activity in the striatum

- **Dopamine**
  - Irregularities in neurons
  - Reductions in the forebrain and striatum

- **GABA**
  - Reductions in the release of GABA

*Meaning of these results is unclear as research is still in early stages*
Interventions

- Home-based services to mothers by community nurses
- Goal is to educate & provide support to improve home environment, parenting skills and child development
- Maternal psychological distress predicts cognitive and behavioral outcomes of children with prenatal drug exposures
Interventions

• Few studies are drug-specific or target the children directly (case management)

• Conflicting results
  • Even when benefit is seen, children in the control group who did not receive services generally attain scores in the average range
Model of Intervention

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<tr>
<th>Services</th>
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Bandstra et al., 2010
Model of Intervention

Bandstra et al., 2010
Mother-Infant Interactions

Strathearn, 2007
Breastfeeding as Potential Intervention

Methadone is the most-studied drug in terms of human milk and its effects

- Concentrations in human milk are low
- No apparent short-term or long-term effects on neurodevelopment
- Promotes positive attachment
- Is protective against child neglect
- Associated with less severe NAS and shorter hospital stays
- Breastfeeding **IS** recommended for methadone-maintained women **who meet specific criteria** regardless of maternal methadone dose

ABM Clinical Protocol #21 (2009)
ACOG Committee Opinion No. 524 (2012)
AAP Section on Breastfeeding (2012)
Summary

*Teratogenic effects of prenatal opioid exposure?*

- Current knowledge is *remarkably limited*
- Reasons to be suspect potential effects
- Need to *guard against rush to judgment*
- **Difficult research to conduct** due to large number of *confounding factors*
Summary

*Teratogenic effects of prenatal opioid exposure?*

- Clear negative effects on **birth outcomes**
- Longer-term effects are **mostly unknown**
- **Difficult to design interventions** when targets are unclear
- Need to focus on interventions (beyond general parenting skills) that strengthen **mother-child attachment**
Questions and Discussion
References

Breastfeeding


References

Dr. Behnke’s presentation:


Dr. Warner’s presentation:

- Critiques of Broussard et al. (Letters to the Editor and Authors’ Replies).
Dr. Warner’s presentation (continued)


