Supporting Babies, Supporting Families:
Understanding and Supporting Developmental Outcomes for Infants Born with Neonatal Abstinence Syndrome

Pediatric Nursing Grand Rounds
Seattle Children’s Hospital
November, 2021
None!

Disclosures
# Learning Objectives

<table>
<thead>
<tr>
<th>Action</th>
<th>Description</th>
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<tbody>
<tr>
<td>Review</td>
<td>Review the neurophysiological impacts of opiate use on maternal and fetal brains</td>
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<tr>
<td>Identify</td>
<td>Identify challenges experienced by children with neonatal abstinence syndrome which can affect developmental outcome</td>
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<td>Recognize</td>
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<tr>
<td>Describe</td>
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Neonatal Abstinence Syndrome: NAS

- Array of symptoms seen in infants after abrupt postnatal withdrawal from in-utero opioid substance exposure
Epidemiology

NAS - 2019

2000→2014 increase from 1.5 to 8 per 1000 hospital births

Rural, public health insurance populations

Non-Hispanic white (10/1,000)> other race/ethnicity (3/1,000)
Epidemiology NAS-2019

Sex at birth

Co-exposure to other substances

Genetic and epigenetic influences
## Maternal Opioid Treatment

<table>
<thead>
<tr>
<th>Methadone – synthetic mu-opioid receptor agonist</th>
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<tbody>
<tr>
<td>• Optimized obstetric care</td>
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<tr>
<td>• Decreased illicit drug use</td>
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<td>• Improved fetal outcomes</td>
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<tr>
<td>• Also increased incidence of NAS</td>
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<tr>
<td>• Over time increased dosage of methadone use in pregnancy</td>
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<table>
<thead>
<tr>
<th>Buprenorphine</th>
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<tr>
<td>• Partial mu-opioid receptor agonist and complete k-opioid receptor agonist</td>
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<td>• Alternative to methadone</td>
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Opioid withdrawal in neonates

**Mechanism unknown**

- Low molecular weight, water soluble and are lipophilic
- Easily transferrable across the placenta
- Transmission of opioids increases as gestation increases
- Synthetic opioids cross the placenta easier than semisynthetics
- Combinations of cocaine or heroin with methadone increase permeability of methadone across the placenta
Opioid withdrawal in neonates

Opiates act through the mu-, kappa-, and gamma-opioid receptors which are distributed across the central nervous system. The abrupt lack of activation of these receptors that have been chronically stimulated with opiates results in a cascade of cellular activity in many different parts of the brain and body.

- **Locus coeruleus of the pons** – increased production of noradrenaline
- **Ventral tegmental area** – decreased production of dopamine
- **Dorsal raphe nucleus** – decreased production of serotonin
Learning Objectives

**Identify**
Identify challenges experienced by children with neonatal abstinence syndrome which can affect developmental outcome
Clinical presentation of NAS

- Hyperthermia
- Hypertension
- Tremors
- Tachycardia
- Irritability
- Anxiety
- Sleep disturbance

Serotonin

Dopamine
- Irritability
- Anxiety

Norepinephrine
- Hyperthermia
- Hypertension
- Tremors
- Tachycardia
<table>
<thead>
<tr>
<th>Increased Cortisol</th>
<th>Increased Acetylcholine</th>
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<tbody>
<tr>
<td>Increased stress</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Hyperphagia (hungry!)</td>
<td>Vomiting</td>
</tr>
<tr>
<td></td>
<td>Yawning</td>
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<tr>
<td></td>
<td>Sneezing</td>
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<td>Sweating</td>
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Neonatal Consequences, NAS

- Mother-infant bonding
- Feeding problems, challenges with weight gain
- Prolonged Hospitalization
Treatment – Therapeutic Options

- Wide variability/availability of treatment options between hospitals across the country
- Nonpharmacologic/Pharmacologic
- LOS and observation periods
Nonpharmacologic treatment
Pharmacological Treatment NAS

Finnegan Scores
Learning Objectives

- Review the neurophysiological impacts of opiate use on maternal and fetal brains
- Review
- Identify challenges experienced by children with neonatal abstinence syndrome which can affect developmental outcome
- Identify
- Recognize the developmental challenges that can be experienced by children with neonatal abstinence syndrome
- Recognize
- Describe long-term outpatient resources to support children and families, to optimize developmental outcomes
- Describe
Brain differences in opioid exposed infants

**Pediatrics 2019** – prospective cohort study of 429 infants with NAS matched with 429 infants without NAS

- significantly smaller head circumference in babies experiencing NAS
Structural Brain Differences in opioid exposed infants

Journal Perinatology 2014 –
Case series of 16 infants born exposed to opiates

• Smaller brain volumes in basal ganglia regions
Developmental outcomes in children prenatally exposed to opiates

2017 Pediatrics - Retrospective Case Control Australia

- High school students had significantly lower literacy and numeracy scores and were more likely to not meet minimum standards at grades 3, 5, 7 and adjusted for race

2018 Pediatrics – Retrospective Case Control

- Cases: 1815; Controls 5441 matched by maternal age and race
- Significantly more children referred for a disability evaluation, diagnosed with a disability and to special education services

2015 Pediatric Research – Case Control 80 children exposed to opiates 50 children not exposed

- IQ at age 8 ½ WISC-R significantly lower in exposed children than not exposed
- Significant even after adjustment for SES – NO RACE data
Learning Objectives

- Review the neurophysiological impacts of opiate use on maternal and fetal brains.
- Identify challenges experienced by children with neonatal abstinence syndrome, which can affect developmental outcomes.
- Recognize the developmental challenges that can be experienced by children with neonatal abstinence syndrome.
- Describe long-term outpatient resources to support children and families, to optimize developmental outcomes.
Supporting families and infants with fetal opioid exposure

- Journal of Developmental and Behavioral Pediatrics - 2019 retrospective cohort study of 256 infants in MA
  - 77% all infants referred to EI and only 48% screened in for services
  - 88% infants discharged home with biological parents referred to EI; 66% infants discharged with foster parents referred to EI
Referral to Early Intervention!

- Prenatal opiate exposure – automatic screen-in to Birth to Three services
- Providers just need to refer
Early Headstart
Seattle-area Resources for Follow-Up

- Hope Rising Program, Wonderland Child and Family Services
- University of Washington Infant Development Follow Up Program
- University of Washington Center for Adoption Medicine
- University of Washington Foster Care Clinic
• Opiate withdrawal causes significant changes in several different neurotransmitters which causes the clinical presentation of NAS

• Synthetic opiates are much more transmissible across the placenta than semi-synthetic, and use of methadone in combination with other opiates potentiate the transfer of methadone across the placenta
Summary

- Irritability, tremulous, sensitive, hyperthermia, tachycardia
- Feeding problems, diarrhea, sweating
- Growth difficulties
- Challenges with bonding
Summary

- Compelling evidence of smaller head circumference
- Data describing differences in other brain anatomy is less strong
- There is evidence of long-term developmental differences associated with opiate exposure, but causality not established

Recognize

Recognize the developmental challenges that can be experienced by children with neonatal abstinence syndrome
Summary

- Birth to Three automatic qualification
- Early Head Start
- Hope Rising, Wonderland
- Infant Development Follow Up Clinic, UW
- Center for Adoption Medicine, UW
- Foster Care Consultation Clinic, UW

Describe

Describe long-term outpatient resources to support children and families, to optimize developmental outcomes
This has been an honor!
Thank you!