Neonatal Opioid Withdrawal Syndrome (NOWS)

Advances in Diagnosis and Management

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Objectives

- **Scope of the problem**
- **Assessment and management:**
  - Signs and symptoms
  - Role of toxicology testing
  - Monitoring
    - EAT, SLEEP, CONSOLE
  - Non pharmacological measures
  - Medications
- **Discharge planning:**
  - Plan for safe care
- **Outpatient follow-up:**
  - Pediatric care
  - Developmental screening
- **Long-term outcomes**
Definition

• Neonatal abstinence syndrome (NAS):
  – Abrupt discontinuation of chronic fetal exposure to substances used or abused by the mother during pregnancy
  – Generally follows opioid exposure
  – *Other drugs* may be implicated

• NOWS – neonatal opioid withdrawal syndrome
Scope of the Problem

- Dramatic ↑ in NAS/NOWS cases in the US
  - 5-fold ↑ between 2004 and 2014
  - 1.2 → 5.8 per 1,000 hospital births
  - 4% of NICU admissions
- Outpacing projections
Scope of the Problem

**NAS/NOWS and Maternal Opioid Use Disorder on the Rise**
Rates per 1,000 Hospital Births

- NAS/NOWS
- OUD

**Growing Hospital Costs for Treatment of NAS/NOWS**
Inflation-Adjusted U.S. Dollars (millions)

THE OPIOID EPIDEMIC BY THE NUMBERS

130+
People died every day from opioid-related drug overdoses
(estimated)

47,600
People died from overdosing on opioids

81,000
People used heroin for the first time

2 million
People misused prescription opioids for the first time

32,656
Deaths attributed to overdosing on synthetic opioids other than methadone (in 12-month period ending February 2019)

10.3 m
People misused prescription opioids in 2018

2.0 million
People had an opioid use disorder in 2018

808,000
People used heroin in 2018

15,349
Deaths attributed to overdosing on heroin (in 12-month period ending February 2019)

SOURCES
1. 2019 National Survey on Drug Use and Health. Mortality in the United States, 2018
2. NCHS Data Brief No. 329, November 2018

Updated October 2019. For more information, visit: http://www.hhs.gov/opioids/
Opioid Use Disorder in Pregnancy

- Prescription opioid medication (2008-2012)
  - 28% of privately insured women
  - 39% of Medicaid enrolled women
- Illicit drugs use in pregnant women, 2012-2013:
  - 5.4% of 15-44 years old
    - Compared to 10.7% in non-pregnant women
  - 14.6% of 15-17 years old
  - 8.6% of 18-25 years old
  - 3.2% 26-44 years old
Economic Impact

- **2.5 billions** in total hospital charges (2016)
- 6.7% of hospital costs in 2014
  - up from 1.6% in 2004
- Medicaid is responsible for 83% of the charges

**Table 2. Birth Hospitalization Mean Length of Stay and Costs for US Infants With Neonatal Abstinence Syndrome by Primary Payer, 2016**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>NAS Rate per 1000 Births</th>
<th>Mean (SD) Length of Stay, d</th>
<th>Cost, $</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Per Birth</td>
</tr>
<tr>
<td>Overall</td>
<td>6.7</td>
<td>15.9 (20.4)</td>
<td>22 552</td>
</tr>
<tr>
<td>Medicaid</td>
<td>12.3</td>
<td>16.2 (20.2)</td>
<td>22 669</td>
</tr>
<tr>
<td>Private</td>
<td>1.5</td>
<td>14.9 (23.4)</td>
<td>25 013</td>
</tr>
<tr>
<td>Uninsured</td>
<td>7.0</td>
<td>11.5 (13.2)</td>
<td>13 516</td>
</tr>
<tr>
<td>Other payer$</td>
<td>3.9</td>
<td>16.3 (23.9)</td>
<td>27 153</td>
</tr>
</tbody>
</table>

Disproportionately Affects Rural/Suburban areas

Figure. Changes in Opioid-Related Diagnoses Among Infants and Mothers by Urban/Rural Status

A. Neonatal abstinence syndrome

B. Maternal opioid use

No. per 1000 Hospital Births

Time, y

Rural Urban
Rate of NAS per 1,000 Newborn Hospitalizations

2016 National rate: 7.0

33.4 per 1000 hospital birth

0.7 per 1000 hospital birth

https://www.hcup-us.ahrq.gov/faststats/NASMap
SAMHSA’s Five-Point Intervention Framework

Pre-pregnancy | Prenatal | Birth | Neonatal | Childhood and beyond

Prevention Across the Life Course - Avoid Stigma

Section II: Infant Care
Objectives

• Scope of the problem
• Assessment and management:
  • Signs and symptoms
  • Role of toxicology testing
  • Monitoring
    • EAT, SLEEP, CONSOLE
  • Non pharmacological measures
  • Medications
• Discharge planning:
  • Plan for safe care
• Outpatient follow-up:
  • Pediatric care
  • Developmental screening
• Long-term outcomes
Case #1

- Baby S:
  - Born at 39 weeks to a 22 year old G3P1201 mother
  - Uncomplicated vaginal delivery
- Mother began prenatal care at 18 weeks
  - Disclosed using oxycontin 10 mg “4 or 5 times” daily for chronic back pain after a fall from a horse
  - Agreed to a referral to a methadone program
    - Pain medication is converted to Methadone (80 mg daily)
- She is planning on breastfeeding
Case #1

- What else do you want to know in the history?
- How long does this infant need to be observed?
- And what are you looking for?
- What is the role of toxicology screening?
NAS/NOWS

• Clinical diagnosis
  – Toxicology confirmation

• Generalized multisystem disorder involving predominantly:
  – CNS
  – ANS
  – GI tract

• Highly variable presentation
  – May be severe and intense
NOWS/NAS Development

- Depends upon:
  - Type of opioid
    - Lower risk if buprenorphine
  - Additional substances
  - Timing of maternal drug usage
  - Infant metabolism
  - Gestational age
  - Birthweight

Risk Factors

- Synergistic / exacerbating substances
  - Tobacco
  - SSRIs
  - Poly-substance exposure(s)
  - Benzodiazepines
  - Psychotropic medications

Associated with prolonged LOS and pharmacological treatment

CYP2B6 positive
Timing of Symptoms Onset

- Heroin ~ 24h
- Methadone 24-72h
  - Higher doses of methadone *are not* associated with higher rates or severity of withdrawal symptoms
- Buprenorphine 40h
  - In some cases as long as 19-200 hours!
- Evidence of withdrawal may be delayed until 5-7 days of age or later
  - \(\rightarrow\) May happen **after** hospital discharge
## Onset and Duration by Opioid Type

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset, h</th>
<th>Frequency, %</th>
<th>Duration, d</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heroin</td>
<td>24–48</td>
<td>40–80&lt;sup&gt;27&lt;/sup&gt;</td>
<td>8–10</td>
</tr>
<tr>
<td>Methadone</td>
<td>48–72</td>
<td>13–94&lt;sup&gt;57&lt;/sup&gt;</td>
<td>Up to 30 or more</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>36–60</td>
<td>22–67&lt;sup&gt;48,49&lt;/sup&gt;</td>
<td>Up to 28 or more</td>
</tr>
<tr>
<td>Prescription opioid medications</td>
<td>36–72</td>
<td>5–20&lt;sup&gt;56,60&lt;/sup&gt;</td>
<td>10–30</td>
</tr>
<tr>
<td><strong>Nonopioids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSRIs</td>
<td>24–48</td>
<td>20–30&lt;sup&gt;64&lt;/sup&gt;</td>
<td>2–6</td>
</tr>
<tr>
<td>TCAs</td>
<td>24–48</td>
<td>20–50&lt;sup&gt;64&lt;/sup&gt;</td>
<td>2–6</td>
</tr>
<tr>
<td>Methamphetamines</td>
<td>24</td>
<td>2–49&lt;sup&gt;101&lt;/sup&gt;</td>
<td>7–10</td>
</tr>
<tr>
<td>Inhalants</td>
<td>24–48</td>
<td>48&lt;sup&gt;70&lt;/sup&gt;</td>
<td>2–7</td>
</tr>
</tbody>
</table>
In Hospital Observation Duration

• American Academy of Pediatrics guideline recommendations:
  – 3 days of observation for short-acting opioids
  – 5–7 days of observation for longer acting opioids
Length of Hospital Stay

- Depends on agent(s) and subsequent treatment
  - Mean LOS: 10-21 days
  - No real differences in LOS for centers that sent infants home on medications

VDH data
## Signs and Symptoms

- Generalized multisystem disorder

<table>
<thead>
<tr>
<th>Central Nervous System</th>
<th>Autonomic Nervous System</th>
<th>GI tract</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypertonia</strong>*</td>
<td>Sweating</td>
<td>Excessive/uncoordinated sucking</td>
</tr>
<tr>
<td><strong>Tremors</strong> (undisturbed)*</td>
<td>Low-grade fever</td>
<td>Poor feeding</td>
</tr>
<tr>
<td>Hyperreflexia</td>
<td>Rhinorrhea / nasal stuffiness</td>
<td>Vomiting</td>
</tr>
<tr>
<td><strong>Exaggerated Moro</strong>*</td>
<td>Sneezing</td>
<td>Loose stools/diarrhoea</td>
</tr>
<tr>
<td><strong>Irritability</strong></td>
<td>Yawning</td>
<td><em>Diaper rash</em></td>
</tr>
<tr>
<td>Restlessness</td>
<td>Skin mottling</td>
<td><em>Skin excoriation</em></td>
</tr>
<tr>
<td><strong>Excessive crying</strong></td>
<td>Tachypnea</td>
<td>Poor swallowing</td>
</tr>
<tr>
<td>High-pitched cry</td>
<td></td>
<td>Dehydration</td>
</tr>
<tr>
<td>Sleep disturbances</td>
<td></td>
<td>Poor weight gain</td>
</tr>
<tr>
<td>Seizures (2-11%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Only items shown to be specific for NOWS

**Bold = most common**

Lack of opioids in chronically stimulated receptors

Super activation of adenyl cyclase

Increased cyclic adenosine monophosphate

Increased protein kinase

Increased transcription factors

Increased release of neurotransmitters

Noradrenaline increase
- Hyperthermia
- Hypertension
- Tremors
- Tachycardia

Serotonin decrease
- Sleep deprivation
- Sleep fragmentation

Dopamine decrease
- Hyperirritability
- Anxiety

Acetylcholine increase
- Diarrhea
- Vomiting
- Yawning
- Sneezing
- Sweating

Other receptor activity increase
- Hyperalgesia
- Allodynia
<table>
<thead>
<tr>
<th>Drugs of abuse</th>
<th>Neurotransmitter effects of drug withdrawal</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioids&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Norepinephrine (↑)</td>
<td>Hyperthermia</td>
</tr>
<tr>
<td>TCAs&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td>Hypertension</td>
</tr>
<tr>
<td>Opioids&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Corticotropin (↑)</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Opioids&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Acetylcholine (↑)</td>
<td>Tremors</td>
</tr>
<tr>
<td>TCAs&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td>Hyperphagia</td>
</tr>
<tr>
<td>SSRIs&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td>Stress</td>
</tr>
<tr>
<td>SNRIs&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Opioids&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Dopamine (↓)</td>
<td>Vomiting</td>
</tr>
<tr>
<td>SSRIs&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td>Sweating</td>
</tr>
<tr>
<td>SNRIs&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td>Sneezing</td>
</tr>
<tr>
<td>Opioids&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Serotonin (↓)</td>
<td>Yawning</td>
</tr>
<tr>
<td>TCAs&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td>Temperature instability</td>
</tr>
<tr>
<td>SSRIs&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td>Anxiety</td>
</tr>
<tr>
<td>SNRIs&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td>Irritability</td>
</tr>
<tr>
<td>Opioids&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td>Sleep disorders</td>
</tr>
<tr>
<td>TCAs&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td>Insomnia</td>
</tr>
<tr>
<td>SSRIs&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SNRIs&lt;sup&gt;d&lt;/sup&gt;</td>
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</tr>
</tbody>
</table>
Toxicology Screening

- Although NOWS is a clinical diagnosis, **toxicological confirmation** is necessary to:
  - Identify exact type of substance use or abused
  - Confirm/rule-out use of other licit/illicit substances
Toxicology Screening

- **Urine** – *Not recommended*
  - Short detection window (24-48h)
  - More false negative (dilute urine)
  - Prone to adulteration (Visine…)

- **Meconium**
  - Most sensitive
  - Long detection window
    - Reflect 2nd/3rd trimester exposures
  - Collection issues
    - In utero or delayed passage
    - Light sensitive

- **Cord**
  - Readily available
  - Long detection window
  - Lower drug concentrations
  - 80-100% agreement with mec

---

*Estimated Detection Window for Various Biological Specimens*^*

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Hours</th>
<th>Days</th>
<th>Weeks</th>
<th>Months</th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Oral Fluid</td>
<td></td>
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<tr>
<td>Breast Milk</td>
<td></td>
<td></td>
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<tr>
<td>Placenta</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweat*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vernix</td>
<td></td>
<td></td>
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<tr>
<td>Amniotic Fluid</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nails*</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Hair, Neonatal</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Umbilical Cord Tissue</td>
<td></td>
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<td></td>
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<tr>
<td>Meconium</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hair, Maternal*</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Collection</th>
<th>Difficult</th>
<th>Easy</th>
<th>Moderate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical Turnaround Time</td>
<td>&lt;4 hrs</td>
<td>1-2 days</td>
<td>12 hrs-2 days</td>
</tr>
<tr>
<td>Window of Detection</td>
<td>Short</td>
<td>Intermediate</td>
<td>Long</td>
</tr>
<tr>
<td>Drug Concentrations</td>
<td>Moderate</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Extent of Characterization</td>
<td>Moderate</td>
<td>Low</td>
<td>High</td>
</tr>
</tbody>
</table>

Ther Drug Monit. 2018 Apr;40(2):166-185.
## Mom UDS Results

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ur Amphetamine Screen Interpretation</td>
<td>Negative</td>
</tr>
<tr>
<td>Ur Barbiturate Screen Interpretation</td>
<td>Negative</td>
</tr>
<tr>
<td>Ur Benzodiazepine Screen Interpretation</td>
<td>Negative</td>
</tr>
<tr>
<td>Ur Cannabinoid Screen Interpretation</td>
<td>Positive</td>
</tr>
<tr>
<td>Ur Cocaine Screen Interpretation</td>
<td>Negative</td>
</tr>
<tr>
<td>Ur Darvon Screen Interpretation</td>
<td>Negative</td>
</tr>
<tr>
<td>Ur Methadone Screen Interpretation</td>
<td>Positive</td>
</tr>
<tr>
<td>Ur Opiate Screen Interpretation</td>
<td>Positive</td>
</tr>
</tbody>
</table>

How would you interpret these results?
Case #1 (continued)

<table>
<thead>
<tr>
<th>Baby UDS Results</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ur Amphetamine Screen Interpretation</td>
<td>Negative</td>
</tr>
<tr>
<td>Ur Barbiturate Screen Interpretation</td>
<td>Negative</td>
</tr>
<tr>
<td>Ur Benzodiazepine Screen Interpretation</td>
<td>Negative</td>
</tr>
<tr>
<td>Ur Cannabinoid Screen Interpretation</td>
<td>Positive</td>
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<tr>
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<td>Negative</td>
</tr>
<tr>
<td>Ur Darvon Screen Interpretation</td>
<td>Negative</td>
</tr>
<tr>
<td>Ur Methadone Screen Interpretation</td>
<td>Positive</td>
</tr>
<tr>
<td>Ur Opiate Screen Interpretation</td>
<td>Negative</td>
</tr>
</tbody>
</table>

How would you interpret these results?
Case #1 (continued)

• Maternal UDS:
  – Mom received methadone as she described
  – In addition, the results suggest she used marijuana and opiates close to the time of delivery

• Baby UDS
  – Exposure to methadone consistent with maternal history
  – Exposure to marijuana and opiate again require further discussion with mother

• Requires additional history taking
Case #1 (continued)

- On further questioning, mom reveals that she continued to have back pain especially the last week before she delivered.
- She found some oxycontin tablets and took one every morning and at bedtime to help reduce her pain.
- She also explained that she smoked marijuana “2 or 3 times a week for nausea.
- She did not communicate her use of oxycontin or marijuana to her counselors at the methadone clinic.

• How does this information affect your plans?
Case #1 (continued)

• The presence of shorter acting opiates may result in more rapid declines in brain and serum levels and earlier symptoms

• No change in monitoring/treatment plan
  – Monitoring should be in place
  – Using your institution scoring system or too

• Will affect the feeding plan
MONITORING
Case #2

- CS is a 3 day old born at 40 2/7 weeks via SVD to a 30 y.o. G4P3013 mother.
- The prenatal course is notable for:
  - Mom in on medication assisted treatment (Buprenorphine)
  - Mom is incarcerated
  - Maternal h/o hepatitis C

- Where should the baby be monitored?
- How would you monitor for withdrawal?
- Preferred feeding method?
Monitoring for NOWS - WHO?

- ALL at risk neonates:
  - Known maternal opioid dependence or abuse
  - Suspected opioid dependence or abuse
  - Positive maternal urine drug screen for opioids
  - Positive infant drug screen (umbilical cord or meconium) for opioids
Monitoring for NOWS – WHEN?

- Begin observation within 4-6 hours of admission
- Every 3-4 hours at the time of other routine infant care
  - ON THE INFANT’S SCHEDULE
- Using **standardized assessment tools**
  - Eat, sleep, console
  - Finnegan
Monitoring for NOWS – WHERE?

- Depends on local set-up
- The goal is to:
  - Promote rooming-in
  - Minimize the separation of the maternal–infant dyad
    - The presence of parents at the bedside is associated with:
      - Fewer days of opioid therapy
      - Shorter LOS
- Avoid NICU admission unless medically necessary
Monitoring for NOWS – HOW?

- Standardized NAS assessment
  - Duration of pharmacological treatment
  - Number of infants discharged on medication
- No good data comparing the different tools:
  - Cost-effectiveness
  - Efficiency in identifying opioid-exposed infants at birth
<table>
<thead>
<tr>
<th>Assessment Tool</th>
<th>Description</th>
<th>Studies</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Finnegan Neonatal Abstinence Severity Score</td>
<td><strong>32 items</strong> (1-5 based on potential for clinically adverse effects). Starts 2h after birth, then q4h Pharmacologic treatment initiated if scores &gt;= 8 x 3 consecutive scorings.</td>
<td>Evaluated in 2 groups of neonates with NAS/NOWS. Treatment time and length were found to decrease in the NAS scoring group and significantly fewer of these neonates required drug treatment. Inter-rater reliability ranged from 0.75 to 0.96.</td>
<td></td>
</tr>
<tr>
<td>Modified Finnegan Neonatal Abstinence Severity Score</td>
<td><strong>21 items</strong> in 3 categories (CNS, GI, metabolic). T Same scoring process and cut-off points for treatment are used.</td>
<td>Used extensively No validation studies. Resource available to support staff education and inter-rater reliability: <a href="http://neoadvances.com/">http://neoadvances.com/</a></td>
<td></td>
</tr>
<tr>
<td>Simplified Finnegan Neonatal Abstinence Severity Score</td>
<td><strong>10 items</strong> in 3 categories (CNS, GI, metabolic). Scores ≥ 6 and ≥ 10 have excellent specificity and negative predictive value for identifying infants with Finnegan Neonatal Abstinence Scores ≥ 8 and ≥ 12.</td>
<td>No validation studies.</td>
<td></td>
</tr>
<tr>
<td>Neonatal Drug Withdrawal Scoring System (Lipsitz)</td>
<td><strong>11 items</strong>. &gt; 4 = significant signs of withdrawal. Score 1 hour after feeding Included in the 1998 and 2012 AAP statement on NAS.</td>
<td>1 validation case control study: inter-rater reliability of 0.92 and 77% sensitivity was reported.</td>
<td></td>
</tr>
<tr>
<td>Eat, Sleep, Console (ESC)</td>
<td>Simplified approach focusing on 3 “functional” criteria 1- EAT - Is the infant feeding well? Tolerates feedings (appropriate amount for gestational and postnatal age) 2- SLEEP - Is the infant sleeping well? Able to sleep for at least 1 hour undisturbed 3- CONSOLE - Is the infant consolable? Can be consulted in 10 minutes or less</td>
<td>Studies indicate that this approach leads in improvements in NAS/NOWS outcomes including decrease need for pharmacologic interventions and decreased length of stay</td>
<td></td>
</tr>
<tr>
<td>Tool and Year Tool Published</td>
<td>No. of Items</td>
<td>Score Range</td>
<td>Score for Treatment</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--------------</td>
<td>-------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Finnegan Neonatal Abstinence Scoring Tool (1975)</td>
<td>21</td>
<td>0–62</td>
<td>≥8 on three consecutive evaluations</td>
</tr>
<tr>
<td>Lipsitz Neonatal Drug Withdrawal Scoring System (1975)</td>
<td>11</td>
<td>0–20</td>
<td>≥4</td>
</tr>
<tr>
<td>Neonatal Narcotic Withdrawal Index (1981)</td>
<td>7</td>
<td>0–14</td>
<td>≥5 on two evaluations in 24 hr</td>
</tr>
<tr>
<td>Neonatal Withdrawal Inventory (1998)</td>
<td>7</td>
<td>0–19</td>
<td>≥8</td>
</tr>
<tr>
<td>MOTHER NAS Scale (2010)</td>
<td>19</td>
<td>0–42</td>
<td>9; rescore before initiation of drug treatment</td>
</tr>
<tr>
<td>Finnegan Neonatal Abstinence Syndrome Scale — Short Form (2013)</td>
<td>7</td>
<td>0–16</td>
<td>≥8</td>
</tr>
</tbody>
</table>

* The data provided in the table are based on overviews and comparisons of the various assessment tools reported by Newnam et al. and Orlando, as well as specific assessments of each tool, which are cited in the table.
† Some definitions are the same as those in the original Finnegan tool (Finnegan Neonatal Abstinence Scoring Tool).
‡ Training materials from the original Finnegan tool may be used.
The Modified FNAS

Initiation of pharmacological treatment:
- 3 consecutive scores of 8 or higher
- 2 consecutive scores of 12 or higher

Weaning pharmacological therapy:
- Contiguous scores less than 8

<table>
<thead>
<tr>
<th>System</th>
<th>Signs and Symptoms</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Nervous System Disturbances</td>
<td>High-Pitched Cry</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Continuous High-Pitched Cry</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Sleeps=1 hour after feeding</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Sleeps=2 hours after feeding</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Sleeps=3 hours after feeding</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Mild Tremors Disturbed</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Mod-Severe Tremors Disturbed</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Mild Tremors Undisturbed</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Mod-Severe Tremors Undisturbed</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Increased Muscle Tone</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Excoriation (specify area)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Myoclonic Jerks</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Generalised Convulsions</td>
<td>5</td>
</tr>
<tr>
<td>Metabolic/Endocrine/Respiratory Disturbances</td>
<td>Fever (37.3°C-38.3°C)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Fever (38.4°C and higher)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Frequent Yawning (&gt;3-4 times)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Nasal Stiffnesses</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Sneezing (&gt;3-4 times)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Nasal Flaming</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Respiratory Rate &gt; 60/min</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Respiratory Rate &gt; 60/min with retractions</td>
<td>2</td>
</tr>
<tr>
<td>Gastrointestinal Disturbances</td>
<td>Excessive sucking</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Poor Feeding</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Regurgitation</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Projectile Vomiting</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Loose Stools</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Watery Stools</td>
<td>3</td>
</tr>
</tbody>
</table>
The Simplified FNAS

* Scores ≥ 6 and ≥ 10 have excellent specificity and negative predictive value for identifying infants with FNAS scores ≥ 8 and ≥ 12.

<table>
<thead>
<tr>
<th>Simplified Finnegarn Neonatal Abstinence Scoring</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Cry (excessive or continuous)</td>
<td>2</td>
</tr>
<tr>
<td>2. Tremors</td>
<td></td>
</tr>
<tr>
<td>Tremors undisturbed (mild, moderate or severe)</td>
<td>5</td>
</tr>
<tr>
<td>Tremors disturbed (mild, moderate or severe)</td>
<td>1</td>
</tr>
<tr>
<td>3. Increased muscle tone</td>
<td>2</td>
</tr>
<tr>
<td>4. Sleep</td>
<td></td>
</tr>
<tr>
<td>&lt;1 hour</td>
<td>3</td>
</tr>
<tr>
<td>&lt;2 or 3 hours</td>
<td></td>
</tr>
<tr>
<td>5. Nasal stuffiness</td>
<td>1</td>
</tr>
<tr>
<td>6. Respiratory rate &gt;60/min</td>
<td>1</td>
</tr>
<tr>
<td>7. Excessive sucking</td>
<td>1</td>
</tr>
<tr>
<td>8. Poor feeding</td>
<td>2</td>
</tr>
<tr>
<td>9. Feed tolerance (Regurgitation/projectile vomiting)</td>
<td>2</td>
</tr>
<tr>
<td>10. Stools Loose/watery stools</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>0-21</strong></td>
</tr>
</tbody>
</table>

6 or greater x 3 scores in a 12-hour period
or
10 or greater x 2 scores within an 8-hour period

Eat, Sleep, Console

- Developed at Yale
- Novel assessment method:
  - Assesses only 3 basic domains: EAT, SLEEP, CONSOLE
  - Simple YES / NO answers
- Shifts:
  - Focus from withdrawal signs to overall assessment of infant’s well-being
  - Management from medical to family-centered
- They were able to significantly decrease:
  - Number of opioid-exposed neonates started on medication
    - From 62% to 12%
  - Length of inpatient stay
    - Average LOS 5.9 days vs. 16 days

“Treat babies like babies and moms like moms”
– Dr. Matt Grossman

Eat, Sleep, Console

- **EAT** - Is the infant feeding well?
  - Breastfeeding well (8-12 times per day with effective latch and milk transfer)
  - Bottle feeding an expected volume for age when showing hunger cues
    - ≥ 1 ounce per feed

- **SLEEP** – Can the infant sleep for at least an hour undisturbed?

- **CONSOLE** - Is the infant consolable?
  - Can be consoled in 10 minutes or less with appropriate comfort measures

No readmissions
No transfers to the ICU
No seizures
Do You Still Need a Scoring System?

- Controversial
- Can be considered if more information is required for decision making
  - NICU patients
    - When the ESC approach cannot be used (i.e. NPO, intubated, hemodynamically unstable)
  - Healthy neonates when more information is deemed helpful to:
    - Assess the severity and progression of the symptoms
    - Assist with discharge decisions
Case #2 (continued)

- The baby was monitored using ESC
  - He was *feeding well* and gaining weight on 20 kcal formula
  - He was *sleeping well*
  - He remained intermittently agitated, tremulous and had mildly increased muscle tone but was *easily consolable*

- Foster mom had been at bedside and felt comfortable taking him home

- He was discharged home after 4 days of observation

*Can infant eat ≥1 ounce per feed or breastfeed well?*
- Yes

*Can infant sleep ≥1 hour?*
- Yes

*Can infant be consoled within 10 minutes?*
- Yes

Infant is considered to be well managed and no further interventions are necessary
MANAGEMENT
Case #3

- CB was born at 37 5/7 weeks to a mother whose pregnancy was complicated by:
  - Late presentation to prenatal care
  - Maternal drug use, maternal tobacco use
  - Maternal hepatitis C exposure
  - Breech presentation
- Mother's delivery urine drug screen positive for cocaine, amphetamine, benzodiazepines and opiates.
Case #3 – Initial Course

- Admitted to the newborn nursery and monitored using ESC
- Formula feeding is advised as mother is positive for multiple drugs

**DAY 1:**
- He is noted to feed well, console easily and sleep well between feedings

**DAY 2:**
- More irritable, requiring constant holding and taking formula in sporadic amounts
- He is sneezing and intermittently jittery
  - Console = NO Feed = NO
  - Modified Finnegan scores is 9 on a few measures
- He is down 7.2% from birth weight

**Now what?**
Can infant eat ≥1 ounce per feed or breastfeed well?

Yes

Can infant sleep ≥1 hour?

No

Nonpharmacologic interventions increased if possible:
- Feeding on demand
- Swaddling and holding
- Low-stimulation environment
- Parental presence

Not improved

Morphine PRN
0.05 mg/kg/dose
Every 3 hours
May be scheduled

No

Can infant be consoled within 10 minutes?

Yes

Infant is considered to be well managed and no further interventions are necessary

No
Nonpharmacologic Care

- **FIRST LINE therapy** in ALL cases
  - Family-centered
  - Decrease stimuli
  - Feed on demand

---

**Nonpharmacologic care of the maternal-infant dyad affected by neonatal abstinence syndrome**

<table>
<thead>
<tr>
<th>Assessment Functioning of the:</th>
<th>With the Goal of:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant</td>
<td>Implementing comforting techniques and environmental modifications that decrease signs of neurobehavioral dysregulation</td>
</tr>
<tr>
<td></td>
<td>Promoting the infant’s self-regulation</td>
</tr>
<tr>
<td></td>
<td>Nurturing healthy development and interactive capabilities</td>
</tr>
<tr>
<td>Mother</td>
<td>Promoting maternal self-regulation</td>
</tr>
<tr>
<td></td>
<td>Encouraging and supporting parenting confidence</td>
</tr>
<tr>
<td></td>
<td>Fostering maternal ability to support her child’s healthy development and to maximize her interactional capacity</td>
</tr>
<tr>
<td>Dyad</td>
<td>Bidirectional communication and dyadic synchrony</td>
</tr>
</tbody>
</table>

Pediatr Clin North Am, 66 (2), 353-367, 2019
Decrease Stimuli

- Promote a quiet, dark and soothing environment
- Cluster care (baby schedule)
  - No disruption when sleeping
- Supportive care (preferably provided by parents/family):
  - Skin-to-skin care
  - The 5 S’s:
    - Shushing
    - Swinging / Head to toe swaying
    - Sucking
    - “C-position” or sideline position
    - Swaddling
  - For babies that are difficult to calm:
    - Vertical rocking (slow and rhythmical)
    - Firm patting or clapping
Decrease Stimuli

• AVOID NICU admission if medically appropriate

• Use of cuddler volunteers
Nonpharmacologic Care

- **Reactivity to sensory stimulation**
  - Touch: gentle, slow
  - Visual: dim environment
  - Sounds: speak quietly
  - Movement: hold, contain
  - Multiple sensitivity swaddling

- **Sleep/Wake control**
  - Assist with transition
  - Gentle handling
  - Appropriate stimulation

- **Motor/Tone**
  - Non-nutritive sucking
  - Containment, holding
  - Swaddling
  - Positioning aides
  - Rocking

- **Autonomic Signs of Stress**
  - Promote rest
  - Adjust environment and stimuli
  - Identify triggers of physiologic signs
  - Understand limits of tolerance
  - Gradual presentation of stimuli
  - Sensitivity to feedback signals
Nutrition

• **Feed on demand**

• **Breastfeeding:**
  – Safe and beneficial to bonding and symptoms management
  – Should be encouraged if:
    • No contraindications
    • Mother adheres to a supervised drug treatment program
    • No active use pattern (including Marijuana)
      – Have tested negative for other drugs
  – Associated with:
    • Less severe withdrawal symptoms that have a later onset
    • Less need for pharmacologic intervention
  – **Very low concentrations of methadone or buprenorphine in breastmilk**
    • Cumulative daily intake of methadone in fully breastfed infants:
      – 0.01-0.15 mg/day during the first 30 days
      – 0.15-0.30 mg/day between 30 and 180 days
  – Lactation support is critical

McQueen, K. and Murphy-Oikonen, J., *NEJM*, 2016
Seminars in Fetal and Neonatal Medicine 24 (2019) 95–104
Nutrition

• Formula feeding:
  – Should not be the default choice
  – Lower lactose containing formula may be helpful

• Weight gain may be an issue
  – Consider high-calorie feeds EARLY
    • Often only required for a short time
    • Typically 2 weeks
  – NG tube for supplementation

McQueen, K. and Murphy-Oikonen, J., *NEJM*, 2016.
Family-Centered

• Neonates should be kept with their mothers whenever possible
  – Promote **rooming-in**
    • With mother or care provider when appropriate
  – Co-regulatory caregiving
    • Dyadic management

• No continuous pulse-ox needed
  – Spot check or continuous if on meds
Family Considerations

- Form a therapeutic alliance with the family:
  - Engaging these mothers and developing a therapeutic alliance is important to improve the infant’s outcomes
  - Recognize this may not always be possible
  - Engage social work to help address needs
Family Considerations

- Practice *compassionate care*:
  - Drug addiction is a disease of the brain, it is not a moral failure
  - Reflect on your personal attitudes toward mothers with SUD
    - Attitudes and stigma have a **PROFOUND effect and are a barrier to recovery**
  - These families need our help, not judgment

1. Mom is medicine
2. Pretend it’s a baby
3. Pretend it’s a mom
Mothers’ Perspectives

- **Hospital environment** is both a source of support and tension for mothers exerting autonomy in the care of their infants.

- Feelings of internal and external **stigma** negatively impact mothers’ self-efficacy:
  - Own feelings of shame led to less confidence
  - Disinterested or judgmental caregivers led to more stress and less confidence

- **Mothers’ histories of abuse and trauma** affect their feeding choice and bonding:
  - Sexual abuse may lead to issues with breastfeeding
  - Prior removal of children may lead to anxiety that this infant will also be taken
  - Mothers’ own recovery makes infant care emotionally and logistically challenging

Mothers’ Perspectives

● Feeding choices and experiences:
  ○ Information drives maternal feeding choices (conflicting information)
  ○ Opioid withdrawal symptoms negatively impact breastfeeding (oromotor dysfunction)

● Having an infant is a source of resilience and provides a sense of purpose for mothers on their path to recovery
  ○ The infant may be the motivation for the mother to continue to strive for recovery
Can infant eat ≥1 ounce per feed or breastfeed well?

Yes

Can infant sleep ≥1 hour?

No

Nonpharmacologic interventions increased if possible:
- Feeding on demand
- Swaddling and holding
- Low-stimulation environment
- Parental presence

Not improved

No

Yes

Can infant be consoled within 10 minutes?

No

Infant is considered to be well managed and no further interventions are necessary

Yes

Morphine PRN
0.05 mg/kg/dose
Every 3 hours
May be scheduled
Pharmacologic Treatment

- Pharmacologic therapy should be initiated
- If using the ESC methodology:
  - If there is a NO response AND Supportive care can no longer be increased
- If using a scoring system, typically:
  - Modified FNAS
    - 3 consecutive scores of 8 or higher
    - 2 consecutive scores of 12 or higher
  - sFNAS
    - Score of 6 or greater x 3 in a 12h period
    - Score of 10 or greater x 2 within an 8h period
Pharmacologic Treatment

- Morphine is preferred
  - Shorter acting than methadone
- Dosing recommendations:
  - Start with PRN dosing
  - 0.05 mg/kg/dose
    - May repeat PRN, no more than Q3h
    - This needs to be a team decision
    - May increase by 0.01 mg/kg/dose Q12h until NAS symptoms are controlled
- If persistently getting “No” to at least one ESC domain:
  - Schedule morphine Q3-6h
  - Max of 0.3 mg/kg/dose
  - Max daily dose 1.2 mg/kg/day
Pharmacologic Treatment

- **Clonidine**
  - Preferred second line agent in opioid-exposed neonates
  - Can also be used first line in non-opioid exposed neonates with withdrawal symptoms
- 1 mcg/kg PO every 6 hours
- Start weaning as soon as possible
## Pharmacologic Treatment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine(^a)</td>
<td>0.05–0.2 mg/kg/dose q3–4 h Max dose 1.3 mg/kg/d Start with PRN dosing</td>
<td>No alcohol</td>
<td>Sedation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Short half-life (9 h)</td>
<td>Apnea</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Constipation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Frequent Dosing</td>
</tr>
<tr>
<td>Methadone</td>
<td>0.05 –0.1/mg/kg/dose q 12 h Max dose 1 mg/kg/d</td>
<td>Long half-life (26 h)</td>
<td>Longer duration of treatment even with shorter</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 hourly doses</td>
<td>hospitalization time</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Associated with shorter hospitalization time</td>
<td>Alcohol 8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>By ~ 2 days</td>
<td>Frequent follow-up needed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Dose 4–5 micrograms/kg/dose q8 h Max dose 60</td>
<td>Sublingual route</td>
<td>Alcohol 30% which is almost as high as tincture</td>
</tr>
<tr>
<td></td>
<td>micrograms/kg/day</td>
<td>Half-life (12 h) which allows levels to be</td>
<td>of opium.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>monitored</td>
<td>Adjuvant medications required</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Shorter duration of treatment and shorter LOS</td>
<td>Limited amount of research available about</td>
</tr>
<tr>
<td></td>
<td></td>
<td>compared to morphine</td>
<td>effectiveness of drug.</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Loading dose 16 mg/kg Maintenance dose 1–4 mg/kg/q12 h</td>
<td>Long half-life (45–100 h)</td>
<td>High treatment failure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Levels can be monitored</td>
<td>Interacts with other drugs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Alcohol content is about 15% which is high for</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>a secondary drug</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sedation</td>
</tr>
<tr>
<td>Clonidine</td>
<td>Initial dose 0.5–1 microgram/kg followed by 0.5–1.25 micrograms/kg per dose q 4–6 h</td>
<td>Non-narcotic antagonist</td>
<td>Hypotension</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No sedation</td>
<td>Abrupt discontinuation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No alcohol</td>
<td>may cause rapid rise of blood pressure and heart rate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Long half-life (44–72 h)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)JAMA Pediatrics 2018; 172(8):741–748.


Linked to worse neurodevelopmental outcomes (RCT, n=116)
Czynski 1 et al, J. Pediatr. Online ahead of print, 2020

Case #3 (continued)

- He was transferred to the General Pediatrics service for further assessment and treatment.
- Mom was able to stay at the bedside and get him to console and sleep.
- However, feeding remained an issue:
  - He was started on prn morphine
  - The caloric density of his feeds was increased
  - Speech was consulted.
- Despite the morphine, he continued to have “No” on his ESC scores.
Case #3 (continued)

- He was started on clonidine thinking his symptoms were benzodiazepine predominant.
- The following day his eating had improved, his weight was up, and he had not required any prn morphine.
- After he was stable for a few days and gaining weight, his clonidine was weaned.
- He went home with his grandmother on day 8 of age and was off of all medications.
- Early Intervention and Developmental Pediatrics follow-up were in place at the time of discharge.
Objectives

- **Scope of the problem**
- **Assessment and management**
  - Signs and symptoms
  - Role of toxicology testing
  - Monitoring
    - EAT, SLEEP, CONSOLE
  - Non pharmacological measures
  - Medications
- **Discharge planning:**
  - Plan for safe care
- **Outpatient follow-up:**
  - Pediatric care
  - Developmental screening
- **Long-term outcomes**
Case #4

- R was 38w4d born to a mother with a pregnancy complicated by chronic Hepatitis C, polysubstance abuse (cocaine, heroin, currently on buprenorphine), DM (poorly controlled). She was also on cyclobenzaprine and buspirone during pregnancy and has a history of tobacco use.

- He was in the NICU for the first 13 days because of respiratory distress and withdrawal symptoms. He was started on methadone, as much as 0.1 mg/kg every 6 hours. He was transferred to the General Pediatric service to continue his methadone wean.

- On DOL #15, clonidine was added to help with withdrawal symptoms.
Case #4

- Throughout his stay, he gained weight on 20 kcal formula.
- His methadone was finally weaned off on DOL#23.
- What are the key elements of discharge planning for this infant?
Discharge Planning

- Establishment of a Safe Care Plan:
  - Begins PRIOR to discharge
    - Ideally begins prior to birth
  - Requires a *multi-disciplinary team* and cross-system collaboration
    - LIPs
    - Bedside nurse
    - Social worker
    - Discharge coordinator
    - Welfare agencies
    - Community agencies
Discharge Planning

Before Birth

• Early engagement the mother
• Opportunities for education on:
  – Expected observation period in the hospital – 4 days MINIMUM
  – Ways to reduce the impact of NAS:
    • Skin-to-skin contact
    • Non-pharmacological interventions
  – Parenting and family support
    • Bonding and healthy attachment
    • Parenting skills
  – Benefits of breastfeeding when appropriate
• Address potential maternal comorbid medical or mental health disorders
Discharge Planning

Before Birth

• In opioid-exposed children at age 5
• A parent–HCP relationship established in pregnancy and continued during the postpartum period:
  – Facilitated a long lasting relationship with childhood professionals
  – ↓ Court-ordered placements reports
  – ↓ Developmental disorders

Discharge Planning

Caregiver Education

• Ensure they know how to:
  – Recognize signs and symptoms of withdrawal
  – Utilize non-pharmacological techniques
  – Recognize and treat diaper rash

• Safe sleep education

• Clearly discuss when evaluation by a HCP is recommended:
  – Trouble eating or sleeping
  – Crying more than expected
  – Loose stools and/or diaper rash
Discharge Planning
Caregiver Education

• Understand need/benefits of home visitations and early intervention services:
  – Educational support:
    • Recognizing withdrawal signs
    • Using non pharmacological techniques
  – Help in creating and maintaining a healthy home environment
  – Parenting skills
Discharge Planning

Healthy Home Environment

• Critical to healthy development
• Discussion points:
  – Home must be secured from safety hazards:
    • Gun safety
    • Child proofing
    • Prescription drugs must be out of reach (preferably stored under lock and key)
  – Food insecurities
  – Violence exposure
  – Partner violence
• Emphasizes modifiable risk factors:
  – Maintaining parental recovery
    • Ongoing engagement of the mother in her treatment and recovery plan is essential to optimize infant outcomes
  – Stable home environment

Discharge Planning

Referrals and Resources

• Plan for routine and acute pediatric care:
  – Includes discussion of transportation plan
  – Referrals to HCPs knowledgeable about NAS
  – Accessible to the family immediately after discharge
• Perinatal home nursing visits
• Early Childhood Intervention referral
• Child Welfare Services if applicable
• Community resources
  – Trauma-informed care services
  – Mentoring resources
Discharge Checklist

Exhibit FS #12.1: Sample Protocol for Discharge and Follow-up Visits*

<table>
<thead>
<tr>
<th>Infant Discharge Checklist</th>
<th>Is Infant Ready for Discharge?†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthcare Professionals Considerations When Determining Infant Discharge Eligibility</td>
<td></td>
</tr>
<tr>
<td>Infant weaned off medication (if applied) and observed for at least 24 hours after weaning, following a hospital protocol.</td>
<td>□</td>
</tr>
<tr>
<td>Infant is successfully feeding.</td>
<td>□</td>
</tr>
<tr>
<td>Caregivers received education about recognition of infant signs of NAS and have the contact information of responsive medical personnel to call with concerns.</td>
<td>□</td>
</tr>
<tr>
<td>Caregivers have received education about techniques to soothe the infant (e.g., dim lights, softly playing white noise, skin-to-skin contact, pacifier, swaddling) and ways to recognize and respond to infant dysregulation.</td>
<td>□</td>
</tr>
<tr>
<td>Caregivers are responding to the infant’s needs in a safe and responsive way.</td>
<td>□</td>
</tr>
<tr>
<td>Caregivers have been educated on the <strong>Safe to Sleep campaign</strong> and the infant has its own place to sleep to reduce the risk of sudden infant death syndrome (SIDS), especially as infants with NAS are at an increased risk for sleep-related deaths.</td>
<td>□</td>
</tr>
<tr>
<td>Caregivers have received education about follow-up plans that include home visits and early pediatric follow-up appointments (within 5 days of discharge).</td>
<td>□</td>
</tr>
</tbody>
</table>

†If all boxes are checked, the infant is ready to be considered for discharge.
Case #4 (continued)

- He was sent home on DOL#25 in the care of maternal grandmother, who also had custody of mom’s other 2 children. He was to continue his clonidine wean at home. Mom was involved but not allowed unsupervised visitation.

- He has had close follow up with his physician and his development has been tracked with the MCHAT.

- At his 2 year well check, he was noted to be developmentally on track. He was still living with his grandmother and his parents were not involved in his care.
Objectives

- **Scope of the problem**
- **Assessment and management:**
  - Signs and symptoms
  - Role of toxicology testing
  - Monitoring
    - **EAT, SLEEP, CONSOLE**
  - Non pharmacological measures
  - Medications
- **Discharge planning:**
  - Plan for safe care
- **Outpatient follow-up:**
  - Pediatric care
  - Developmental screening
- **Long-term outcomes**
Routine Pediatric Health Care

• Early visits
• Assess for the presence of withdrawal symptoms after discharge:
  – Periodic fast breathing
  – Nasal stuffiness/congestion
  – Reflux, spitting up
  – Tremors
  – Crying spells, irritability
  – Mottling
  – Hypertonia

• Overall assessment of functioning:
  – Continue to use the eat, sleep, console method

May last for months
Routine Pediatric Health Care

• Monitor growth and development:
  – Infants with NOWS are at risk for failure to thrive

• Continued education non-pharmacologic techniques:
  – Skin-to-skin
  – Low stimulus environment
  – Calming strategies (the 5 S’s)

• Discuss enrichment activities:
  – Stretches, range of motion
  – Tummy time
Review Feeding Concerns

• Support breastfeeding if applicable (mother in a stable treatment program)
  – Does NOT ↑ the risk for withdrawal if/when mothers stop breastfeeding
  – Little methadone or buprenorphine excreted in breastmilk
  – May ↑ compliance with medication assisted treatment (MAT)

• BUT:
  – Mothers need help after discharge
  – As many as 60% of those who initiate breastfeeding stop after 6 days
Review Feeding Concerns

• Infant with NOWS often experience:
  – Poor feeding coordination and hyperphagia
  – Poor weight gain
  – Feeding intolerance

• Providers report success with formulas containing partially hydrolyzed proteins

• If continued GI distress extensively hydrolyzed formulas may help

• Increase caloric density of formula
Additional Recommendations

• Screen for sensory processing difficulties
• Visual screen at 6 months
• Growing evidence of increased risk of:
  – Strabismus
  – Reduced visual acuity
  – Nystagmus
  – Refractive errors
  – Cerebral visual impairment

Monnelly et al. Dev Med Child Neurol. Epub 2018 Dec 3
WCC visit completion over time.

Be Aware of the Risk of Readmission

• Australian-based population study from 2000-2011
• 3842 infants with NAS compared to 1,018,421 controls
Risk of Readmission

• Infants with NAS were more likely to:
  – At birth:
    • Require admission at birth (OR 15.6; 14.5-16.8)
    • Be in the hospital longer after birth (10 vs. 3 days)
  – In childhood
    • Be rehospitalized (OR 1.6, 1.5-1.7)
    • Die during hospitalization (OR 3.3, 2.1-5.1)
    • Be hospitalized for:
      – Assaults (OR 15.2, 11.3-20.6)
      – Maltreatment (OR 21.0, 14.3-30.9)
      – Poisoning (OR 3.6, 2.6-4.8)
      – Mental/behavioral disorders (OR 2.6, 2.1-3.2)
      – Visual disorders (OR 2.9, 2.5-3.5)
Risk of Readmission

- Mothers of infants with NAS were more likely to:
  - Be Indigenous (OR 6.4, 6.0-7.0),
  - Have no antenatal care (OR 6.6, 5.9-7.4)
  - Be socio-economically deprived (OR 1.6, 1.5-1.7).

- On regression analyses, NAS was the most important predictor of admissions for:
  - Maltreatment (OR 4.5, 3.4-6.1)
  - Mental and behavioral disorders (OR 2.3, 1.9-2.9)
  - Even after accounting for prematurity, maternal age, and Indigenous status
Mean age of admission for specific conditions. *P < .05, **P < .005, ***P < .001.
Recommendations: Developmental Follow-up

• All children should have:
  – Routine developmental screening
  – *Early referral* for specialized assessments if concerns arise (from HCP or caregiver)
  – Receive early intervention services

• Review normal developmental milestones with caregivers
  – So families can better understand the importance of achieving these milestones within a certain timeframe
  – Also helps give families realistic expectations of what the infant should be doing at different developmental stages
## Routine Developmental Screening

<table>
<thead>
<tr>
<th>Measure</th>
<th>Description</th>
<th>Age Range</th>
<th>Format</th>
<th>Time</th>
</tr>
</thead>
</table>
| Ages & Stages Questionnaire®, Third Edition (ASQ-3™) | • Screens infants and young children for developmental delays.  
• 30 questions provide scores on 5 skills: fine motor, gross motor, problem solving, personal—social, and communication. | 1—66 months | Parent or caregiver, teacher, or clinician | 10—20 minutes |
| Developmental Activities Screening Inventory, Second Edition (DASI-II) | • Provides early detection of children with developmental disabilities.  
• 67 questions cover 15 skills including sensory intactness, means-end relationships, and causality to memory, seriation, and reasoning yielding a developmental quotient. | Birth—60 months | Teacher or clinician | 25—30 minutes |
Objectives

- Scope of the problem
- Assessment and management:
  - Signs and symptoms
  - Role of toxicology testing
  - Monitoring
    - EAT, SLEEP, CONSOLE
  - Non pharmacological measures
  - Medications
- Discharge planning:
  - Plan for safe care
- Outpatient follow-up:
  - Pediatric care
  - Developmental screening
- Long-term outcomes
Fig. 1. Factors that may exert programming effects on the developing fetus exposed to opioids in utero. Adapted from Conradt et al. (2018).
Effects of Prenatal Drug Exposures

### TABLE 2 Summary of Effects of Prenatal Drug Exposure

<table>
<thead>
<tr>
<th></th>
<th>Nicotine</th>
<th>Alcohol</th>
<th>Marijuana</th>
<th>Opiates</th>
<th>Cocaine</th>
<th>Methamphetamine</th>
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<tbody>
<tr>
<td><strong>Short-term effects/birth outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Fetal growth</td>
<td>Effect</td>
<td>Strong effect</td>
<td>No effect</td>
<td>Effect</td>
<td>Effect</td>
<td>Effect</td>
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<tr>
<td>Anomalies</td>
<td>No consensus on effect</td>
<td>Strong effect</td>
<td>No effect</td>
<td>No effect</td>
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<tr>
<td>Withdrawal</td>
<td>No effect</td>
<td>No effect</td>
<td>No effect</td>
<td>Strong effect</td>
<td>No effect</td>
<td>No effect *</td>
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<tr>
<td>Neurobehavior</td>
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<td>Effect</td>
<td>Effect</td>
<td>Effect</td>
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<td><strong>Long-term effects</strong></td>
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<tr>
<td>Growth</td>
<td>No consensus on effect</td>
<td>Strong effect</td>
<td>No effect</td>
<td>No effect</td>
<td>No consensus on effect</td>
<td>*</td>
</tr>
<tr>
<td>Behavior</td>
<td>Effect</td>
<td>Strong effect</td>
<td>Effect</td>
<td>Effect</td>
<td>Effect</td>
<td>*</td>
</tr>
<tr>
<td>Cognition</td>
<td>Effect</td>
<td>Strong effect</td>
<td>Effect</td>
<td>Effect</td>
<td>Effect</td>
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<tr>
<td>Language</td>
<td>Effect</td>
<td>Strong effect</td>
<td>Effect</td>
<td>No effect</td>
<td>No consensus on effect</td>
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<tr>
<td>Achievement</td>
<td>Effect</td>
<td>Strong effect</td>
<td>Effect</td>
<td>Effect</td>
<td>Effect</td>
<td>*</td>
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</table>

* Limited or no data available.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Sample Size Exposed/Control*</th>
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<th>Outcomes</th>
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<tr>
<td>Beckwith &amp; Burke, 2015</td>
<td>28</td>
<td>Opiates</td>
<td>Language, motor, cognition</td>
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<td>Chasnoff and colleagues, 1984</td>
<td>58/27</td>
<td>Methadone</td>
<td>Growth</td>
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<td>Gill and colleagues, 2003</td>
<td>49</td>
<td>Opiates</td>
<td>Strabismus</td>
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<tr>
<td>Hamilton and colleagues, 2010</td>
<td>20</td>
<td>Methadone</td>
<td>Ophthalmic abnormalities</td>
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<tr>
<td>Hunt and colleagues, 2008</td>
<td>133/103</td>
<td>Opiates</td>
<td>Neurodevelopmental</td>
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<tr>
<td>Johnson and colleagues, 1984</td>
<td>61/32</td>
<td>Methadone</td>
<td>Neurobehavioral</td>
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<tr>
<td>Kahila and colleagues, 2007</td>
<td>67</td>
<td>Buprenorphine</td>
<td>SIDS</td>
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<tr>
<td>Kaltenbach and colleagues, 1987</td>
<td>105/63</td>
<td>Methadone</td>
<td>Developmental</td>
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<td>McGlone and colleagues, 2014</td>
<td>81/26</td>
<td>Methadone</td>
<td>Nystagmus</td>
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<td>Mulvihill and colleagues, 2007</td>
<td>14</td>
<td>Opiates</td>
<td>Nystagmus</td>
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<td>Ornoy and colleagues, 2001</td>
<td>65/62</td>
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<td>Developmental/cognitive</td>
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<td>Ornoy, 2003</td>
<td>93/87</td>
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<td>Developmental, behavioral</td>
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<td>Rosen &amp; Johnson, 1982</td>
<td>38/23</td>
<td>Methadone</td>
<td>Neurologic, motor, otitis media, vision/behavioral/cognitive</td>
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<tr>
<td>Sandtorv and colleagues, 2009</td>
<td>15</td>
<td>Polysubstances</td>
<td>SIDS</td>
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<tr>
<td>Spiteri Cornish and colleagues, 2013</td>
<td>301/7,887</td>
<td>Polycioids</td>
<td>Nystagmus, strabismus</td>
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<td>Strauss and colleagues, 1976</td>
<td>60/53</td>
<td>Methadone</td>
<td>Behavioral/motor</td>
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<td>Sundelin Wahlsten &amp; Sarman, 2013</td>
<td>28</td>
<td>Buprenorphine</td>
<td>Neurobehavioral/attention</td>
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<td>Wachman and colleagues, 2013†</td>
<td>86</td>
<td>Methadone</td>
<td>Hospital stay</td>
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<tr>
<td>Wachman and colleagues, 2014†</td>
<td>86</td>
<td>Methadone</td>
<td>Gene variation</td>
</tr>
<tr>
<td>Wachman and colleagues, 2015†</td>
<td>86</td>
<td>Methadone</td>
<td>Gene variation</td>
</tr>
<tr>
<td>Wallhovd and colleagues, 2015</td>
<td>23/24</td>
<td>Detoxified opioid and polysubstance</td>
<td>Visual acuity</td>
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<td>Wilson and colleagues, 1979</td>
<td>22/20</td>
<td>Heroin</td>
<td>Growth/cognitive</td>
</tr>
<tr>
<td>Wilson and colleagues, 1981</td>
<td>69/58</td>
<td>Narcotics or methadone</td>
<td>Health, developmental</td>
</tr>
</tbody>
</table>
Impact of NAS on Long-Term Neurocognitive Outcomes

- **Difficult to ascertain**
- *Complex interplay of prenatal and environmental factors*
  - Family characteristics
  - Prenatal care
  - Exposure to multiple substances (alcohol and tobacco)
  - Early childhood experiences
    - Unsafe and unstable home environment
    - Adverse childhood experiences (ACEs)
  - Other health and psychosocial factors

ACOG, 2012; Bandstraet al., 2010; Baldacchino et al., 2014; Nygaard et al., 2015
Impact on Cognitive Function

• Longitudinal study in Norway of:
  – 45 children born to mothers who used heroin ± poly-drugs
  – 48 children without prenatal drug exposure
• Followed up to age 17-21 years

Nygaard et al. Child Neuropsychol 2017; 23:159-87
Impact on Cognitive Function

• Significantly worse:
  – Cognitive function
  – Fine motor function
  – But still within the normal range

Nygaard et al. Child Neuropsychol 2017; 23:159-87
Impact on Cognitive Function

• The big question:
  – Due to heroin-exposure?
  – Or social determinants?
  • Most were in the foster care system by age 1

Adverse impact of:
- Lower birthweight
- Multiple caregivers
- Poly-drug use

Nygaard et al. Child Neuropsychol 2017; 23:159-87
Impact on Mental Health and Behavior

• 23 children of heroin dependent parents
  – Assessed at age 6-17.9 year-old
  – Compared to 152 controls
• Found to have:
  – 8-fold ↑ risk of depression
  – 3-fold ↑ risk of attention disorders
  – 16-fold ↑ risk of SUD in young adulthood
Impact on Behavior

- Increased risk of poor emotional and behavioral function:
  - ↑ Oppositional behavior
  - ↑ Aggressive behavior
  - ↓ Self-esteem and social competence

- In adults, ↑ risk of:
  - Externalizing behaviors
  - Impulsivity and attention problems
But…

• ALL these outcomes can be improved by programs focusing:
  – Fostering resilience in the individual and family
  – Decreasing the dose of trauma exposure

Need for **prospective studies** that adequately control for prenatal exposures, NAS management, and parental socio-demographic factors.
How about Medication Assisted Treatment?

• Data:
  – Methadone > buprenorphine >> naltrexone

• Most studies do not control for confounding factors

• Overall lack of consensus on any neurodevelopmental impact of *in utero* opioid exposure up to age 5 years
How about MAT?

• 96 children whose mothers participated in the MOTHER trial
• At 36 months:
  – No difference between buprenorphine vs. methadone
  – No impact of NAS treatment requirements
• All studied parameters fell within the normal range:
  • Growth
  • Cognitive and language development
  • Sensory processing
  • Temperament
• Data from a randomized double-control trial suggest that prenatal opioid agonist exposure is not deleterious to normal physical and mental development
Committee on Obstetric Practice

• After controlling for confounding factors:
  – Socio-economic status
  – Maternal psychological distress
  – Instability in the home environment
• NO significant difference in cognitive outcomes up to age 5 between children exposed to methadone or buprenorphine and controls
• BUT:
  – Limited data
  – Observational studies
  – Significant concerns remain
2018 Meta-Analysis

- Children born to opioid-dependent mothers prescribed methadone are at risk of neurodevelopmental impairment
  - Lower mental developmental index and psychomotor developmental index scores than unexposed children at age 2
  - Atypical visual evoked potentials
  - Strabismus and nystagmus
- Estimates of impairment may be biased by intermediate to poor quality evidence
2019 Meta-Analysis

• 26 studies
  – 1,455 children exposed to prenatal opioids
  – 2,982 controls
• Prenatal opioid exposure was significantly associated with:
  – Poorer mental and physical development from as early as 6 months
  – Cognitive differences persisted into early childhood with standardized mean differences (95% CI) in test scores of:
    • 0.52 (0.31–0.74) at age 0–2 years
    • 0.38 (0.07–0.69) at ages 2–6 years
    • 0.44 (−0.28–1.16) at ages 6–18 years (not significant at this age)
  – Lower motor scores 0.49 (0.23–0.74) between 2 and 6 years

JAMA Netw Open. 2019 Jul 3;2(7):e197025
Impact on Brain Development?

- Prenatal methadone exposure is associated with microstructural alteration in major white matter tracts at birth.
Impact on Brain Growth?

- Prospective study – Impact on head circumference at birth
  - 429 neonates with NAS
    - 87% born to mother receiving opioid agonist MAT
      - 75% buprenorphine
      - 12% methadone
  - 429 controls

- Results:
  - ↓ in average HC:
    - $33.04 \pm 1.9$ cm vs. $33.99 \pm 2.0$ cm ($p<0.0001$)
  - 30% had HC < 10th percentile
  - Only chronic opioid use was a significant risk factor on multivariate analysis

- Chronic opioid use during pregnancy, sufficient to cause NAS, is associated with smaller HCs at birth
Later Substance Use Disorder Risk

• ↑ risk in children of parents with SUDs
  – Genetic factors:
    • Genetic variability of μ-, δ-, and κ-opioid receptor genes (OPRM1, OPRD1, OPRK1) modulate the efficacy of opioid treatments
    • The same genes that ↑ a person’s risk for problems with alcohol might also ↑ the risk of other SUDs.
    • These same genes might ↑ the risk for psychiatric problems (conduct disorder, adult antisocial behavior)
  – Social factors:
    • Unstable, unsafe home environment

• BUT a stable, healthy home environment ↓ that risk
  – Maintain parental recovery
  – Support a stable home environment

Illustrative Case #5

- RP was born at 40 weeks to a 30 year old mother whose prenatal course was complicated by:
  - Fentanyl and intranasal heroin use (last the day prior to delivery), as well as tobacco use
  - Late prenatal care (33 weeks)
  - Anemia, chlamydia infection, genital warts, depression
  - Mild polyhydramnios
- She was diagnosed with hepatitis C at the time of delivery
- As the mother was showing signs of withdrawal prior to delivery, she received buprenorphine, hydroxyzine, and lorazepam.
- The infant had respiratory distress after delivery and was admitted to the NICU on CPAP
- Umbilical drug screen positive for codeine, morphine, and hydromorphone
Illustrative Case #5

- As the infant was initially in the NICU on CPAP, the sFNAS used:
  - Morphine 0.05 mg/kg PRN was started almost immediately for elevated scores
  - Required scheduled dosing every 3 hour dosing for persistent symptoms
- Because of the multidrug use, the infant was started on 20 kcal formula feeds instead of breastfeeding
- Mom was able to be at the bedside some.
- Social work was consulted and did involve CPS
The infant is not gaining weight. What would be your next step?

Continue current feeding regimen and involve speech

Place an NG tube for supplemental calories

Increase the Kcals in the formula
Illustrative Case #5

• Transferred to the General Pediatrics service on DOL#5, still on morphine 0.05 mg/kg/dose every 3 hours
• Despite that, she was still scoring “no” on ESC so clonidine was added
• By DOL#10, her morphine dose was increased because of worsening symptoms
• DOL#15, the morphine wean was successfully started
• However, on DOL#19 the dose was increased again
• She was finally weaned off all morphine and went home on DOL#32 to wean off clonidine as an outpatient
Illustrative Case #5

• Medical team concerns about the mother:
  – Participation in the baby’s care
  – Inability to reach her at times
  – Prolonged absences from bedside

• Mother’s concerns and comments:
  – Concerns regarding care:
    • Feels there have been inconsistencies with scoring withdrawal symptoms
    • Particularly as it relates to environmental variables
  – Feels ‘judged’ and reported that she doesn't feel she is being treated ‘fairly’
  – Appropriately anxious about discharge and baby’s progress, but she feels they will transition home smoothly and is looking forward to discharge
Illustrative Case #5

- **Social work intervention and recommendations:**
  - Provided space for mother to share her concerns
  - Working with CPS to ensure:
    - Continued support for the family
    - That services are in place to help support her

- **CPS:**
  - Requests that medical providers clearly communicate expectations of mother's presence at bedside
  - Actively working with mother on initiating services
  - Planning to make a home visit same day as discharge

- **Discharge plan:**
  - Patient will go home with mother

"While there are identified risk factors, mother has also identified many strengths surrounding her ability to be forthcoming surrounding substance use and mental health needs, and awareness of seeking support and help to address the above concerns/needs. Mother has identified many family supports and has her own transportation to assist with visiting pt and attending necessary appointments for herself."
Illustrative Case #5

- After discharge, mom was worried about withdrawal symptoms when weaning the clonidine and called her PCP:
  - Told to go back to the previous dose every 6h until her appointment
    - Improvement in stooling but she is still crying a lot
  - Mom feels her symptoms get worse every 5 hours before her dose is due
  - She initially had a diaper rash but it is improved with barrier cream
  - She is eating a little less than in the hospital but still eating well, spits up a lot
    - Mom got gas drops but isn't sure they help.
  - Going in the car or being bounced helps with the crying.
  - She is also not sleeping well:
    - Will sleep in 45 min chunks; will get 7-8 hours sleep total in 24h
    - Easily restless and screaming
  - Mom feels she is overstimulated since being home (lots of visitors)
Illustrative Case #5

• At the PCP:
  – Assessment:
    • 5 week old female with h/o NOWS currently on a clonidine wean here with increased fussiness.
    • Fussy on exam, consolable
    • Eats well and is gaining great weight
  – Plan:
    • Discussed extensively with parents that her dose of clonidine is now exceedingly small (2 mcg/kg/d) and she has no vital sign changes or other symptoms of withdrawal
      – Parents encouraged to resume wean per calendar
    • Discussed colic and the crying curve and encouraged the 5 S's and other soothing techniques.
      – Can try probiotics and continue with gas drops if helpful.
    • Referral placed for home health newborn follow up program to help parents with strategies for comfort as well as monitoring her for other signs of withdrawal.
    • Will follow closely in clinic in 1 week
      – Call sooner with concerns, fever, worse inconsolability or refusal to feed.
Summary

- NOWS cases are rapidly increasing worldwide
- NOWS consists of mostly CNS and GI related signs
  - Onset can be within the first 24h or be delayed for several days
  - Duration is variable depending upon many factors
- Non-pharmacologic interventions are the mainstay of NOWS treatment and should always be optimized prior to consideration of pharmacologic interventions
  - Family centered
  - Decrease stimuli
  - Feed on demand
- Pharmacologic treatment with morphine PRN is indicated as first-line treatment for infant unable to eat, sleep or console
Summary

- Optimal outpatient follow-up of infants with NOWS includes:
  - Pre-hospital discharge planning for acute and routine pediatric care
  - Routine developmental screening
  - Early referral for specialized assessments if concerns arise (from HCP or caregiver)
  - Participation in early intervention services
  - Home nursing visits
Summary

• Exposure to opioids *in utero*:  
  – STRONG effect on short-term outcomes (NOWS)  
  – But NOT conclusively shown to adversely impact neurocognitive development up to age 5 years, when confounders are accounted for  
  – Unlike clear long-term impact of other exposures (particularly alcohol)  

• Because there is a lack of good quality evidence → significant concerns remain  

• Recommendations for neuro-developmental follow-up:  
  – Assess development using screening tools at each visit  
  – Early referral for specialized testing if concerns arise
Thank You

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