Neonatal Abstinence Syndrome: What You Need to Know

Camille Fung, MD
Assistant Professor
Division of Neonatology
University of Utah
Salt Lake City, Utah
February 9, 2018
DISCLOSURES

The content of this presentation does not relate to any product of a commercial entity; therefore, I have no relationships to report.

I will discusses off-label use of medications.
After participating in the presentation, you should have increased knowledge and enhanced competence to...

1. Define the prevalence of neonatal abstinence syndrome (NAS) nationally and locally
2. Define the clinical features of NAS
3. Illustrate management protocols that are in use to manage NAS
Opioid Pain Relievers (OPRs)

- Prescription opioid use is widespread in the U.S.
- Now account for more overdose deaths than cocaine and heroin combined; More deaths than car accidents
- In 2010, enough OPRs were prescribed “to medicate every American adult with a standard pain treatment dose of 5mg of hydrocodone taken every 4 hours for a month”
- Most commonly prescribed short-acting opioids: codeine, hydrocodone, and oxycodone (1/10, 1, 1.5-2x potent than morphine respectively); long-acting opioids are methadone and buprenorphine to stabilize maternal opiate/opioid withdrawal symptoms
- Beware of opioid diversion! This has led to increased use of heroin as people are unable to obtain prescribed opiates/opioids.
Public Health Problem: Opioid Prescription and Deaths in U.S.
Ignored Public Health Problem: Drug Overdose Death Rates Among Women

The rate of overdose deaths has risen rapidly among women, with opioids the biggest killer.

Age-adjusted death rate for drug overdose deaths among women.

SOURCE: Centers for Disease Control and Prevention
The term NAS has been principally used to describe neonatal withdrawal signs/symptoms occurring after in utero exposure to opioids

- Versus neonatal discontinuation syndrome (other prescribed medications like SSRIs, SSNRIIs, benzodiazepines, etc.)
Clinical features of NAS

• Neurologic excitability
  – Hyperactive primitive reflexes
  – Irritability/high pitched cry
  – Sleep/wake disturbance
  – Hypertonia
  – Tremors
  – Seizures

• Gastrointestinal dysfunction
  – Feeding difficulties
  – Uncoordinated sucking and swallowing
  – Vomiting/diarrhea

• Autonomic signs
  – Fever
  – Sweating
  – Nasal stuffiness/Sneezing
  – Mottling
  – Yawning

At increased risk for failure to thrive!
Clinical features of NAS

• Vary due to:
  – Maternal drug history (both illicit, licit, and prescribed)
  – Maternal drug metabolism
  – Net transfer of drug across placenta
  – Placental metabolism
  – Fetal metabolism

  – Difficult to predict which baby will withdraw, for how long, and how severe, and when especially in light of poly-substance abuse!
Onset of NAS symptoms

• Majority start showing signs within 72 hours
  – Range is from minutes to hours after birth to up to 2 weeks
  – Reports of late presentation of withdrawal symptoms not described in detail in literature

• NAS occurs in 55-94% of opioid exposed newborns

• Heroin and short-acting opioids
  – Usually by 24 hours, seldom beyond 48 hours

• Methadone/Buprenorphine
  – 24-72 hours, may be delayed until 5-7 days

Neonatal Abstinence Syndrome and Associated Health Care Expenditures
United States, 2000-2009

Patrick et al. JAMA 2012;307(18):1934-40

• Goal: provide national estimates
  – NAS and its complications
  – Maternal opiate use at time of birth
  – Healthcare utilization patterns of NAS

• Data sources:
  – Hospital billing data (2000-2009)
  – Agency for Healthcare Research and Quality
    • Kids’ Inpatient Database (KID) for newborns
    • Nationwide Inpatient Sample (NIS) for mothers
Neonatal Abstinence Syndrome and Associated Health Care Expenditures
United States, 2000-2009

3-fold increase in NAS during study period
One baby born per hour in the U.S. suffers NAS

Patrick et al. JAMA 2012;307(18):1934-40
Neonatal Abstinence Syndrome and Associated Health Care Expenditures
United States, 2000-2009

Patrick et al. JAMA 2012;307(18):1934-40

Figure 2. Weighted National Estimates of the Rates of Maternal Opiate Use per 1000 Hospital Births per Year

5-fold increase in maternal opiate use
# Neonatal Abstinence Syndrome and Associated Health Care Expenditures

**United States, 2000-2009**

Patrick et al. JAMA 2012;307(18):1934-40

## Table 3. Mean Hospital Charges and Length of Stay for Neonatal Abstinence Syndrome vs All Other US Births

<table>
<thead>
<tr>
<th></th>
<th>Mean (95% CI)</th>
<th>2000</th>
<th>2003</th>
<th>2006</th>
<th>2009</th>
<th>P for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neonatal Abstinence Syndrome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unweighted sample, No.</td>
<td>2820</td>
<td>3761</td>
<td>5200</td>
<td>9674</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of stay, d</td>
<td>15.8 (14.2-17.3)</td>
<td>15.9 (14.5-17.3)</td>
<td>15.3 (14.6-16.0)</td>
<td>16.4 (15.8-17.1)</td>
<td>.06</td>
<td></td>
</tr>
<tr>
<td>Hospital charges, 2009 US $</td>
<td>39,400 (33,400-45,400)</td>
<td>47,900 (40,800-55,100)</td>
<td>44,600 (40,400-48,900)</td>
<td>53,400 (49,000-57,700)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td><strong>All Other US Births</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unweighted sample, No.</td>
<td>784,191</td>
<td>890,582</td>
<td>1,000,203</td>
<td>1,113,123</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of stay, d</td>
<td>3.1 (3.0-3.1)</td>
<td>3.2 (3.1-3.2)</td>
<td>3.2 (3.2-3.3)</td>
<td>3.3 (3.3-3.4)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Hospital charges, 2009 US $</td>
<td>6600 (5800-7300)</td>
<td>7300 (6900-7600)</td>
<td>8200 (7800-8600)</td>
<td>9500 (9000-9900)</td>
<td>&lt;.001</td>
<td></td>
</tr>
</tbody>
</table>

## Hospital charges quadrupled adjusting for inflation!

## Table 4. Proportions of US Hospital Charges for Neonatal Abstinence Syndrome by Payer

<table>
<thead>
<tr>
<th>Year</th>
<th>Unweighted Sample, No.</th>
<th>Medicaid (95% CI)</th>
<th>Private Payer (95% CI)</th>
<th>Self-pay (95% CI)</th>
<th>Other Payer (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>2920</td>
<td>68.7 (63.3-76.7)</td>
<td>18.2 (14.6-22.5)</td>
<td>8.7 (5.6-13.3)</td>
<td>4.4 (2.0-9.3)</td>
</tr>
<tr>
<td>2003</td>
<td>3761</td>
<td>69.9 (65.9-73.6)</td>
<td>19.8 (16.9-23.1)</td>
<td>6.5 (4.5-9.3)</td>
<td>3.8 (1.6-8.7)</td>
</tr>
<tr>
<td>2006</td>
<td>5200</td>
<td>73.7 (70.4-76.7)</td>
<td>19.0 (16.4-22.0)</td>
<td>5.5 (4.4-6.9)</td>
<td>1.9 (1.3-2.8)</td>
</tr>
<tr>
<td>2009</td>
<td>9674</td>
<td>77.6 (74.4-80.4)</td>
<td>17.6 (15.1-20.4)</td>
<td>2.9 (2.4-3.4)</td>
<td>2.0 (1.4-2.9)</td>
</tr>
</tbody>
</table>

*Percentages may not sum to 100 because of rounding.*
Increasing Incidence of the Neonatal Abstinence Syndrome in U.S. Neonatal ICUs

Total % of NICU days nationwide attributed to NAS increased from 0.6% to 4%, with 8 centers reporting >20% of all NICU days attributed to NAS.
National Estimates of NAS
Morbidity and Mortality Weekly Report

Incidence of Neonatal Abstinence Syndrome — 28 States, 1999–2013

Jean Y. Ko, PhD1; Stephen W. Patrick, MD2; Van T. Tong, MPH1; Roshni Patel, MPH1; Jennifer N. Lind, PharmD3; Wanda D. Barfield, MD1

- Of ~30 million births that occurred from 1999-2013 in 28 states, ~75,000 NAS cases = 2.5 cases/1,000 hospital births

- 1.5 cases/1,000 births (1999, 14 states) → 6.0 cases/1,000 births (2013, 21 states) = ↑~300%

- Kentucky, Maine, Vermont, West Virginia had highest NAS incidence (Tennessee, New Hampshire not included)
### National Estimates of NAS

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Arizona</td>
<td>1.3</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.1</td>
<td>1.1</td>
<td>1.1</td>
<td>1.0</td>
<td>1.2</td>
<td>1.5</td>
<td>1.7</td>
<td>2.6</td>
<td>3.6</td>
<td>3.6</td>
<td>3.9</td>
</tr>
<tr>
<td>Arkansas</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0.4</td>
<td>0.9</td>
<td>0.4</td>
<td>0.7</td>
<td>1.0</td>
<td>1.3</td>
<td>1.4</td>
<td>2.2</td>
</tr>
<tr>
<td>California</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0.4</td>
<td>1.0</td>
<td>1.0</td>
<td>1.2</td>
<td>1.2</td>
<td>1.3</td>
<td>1.3</td>
<td>—</td>
</tr>
<tr>
<td>Colorado</td>
<td>0.4</td>
<td>0.6</td>
<td>0.6</td>
<td>0.7</td>
<td>0.6</td>
<td>0.9</td>
<td>0.9</td>
<td>0.9</td>
<td>1.3</td>
<td>1.3</td>
<td>1.3</td>
<td>1.4</td>
<td>2.3</td>
<td>2.5</td>
<td>2.8</td>
</tr>
<tr>
<td>Florida</td>
<td>0.4</td>
<td>0.4</td>
<td>0.5</td>
<td>0.6</td>
<td>0.7</td>
<td>0.9</td>
<td>0.9</td>
<td>1.3</td>
<td>1.7</td>
<td>2.3</td>
<td>3.3</td>
<td>4.9</td>
<td>5.9</td>
<td>5.9</td>
<td>6.3</td>
</tr>
<tr>
<td>Hawaii</td>
<td>—</td>
<td>0.1</td>
<td>0.4</td>
<td>0.1</td>
<td>0.4</td>
<td>0.6</td>
<td>—</td>
<td>0.6</td>
<td>0.5</td>
<td>0.7</td>
<td>0.5</td>
<td>0.7</td>
<td>0.8</td>
<td>0.8</td>
<td>0.7</td>
</tr>
<tr>
<td>Iowa</td>
<td>0.3</td>
<td>0.4</td>
<td>0.3</td>
<td>0.5</td>
<td>0.6</td>
<td>0.4</td>
<td>0.4</td>
<td>0.5</td>
<td>0.6</td>
<td>0.7</td>
<td>0.8</td>
<td>1.1</td>
<td>1.3</td>
<td>1.9</td>
<td>2.2</td>
</tr>
<tr>
<td>Kentucky</td>
<td>—</td>
<td>0.4</td>
<td>0.9</td>
<td>1.3</td>
<td>2.0</td>
<td>2.4</td>
<td>2.5</td>
<td>3.3</td>
<td>3.8</td>
<td>4.7</td>
<td>6.4</td>
<td>7.8</td>
<td>10.5</td>
<td>12.3</td>
<td>15.0</td>
</tr>
<tr>
<td>Maine</td>
<td>1.1</td>
<td>0.9</td>
<td>2.0</td>
<td>3.0</td>
<td>5.2</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>12.6</td>
<td>15.5</td>
<td>19.0</td>
<td>21.5</td>
<td>23.1</td>
<td>30.4</td>
<td>—</td>
</tr>
<tr>
<td>Maryland</td>
<td>7.6</td>
<td>6.5</td>
<td>7.1</td>
<td>6.7</td>
<td>6.3</td>
<td>6.2</td>
<td>6.6</td>
<td>6.6</td>
<td>6.5</td>
<td>7.1</td>
<td>8.2</td>
<td>9.5</td>
<td>10.6</td>
<td>11.4</td>
<td>—</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>2.2</td>
<td>2.5</td>
<td>2.7</td>
<td>2.6</td>
<td>2.9</td>
<td>3.8</td>
<td>4.4</td>
<td>5.0</td>
<td>6.1</td>
<td>6.7</td>
<td>8.5</td>
<td>10.0</td>
<td>10.8</td>
<td>12.5</td>
<td>—</td>
</tr>
<tr>
<td>Michigan</td>
<td>—</td>
<td>0.4</td>
<td>0.5</td>
<td>0.6</td>
<td>0.8</td>
<td>0.9</td>
<td>1.2</td>
<td>1.2</td>
<td>1.7</td>
<td>2.0</td>
<td>2.9</td>
<td>3.6</td>
<td>5.0</td>
<td>5.4</td>
<td>6.7</td>
</tr>
<tr>
<td>Mississippi</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.2</td>
<td>1.3</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Nebraska</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0.2</td>
<td>0.3</td>
<td>0.2</td>
<td>0.7</td>
<td>0.4</td>
<td>0.2</td>
<td>0.4</td>
<td>0.7</td>
<td>1.0</td>
<td>0.8</td>
</tr>
<tr>
<td>Nevada</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.1</td>
<td>0.8</td>
<td>1.3</td>
<td>1.5</td>
<td>1.2</td>
<td>1.3</td>
<td>1.6</td>
<td>2.0</td>
<td>3.0</td>
<td>3.3</td>
</tr>
<tr>
<td>New Jersey</td>
<td>3.3</td>
<td>3.2</td>
<td>3.5</td>
<td>3.0</td>
<td>3.1</td>
<td>2.6</td>
<td>2.9</td>
<td>2.5</td>
<td>2.7</td>
<td>2.8</td>
<td>3.4</td>
<td>4.1</td>
<td>4.6</td>
<td>5.0</td>
<td>5.2</td>
</tr>
<tr>
<td>New Mexico</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>3.7</td>
<td>4.2</td>
<td>5.8</td>
</tr>
<tr>
<td>New York</td>
<td>1.4</td>
<td>1.5</td>
<td>1.3</td>
<td>1.2</td>
<td>1.3</td>
<td>1.2</td>
<td>1.2</td>
<td>1.4</td>
<td>1.5</td>
<td>1.8</td>
<td>1.9</td>
<td>2.6</td>
<td>2.8</td>
<td>3.6</td>
<td>0.1</td>
</tr>
<tr>
<td>North Carolina</td>
<td>—</td>
<td>0.3</td>
<td>0.4</td>
<td>0.7</td>
<td>0.9</td>
<td>1.3</td>
<td>1.3</td>
<td>1.6</td>
<td>1.7</td>
<td>2.7</td>
<td>3.5</td>
<td>4.2</td>
<td>5.3</td>
<td>6.4</td>
<td>0.6</td>
</tr>
<tr>
<td>Oregon</td>
<td>1.0</td>
<td>1.0</td>
<td>1.2</td>
<td>1.5</td>
<td>2.1</td>
<td>2.1</td>
<td>2.0</td>
<td>2.0</td>
<td>2.3</td>
<td>2.9</td>
<td>3.7</td>
<td>4.4</td>
<td>4.5</td>
<td>5.0</td>
<td>0.3</td>
</tr>
<tr>
<td>Rhode Island</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>2.8</td>
<td>3.3</td>
<td>3.5</td>
<td>4.6</td>
<td>3.4</td>
<td>5.1</td>
<td>5.6</td>
<td>6.0</td>
</tr>
<tr>
<td>South Carolina</td>
<td>1.3</td>
<td>0.9</td>
<td>0.6</td>
<td>0.7</td>
<td>1.1</td>
<td>1.1</td>
<td>1.5</td>
<td>1.3</td>
<td>1.5</td>
<td>1.9</td>
<td>2.2</td>
<td>2.7</td>
<td>3.3</td>
<td>3.9</td>
<td>0.2</td>
</tr>
<tr>
<td>South Dakota</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0.7</td>
<td>0.9</td>
<td>0.8</td>
<td>1.0</td>
<td>1.3</td>
<td>1.3</td>
<td>0.8</td>
<td>—</td>
</tr>
<tr>
<td>Utah</td>
<td>—</td>
<td>0.8</td>
<td>0.9</td>
<td>1.3</td>
<td>1.0</td>
<td>1.3</td>
<td>2.0</td>
<td>1.9</td>
<td>2.3</td>
<td>2.5</td>
<td>2.5</td>
<td>3.5</td>
<td>3.4</td>
<td>4.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Vermont</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0.7</td>
<td>2.7</td>
<td>3.7</td>
<td>4.1</td>
<td>8.1</td>
<td>9.1</td>
<td>12.5</td>
<td>15.8</td>
<td>20.9</td>
<td>25.3</td>
<td>26.2</td>
<td>30.5</td>
</tr>
<tr>
<td>Washington</td>
<td>1.5</td>
<td>1.3</td>
<td>1.6</td>
<td>1.7</td>
<td>2.1</td>
<td>2.7</td>
<td>3.5</td>
<td>3.4</td>
<td>3.2</td>
<td>3.6</td>
<td>4.5</td>
<td>5.6</td>
<td>6.7</td>
<td>6.9</td>
<td>7.9</td>
</tr>
<tr>
<td>West Virginia</td>
<td>—</td>
<td>0.5</td>
<td>1.0</td>
<td>1.7</td>
<td>3.3</td>
<td>3.4</td>
<td>6.9</td>
<td>7.1</td>
<td>7.5</td>
<td>10.2</td>
<td>11.0</td>
<td>14.2</td>
<td>16.9</td>
<td>21.7</td>
<td>33.4</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>0.4</td>
<td>0.4</td>
<td>0.3</td>
<td>0.5</td>
<td>0.6</td>
<td>1.1</td>
<td>0.9</td>
<td>1.7</td>
<td>1.9</td>
<td>2.5</td>
<td>2.9</td>
<td>4.1</td>
<td>5.5</td>
<td>5.7</td>
<td>7.9</td>
</tr>
</tbody>
</table>

**Annual change in incidence rate**

- Arizona: 0.2
- Arkansas: 0.3
- California: 0.6
- Colorado: 0.2
- Florida: 0.6
- Hawaii: 0.05
- Iowa: 0.1
- Kentucky: 1.3
- Maine: 3.0
- Maryland: 0.3
- Massachusetts: 0.9
- Michigan: 0.6
- Mississippi: 0.4
- Nebraska: 0.1
- Nevada: 0.4
- New Jersey: 0.1
- New Mexico: 1.5
- New York: 0.1
- North Carolina: 0.6
- Oregon: 0.3
- Rhode Island: 0.5
- South Carolina: 0.2
- South Dakota: 0.8
- Utah: 0.3
- Vermont: 3.6
- Washington: 0.5
- West Virginia: 2.7
- Wisconsin: 0.7
NAS in Utah

Complicated Pregnancies or Births due to a Mother’s Drug Dependence

Figure 1. Number of hospital discharges as a result of complicated pregnancies or births due to a mother’s drug dependence, Utah, 2002–2011

Source: Utah Hospital Discharge Data
NAS in Utah

• Over the past decade, the number of Utah newborns diagnosed with NAS increased ~243% (not including latest numbers)

[Graph showing the number of newborns with NAS from 2002 to 2011]

Latest numbers
2012: 272
2013: 275
2014: 310
Skyrocketing increase in NAS

- Every nursery should:
  - Have a policy for assessing maternal substance abuse
  - Have a standardized plan for the evaluation and management of infants at risk for or showing withdrawal

Drug-Exposed Newborn

- Confirm maternal history (illicit and prescribed drugs, smoking, alcohol)
- Perform drug testing
- Involve social work to assess home safety

Is newborn at risk for developing Neonatal Abstinence Syndrome?

YES-exposure involves opioids

Short-acting opioids (heroin, fentanyl, morphine, hydromorphone, oxymorphone, codeine, hydrocodone, oxycodone, dihydrocodeine, tramadol, propoxyphene)

Start Neonatal Abstinence Scoring
Observe for at least 72 hours

If scores reach threshold for pharmacotherapy, start Morphine

NO-exposure does not involve opioids

Long-acting opioids (levorphanol, methadone, buprenorphine, any controlled-release or extended release will prolong half-lives of opioids)

Start Neonatal Abstinence Scoring
Observe for at least 96 hours

Stimulants (cocaine, methamphetamine), SSRIs/SSNRIs, and Benzodiazepines can cause discontinuation signs of CNS irritability but rarely require pharmacotherapy

Provide non-pharmacologic care
Developmental follow-up in the medical home
Drug-Exposed Newborn

- Confirm maternal history (illicit and prescribed drugs, smoking, alcohol)

Is newborn at risk for developing Neonatal Abstinence Syndrome?

YES-exposure involves opioids

Short-acting opioids (heroin, fentanyl, morphine, hydromorphone, oxymorphone, codeine, hydrocodone, oxycodone, dihydrocodeine, tramadol, propoxyphene)

Start Neonatal Abstinence Scoring
Observe for at least 72 hours

Start Neonatal Abstinence Scoring
Observe for at least 72 hours

If scores reach threshold for pharmacotherapy, start Morphine

NO-exposure does not involve opioids

Long-acting opioids (levorphanol, methadone, buprenorphine, any controlled-release or extended release will prolong half-lives of opioids)

Start Neonatal Abstinence Scoring
Observe for at least 96 hours

If scores reach threshold for pharmacotherapy, start Morphine

Stimulants (cocaine, methamphetamine), SSRIs/SSNRIs, and Benzodiazepines can cause discontinuation signs of CNS irritability but rarely require pharmacotherapy

Provide non-pharmacologic care
Developmental follow-up in the medical home
Maternal History (5 “P”s)

Parents
Did your parents have problems with alcohol or other drug use?

Peers
Do any of your friends have problems with alcohol or other drug use?

Partner
Does your partner have problems with alcohol or other drug use?

Past
In the past, have you had difficulties in your life due to alcohol or other drugs, including prescription medications

Present
In the past month, have you drunk any alcohol or used other drugs?

Maternal History High Risk Characteristics

No prenatal care  
Previous unexplained fetal demise  
Precipitous labor  
Abruptio placentae  
Hypertensive episodes  
Severe mood swings  
Cerebrovascular accidents/stroke  
Myocardial infarction  
Unexplained repeated spontaneous abortions
Neonatal History
High Risk Characteristics

- Unexplained seizures or apneic spells
- Unexplained symmetric intrauterine growth restriction
- Atypical vascular incidents such as stroke
- Myocardial infarction
- Unexplained NEC
- Signs of neonatal abstinence syndrome
Drug-Exposed Newborn

- Perform drug testing

Is newborn at risk for developing Neonatal Abstinence Syndrome?

YES-exposure involves opioids

Short-acting opioids (heroin, fentanyl, morphine, hydromorphone, oxymorphone, codeine, hydrocodone, oxycodone, dihydrocodeine, tramadol, propoxyphene)

Start Neonatal Abstinence Scoring
Observe for at least 72 hours

Long-acting opioids (levorphanol, methadone, buprenorphine, any controlled-release or extended release will prolong half-lives of opioids)

Start Neonatal Abstinence Scoring
Observe for at least 96 hours

If scores reach threshold for pharmacotherapy, start Morphine

NO-exposure does not involve opioids

Stimulants (cocaine, methamphetamine), SSRIs/SSNRIs, and Benzodiazepines can cause discontinuation signs of CNS irritability but rarely require pharmacotherapy

Provide non-pharmacologic care
Developmental follow-up in the medical home
Determining drug exposure

Maternal or neonatal urine
Only reflects ~ 72 hours of exposure
Meconium

• Newborn’s first stool
  – Reflects drug-exposure from 12-18 weeks gestation onward
  – Collection can be challenging/missed especially with unknown exposure history
  – Delayed passage in preterm infants
Umbilical cord

Reflects use from ~12 weeks gestation onward
Shown to be similar to meconium in sensitivity
Easier to collect
Qualitatively detects nearly 60 drugs/drug metabolites in cord tissue (ARUP Laboratories, Salt Lake City, UT; no further confirmatory testing needed)
Turnaround time in 1-3 days

Drug-Exposed Newborn

- **Involve social work to assess home safety**

Is newborn at risk for developing Neonatal Abstinence Syndrome?

YES-exposure involves opioids

NO-exposure does not involve opioids

**Short-acting opioids**
(heroin, fentanyl, morphine, hydromorphone, oxymorphone, codeine, hydrocodone, oxycodone, dihydrocodeine, tramadol, propoxyphene)

Start Neonatal Abstinence Scoring
Observe for at least 72 hours

If scores reach threshold for pharmacotherapy, start Morphine

**Long-acting opioids**
(levorphanol, methadone, buprenorphine, any controlled-release or extended release will prolong half-lives of opioids)

Start Neonatal Abstinence Scoring
Observe for at least 96 hours

Provide non-pharmacologic care
Developmental follow-up in the medical home

**Stimulants (cocaine, methamphetamine), SSRIs/SSNRIs, and Benzodiazepines can cause discontinuation signs of CNS irritability but rarely require pharmacotherapy**
Drug-Exposed Newborn

• Confirm maternal history (illicit and prescribed drugs, smoking, alcohol)
• Perform drug testing
• Involve social work to assess home safety

Is newborn at risk for developing Neonatal Abstinence Syndrome?

YES-exposure involves opioids

Short-acting opioids
(heroin, fentanyl, morphine, hydromorphone, oxymorphone, codeine, hydrocodone, oxycodone, dihydrocodeine, tramadol, propoxyphene)

Start Neonatal Abstinence Scoring
Observe for at least 72 hours

If scores reach threshold for pharmacotherapy, start Morphine

NO-exposure does not involve opioids

Long-acting opioids
(levorphanol, methadone, buprenorphine, any controlled-release or extended release will prolong half-lives of opioids)

Start Neonatal Abstinence Scoring
Observe for at least 96 hours

If scores reach threshold for pharmacotherapy, start Morphine

Stimulants (cocaine, methamphetamine), SSRIs/SSNRIs, and Benzodiazepines can cause discontinuation signs of CNS irritability but rarely require pharmacotherapy

Provide non-pharmacologic care
Developmental follow-up in the medical home
Non-Pharmacologic Treatment

Swaddling with soft blankets
Quiet, dark environment
Frequent small feedings of hypercaloric formula (controversial)
Try a pacifier
Kangaroo care
Organize care to minimize handling
Swings – helpful for some
Determine level of stimulation infant can tolerate

Non-Pharmacologic Treatment

Parent teaching

- Explain how withdrawal is affecting the infant’s ability to cope with stimulation
- Explain how to decrease stimulation
- Help parents find out how much the infant will tolerate
Drug-Exposed Newborn

- Confirm maternal history (illicit and prescribed drugs, smoking, alcohol)
- Perform drug testing
- Involve social work to assess home safety

Is newborn at risk for developing Neonatal Abstinence Syndrome?

**YES**-exposure involves opioids

- Short-acting opioids (heroin, fentanyl, morphine, hydromorphone, oxymorphone, codeine, hydrocodone, oxycodone, dihydrocodeine, tramadol, propoxyphene)
  - Start Neonatal Abstinence Scoring
  - Observe for at least 72 hours
  - If scores reach threshold for pharmacotherapy, start Morphine

- Long-acting opioids (levorphanol, methadone, buprenorphine, any controlled-release or extended release will prolong half-lives of opioids)
  - Start Neonatal Abstinence Scoring
  - Observe for at least 96 hours
  - If scores reach threshold for pharmacotherapy, start Morphine

**NO**-exposure does not involve opioids

- Marijuana
  - **Stimulants (cocaine, methamphetamine), SSRIs/SSNRIs, and Benzodiazepines** can cause discontinuation signs of CNS irritability but rarely require pharmacotherapy
  - Provide non-pharmacologic care
  - Developmental follow-up in the medical home

Marijuana

The University of Utah
Division of Neonatology
Drug-Exposed Newborn

- Confirm maternal history (illicit and prescribed drugs, smoking, alcohol)
- Perform drug testing
- Involve social work to assess home safety

Is newborn at risk for developing Neonatal Abstinence Syndrome?

YES-exposure involves opioids

- Short-acting opioids (heroin, fentanyl, morphine, hydromorphone, oxymorphone, codeine, hydrocodone, oxycodone, dihydrocodeine, tramadol, propoxyphene)
  - Start Neonatal Abstinence Scoring
  - Observe for at least 72 hours
  - If scores reach threshold for pharmacotherapy, start Morphine

NO-exposure does not involve opioids

- Long-acting opioids (levorphanol, methadone, buprenorphine, any controlled-release or extended release will prolong half-lives of opioids)
  - Start Neonatal Abstinence Scoring
  - Observe for at least 96 hours

- Stimulants (cocaine, methamphetamine), SSRIs/SSNRIs, and Benzodiazepines can cause discontinuation signs of CNS irritability but rarely require pharmacotherapy
  - Provide non-pharmacologic care
  - Developmental follow-up in the medical home
Drug-Exposed Newborn

- Confirm maternal history (illicit and prescribed drugs, smoking, alcohol)
- Perform drug testing
- Involve social work to assess home safety

Is newborn at risk for developing Neonatal Abstinence Syndrome?

YES-exposure involves opioids

- Short-acting opioids (heroin, fentanyl, morphine, hydromorphone, oxymorphone, codeine, hydrocodone, oxycodone, dihydrocodeine, tramadol, propoxyphene)
  - Start Neonatal Abstinence Scoring
  - Observe for at least 72 hours
  - If scores reach threshold for pharmacotherapy, start Morphine

NO-exposure does not involve opioids

- Long-acting opioids (levorphanol, methadone, buprenorphine, any controlled-release or extended release will prolong half-lives of opioids)
  - Start Neonatal Abstinence Scoring
  - Observe for at least 96 hours

- Stimulants (cocaine, methamphetamine), SSRIs/SSNRIs, and Benzodiazepines can cause discontinuation signs of CNS irritability but rarely require pharmacotherapy
  - Provide non-pharmacologic care
  - Developmental follow-up in the medical home
Drug-Exposed Newborn

- Confirm maternal history (illicit and prescribed drugs, smoking, alcohol)
- Perform drug testing
- Involve social work to assess home safety

Is newborn at risk for developing Neonatal Abstinence Syndrome?

YES-exposure involves opioids

Short-acting opioids (heroin, fentanyl, morphine, hydromorphone, oxymorphone, codeine, hydrocodone, oxycodone, dihydrocodeine, tramadol, propoxyphene)

Start Neonatal Abstinence Scoring
Observe for at least 72 hours

If scores reach threshold for pharmacotherapy, start Morphine

NO-exposure does not involve opioids

Long-acting opioids (levorphanol, methadone, buprenorphine, any controlled-release or extended release will prolong half-lives of opioids)

Start Neonatal Abstinence Scoring
Observe for at least 96 hours

Stimulants (cocaine, methamphetamine), SSRIs/SSNRIs, and Benzodiazepines can cause discontinuation signs of CNS irritability but rarely require pharmacotherapy

Provide non-pharmacologic care
Developmental follow-up in the medical home
Length of observation

- 5 days of observation detected over 95% of newborns with NAS requiring pharmacotherapy

Behavioral scoring systems

Neonatal Abstinence Scoring System
  Finnegan, 1975 (gold standard)
Neonatal Drug Withdrawal Scoring System
  Lipsitz, 1975
Neonatal Withdrawal Inventory
  Zahorodny, 1998
## FINNEGAN NEONATAL ABSTINENCE SCORE

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Score</th>
<th>AM</th>
<th>PM</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excessive High Pitched Cry</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous High Pitched Cry</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleeps &lt; 1 Hour After Feeding</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleeps &lt; 2 Hours After Feeding</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleeps &lt; 3 Hours After Feeding</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperactive Moro Reflex</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Markedly Hyperactive Moro Reflex</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild Tremors Disturbed</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate-Severe Tremors Disturbed</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild Tremors Undisturbed</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate-Severe Tremors Undisturbed</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased Muscle Tone</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excoriation (Specify Area:__________)</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myoclonic Jerks</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generalized Convulsions</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweating</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever &lt; 38.3</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever &gt; 38.3</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequent Yawning</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mottling</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal Stuffiness</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sneezing</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal Flaring</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory Rate &gt; 60/min</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory Rate &gt; 60 with retractions</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excessive Sucking</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor Feeding</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regurgitation</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Projectile Vomiting</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loose Stools</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Watery Stools</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTAL SCORE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INITIALS OF SCORER</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signs</td>
<td>Score</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>----------------</td>
<td>--------------------------------</td>
<td>----------------------------------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td>Tremors (muscle activity of limbs)</td>
<td>Normal</td>
<td>Minimally increased when hungry or disturbed</td>
<td>Moderate or marked increased when undisturbed—subside when fed or held snugly</td>
<td>Marked increase or continuous even when undisturbed, going on to seizure-like movements</td>
</tr>
<tr>
<td>Irritability (excessive crying)</td>
<td>None</td>
<td>Slightly increased</td>
<td>Moderate to severe when disturbed or hungry</td>
<td>Marked even when undisturbed</td>
</tr>
<tr>
<td>Reflexes</td>
<td>Normal</td>
<td>Increased</td>
<td>Markedly increased</td>
<td></td>
</tr>
<tr>
<td>Stools</td>
<td>Normal</td>
<td>Explosive, but normal frequency</td>
<td>Explosive, more than 8 per day</td>
<td></td>
</tr>
<tr>
<td>Muscle tone</td>
<td>Normal</td>
<td>Increased</td>
<td>Rigidity</td>
<td></td>
</tr>
<tr>
<td>Skin abrasions</td>
<td>No</td>
<td>Redness of knees and elbows</td>
<td>Skin breakdown</td>
<td></td>
</tr>
<tr>
<td>Respiratory rate/min</td>
<td>&lt; 55</td>
<td>55-75</td>
<td>&gt;76</td>
<td></td>
</tr>
<tr>
<td>Repetitive sneezing</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Repetitive yawning</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>No</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Neonatal Withdrawal Inventory NWI
(adopted by IHC and UUHC, Utah)

<table>
<thead>
<tr>
<th>PRE-Stimulus Observation</th>
<th>Stimulus Observation</th>
<th>POST-Stimulus Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 minute of observation prior to touching infant</td>
<td>Scoring during provision of cares, diaper change, feeding, comfort measures</td>
<td>1 minute of observation after cares and comfort measures completed</td>
</tr>
<tr>
<td>• Record respiratory rate</td>
<td>• Record axillary temp (°C)</td>
<td>• Irritability (1 pt)</td>
</tr>
<tr>
<td>• Tremors when undisturbed (4 pts)</td>
<td>• Tremors when disturbed (3 pts)</td>
<td>• Crying or fist-sucking (2 pts)</td>
</tr>
<tr>
<td></td>
<td>• Assessment of tone</td>
<td>• Signs of fresh excoriation of limbs (3 pts)</td>
</tr>
<tr>
<td></td>
<td>• Hyperactive Moro reflex (2 pts)</td>
<td>• Continuous crying (4 pts)</td>
</tr>
<tr>
<td></td>
<td>• Hypertonicity (2 pts)</td>
<td></td>
</tr>
</tbody>
</table>
Neonatal Withdrawal Inventory

• 11-item scoring (maximum 19 points)
• Shown to have better inter-rater reliability compared to Finnegan scoring

• Reportable scores:
• Scores 5-7
  – Reinforce non-pharmacologic care
• Scores ≥8
  – Initiate pharmacologic treatment
Drug-Exposed Newborn

- Confirm maternal history (illicit and prescribed drugs, smoking, alcohol)
- Perform drug testing
- Involve social work to assess home safety

Is newborn at risk for developing Neonatal Abstinence Syndrome?

YES-exposure involves opioids

Short-acting opioids (heroin, fentanyl, morphine, hydromorphone, oxymorphone, codeine, hydrocodone, oxycodone, dihydrocodeine, tramadol, propoxyphene)

Start Neonatal Abstinence Scoring
Observe for at least 72 hours

If scores reach threshold for pharmacotherapy, start Morphine

NO-exposure does not involve opioids

Long-acting opioids (levorphanol, methadone, buprenorphine, any controlled-release or extended release will prolong half-lives of opioids)

Start Neonatal Abstinence Scoring
Observe for at least 96 hours

Stimulants (cocaine, methamphetamine), SSRIs/SSNRIs, and Benzodiazepines can cause discontinuation signs of CNS irritability but rarely require pharmacotherapy

Provide non-pharmacologic care
Developmental follow-up in the medical home

Short-acting opioids

Long-acting opioids
NAS Treatment

Goals:

Relieve symptoms that are interfering with:

Physiologic stability
Feeding/Weight gain
Sleep
Ability to be consoled

Improve mother-infant interactions/bonding
Rooming In with Mother

• Evidence that it can shorten the length of stay and reduce need for pharmacotherapy
  – Canada
  – Germany

Saiki et al., Eur J Peds 2010; 169: 95-98
Hunseler et al., Klin Ped 2013; 225:247-251
Pharmacologic Treatment

Pharmacologic Intervention

Factors to consider

- Opiates only vs polysubstance exposure?
- Presenting with primarily CNS symptoms?
- Presenting with primarily GI symptoms?
Pharmacologic Treatment: **Morphine**

Morphine solution (follow dosing schedule)
- Wean if 2 consecutive scores ≤7 without GI symptoms
- If weaned according to protocol, take 8 days to complete treatment

**Goal is to allow infant to eat, sleep, and gain weight**
# Morphine IV Weaning Schedule

<table>
<thead>
<tr>
<th>Wt (g)</th>
<th>Level 1</th>
<th>Level 2</th>
<th>Level 3</th>
<th>Level 4</th>
<th>Level 5</th>
<th>Level 6</th>
<th>Level 7</th>
<th>Level 8</th>
<th>Level 9</th>
<th>Level 10</th>
<th>Level 11</th>
<th>Level 12</th>
<th>Level 13</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.05mg/kg</td>
<td>0.045mg/kg</td>
<td>0.04mg/kg</td>
<td>0.035mg/kg</td>
<td>0.03mg/kg</td>
<td>0.025mg/kg</td>
<td>0.02mg/kg</td>
<td>0.015mg/kg</td>
<td>0.01mg/kg</td>
<td>0.01mg/kg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>600</td>
<td>0.03 mg</td>
<td>0.03 mg</td>
<td>0.02 mg</td>
<td>0.02 mg</td>
<td>po only</td>
<td>po only</td>
<td>po only</td>
<td>po only</td>
<td>po only</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>800</td>
<td>0.04 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td>0.02 mg</td>
<td>po only</td>
<td>po only</td>
<td>po only</td>
<td>po only</td>
<td>po only</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1000</td>
<td>0.05 mg</td>
<td>0.05 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td>0.02 mg</td>
<td>po only</td>
<td>po only</td>
<td>po only</td>
<td>po only</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1200</td>
<td>0.06 mg</td>
<td>0.05 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td>0.02 mg</td>
<td>po only</td>
<td>po only</td>
<td>po only</td>
<td>po only</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1400</td>
<td>0.07 mg</td>
<td>0.06 mg</td>
<td>0.05 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td>0.02 mg</td>
<td>po only</td>
<td>po only</td>
<td>po only</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1600</td>
<td>0.08 mg</td>
<td>0.07 mg</td>
<td>0.06 mg</td>
<td>0.05 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td>0.02 mg</td>
<td>po only</td>
<td>po only</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1800</td>
<td>0.09 mg</td>
<td>0.08 mg</td>
<td>0.07 mg</td>
<td>0.06 mg</td>
<td>0.05 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td>0.02 mg</td>
<td>po only</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>0.1 mg</td>
<td>0.09 mg</td>
<td>0.08 mg</td>
<td>0.07 mg</td>
<td>0.06 mg</td>
<td>0.05 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td>0.02 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2200</td>
<td>0.11 mg</td>
<td>0.1 mg</td>
<td>0.09 mg</td>
<td>0.08 mg</td>
<td>0.07 mg</td>
<td>0.06 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td>0.02 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2400</td>
<td>0.12 mg</td>
<td>0.11 mg</td>
<td>0.1 mg</td>
<td>0.08 mg</td>
<td>0.07 mg</td>
<td>0.06 mg</td>
<td>0.05 mg</td>
<td>0.04 mg</td>
<td>0.02 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2600</td>
<td>0.13 mg</td>
<td>0.12 mg</td>
<td>0.1 mg</td>
<td>0.09 mg</td>
<td>0.08 mg</td>
<td>0.07 mg</td>
<td>0.05 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2800</td>
<td>0.14 mg</td>
<td>0.13 mg</td>
<td>0.11 mg</td>
<td>0.1 mg</td>
<td>0.08 mg</td>
<td>0.07 mg</td>
<td>0.06 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3000</td>
<td>0.15 mg</td>
<td>0.14 mg</td>
<td>0.12 mg</td>
<td>0.11 mg</td>
<td>0.09 mg</td>
<td>0.08 mg</td>
<td>0.06 mg</td>
<td>0.05 mg</td>
<td>0.03 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3200</td>
<td>0.16 mg</td>
<td>0.14 mg</td>
<td>0.13 mg</td>
<td>0.11 mg</td>
<td>0.1 mg</td>
<td>0.08 mg</td>
<td>0.06 mg</td>
<td>0.05 mg</td>
<td>0.03 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3400</td>
<td>0.17 mg</td>
<td>0.15 mg</td>
<td>0.14 mg</td>
<td>0.12 mg</td>
<td>0.1 mg</td>
<td>0.09 mg</td>
<td>0.07 mg</td>
<td>0.05 mg</td>
<td>0.03 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3600</td>
<td>0.18 mg</td>
<td>0.16 mg</td>
<td>0.14 mg</td>
<td>0.13 mg</td>
<td>0.11 mg</td>
<td>0.09 mg</td>
<td>0.07 mg</td>
<td>0.05 mg</td>
<td>0.03 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3800</td>
<td>0.19 mg</td>
<td>0.17 mg</td>
<td>0.15 mg</td>
<td>0.13 mg</td>
<td>0.11 mg</td>
<td>0.1 mg</td>
<td>0.08 mg</td>
<td>0.06 mg</td>
<td>0.04 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4000</td>
<td>0.2 mg</td>
<td>0.18 mg</td>
<td>0.16 mg</td>
<td>0.14 mg</td>
<td>0.12 mg</td>
<td>0.1 mg</td>
<td>0.09 mg</td>
<td>0.07 mg</td>
<td>0.05 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4200</td>
<td>0.21 mg</td>
<td>0.19 mg</td>
<td>0.17 mg</td>
<td>0.15 mg</td>
<td>0.13 mg</td>
<td>0.11 mg</td>
<td>0.08 mg</td>
<td>0.06 mg</td>
<td>0.04 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4400</td>
<td>0.22 mg</td>
<td>0.2 mg</td>
<td>0.18 mg</td>
<td>0.15 mg</td>
<td>0.13 mg</td>
<td>0.11 mg</td>
<td>0.09 mg</td>
<td>0.07 mg</td>
<td>0.04 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4600</td>
<td>0.23 mg</td>
<td>0.21 mg</td>
<td>0.18 mg</td>
<td>0.16 mg</td>
<td>0.14 mg</td>
<td>0.12 mg</td>
<td>0.09 mg</td>
<td>0.07 mg</td>
<td>0.05 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4800</td>
<td>0.24 mg</td>
<td>0.22 mg</td>
<td>0.19 mg</td>
<td>0.17 mg</td>
<td>0.14 mg</td>
<td>0.12 mg</td>
<td>0.1 mg</td>
<td>0.07 mg</td>
<td>0.05 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5000</td>
<td>0.25 mg</td>
<td>0.23 mg</td>
<td>0.2 mg</td>
<td>0.18 mg</td>
<td>0.15 mg</td>
<td>0.13 mg</td>
<td>0.1 mg</td>
<td>0.08 mg</td>
<td>0.05 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Morphine PO Weaning Schedule

<table>
<thead>
<tr>
<th>Wt (g)</th>
<th>Level 1</th>
<th>Level 2</th>
<th>Level 3</th>
<th>Level 4</th>
<th>Level 5</th>
<th>Level 6</th>
<th>Level 7</th>
<th>Level 8</th>
<th>Level 9</th>
<th>Level 10</th>
<th>Level 11</th>
<th>Level 12</th>
<th>Level 13</th>
</tr>
</thead>
<tbody>
<tr>
<td>600</td>
<td>0.05 mg</td>
<td>0.04 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td>0.03 mg</td>
<td>0.02 mg</td>
<td>0.02 mg</td>
<td>0.01 mg</td>
<td>0.01 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>800</td>
<td>0.06 mg</td>
<td>0.05 mg</td>
<td>0.05 mg</td>
<td>0.04 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td>0.02 mg</td>
<td>0.02 mg</td>
<td>0.01 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1000</td>
<td>0.08 mg</td>
<td>0.07 mg</td>
<td>0.06 mg</td>
<td>0.05 mg</td>
<td>0.05 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td>0.02 mg</td>
<td>0.02 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1200</td>
<td>0.09 mg</td>
<td>0.08 mg</td>
<td>0.07 mg</td>
<td>0.06 mg</td>
<td>0.05 mg</td>
<td>0.04 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td>0.02 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1400</td>
<td>0.11 mg</td>
<td>0.09 mg</td>
<td>0.08 mg</td>
<td>0.07 mg</td>
<td>0.06 mg</td>
<td>0.05 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td>0.02 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1600</td>
<td>0.12 mg</td>
<td>0.11 mg</td>
<td>0.10 mg</td>
<td>0.08 mg</td>
<td>0.07 mg</td>
<td>0.06 mg</td>
<td>0.05 mg</td>
<td>0.04 mg</td>
<td>0.02 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1800</td>
<td>0.14 mg</td>
<td>0.12 mg</td>
<td>0.11 mg</td>
<td>0.10 mg</td>
<td>0.08 mg</td>
<td>0.07 mg</td>
<td>0.05 mg</td>
<td>0.04 mg</td>
<td>0.03 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>0.15 mg</td>
<td>0.13 mg</td>
<td>0.12 mg</td>
<td>0.11 mg</td>
<td>0.09 mg</td>
<td>0.07 mg</td>
<td>0.06 mg</td>
<td>0.05 mg</td>
<td>0.03 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2200</td>
<td>0.17 mg</td>
<td>0.15 mg</td>
<td>0.13 mg</td>
<td>0.12 mg</td>
<td>0.10 mg</td>
<td>0.08 mg</td>
<td>0.07 mg</td>
<td>0.05 mg</td>
<td>0.03 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2400</td>
<td>0.18 mg</td>
<td>0.16 mg</td>
<td>0.14 mg</td>
<td>0.13 mg</td>
<td>0.11 mg</td>
<td>0.09 mg</td>
<td>0.07 mg</td>
<td>0.06 mg</td>
<td>0.04 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2600</td>
<td>0.20 mg</td>
<td>0.17 mg</td>
<td>0.16 mg</td>
<td>0.14 mg</td>
<td>0.12 mg</td>
<td>0.10 mg</td>
<td>0.08 mg</td>
<td>0.06 mg</td>
<td>0.04 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2800</td>
<td>0.21 mg</td>
<td>0.19 mg</td>
<td>0.17 mg</td>
<td>0.15 mg</td>
<td>0.13 mg</td>
<td>0.10 mg</td>
<td>0.08 mg</td>
<td>0.06 mg</td>
<td>0.04 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3000</td>
<td>0.23 mg</td>
<td>0.20 mg</td>
<td>0.18 mg</td>
<td>0.16 mg</td>
<td>0.14 mg</td>
<td>0.11 mg</td>
<td>0.09 mg</td>
<td>0.07 mg</td>
<td>0.05 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3200</td>
<td>0.24 mg</td>
<td>0.21 mg</td>
<td>0.19 mg</td>
<td>0.17 mg</td>
<td>0.14 mg</td>
<td>0.12 mg</td>
<td>0.10 mg</td>
<td>0.08 mg</td>
<td>0.05 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3400</td>
<td>0.26 mg</td>
<td>0.23 mg</td>
<td>0.20 mg</td>
<td>0.18 mg</td>
<td>0.15 mg</td>
<td>0.13 mg</td>
<td>0.10 mg</td>
<td>0.08 mg</td>
<td>0.05 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3600</td>
<td>0.27 mg</td>
<td>0.24 mg</td>
<td>0.22 mg</td>
<td>0.19 mg</td>
<td>0.16 mg</td>
<td>0.13 mg</td>
<td>0.11 mg</td>
<td>0.08 mg</td>
<td>0.05 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3800</td>
<td>0.29 mg</td>
<td>0.25 mg</td>
<td>0.23 mg</td>
<td>0.20 mg</td>
<td>0.17 mg</td>
<td>0.14 mg</td>
<td>0.11 mg</td>
<td>0.09 mg</td>
<td>0.06 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4000</td>
<td>0.30 mg</td>
<td>0.27 mg</td>
<td>0.24 mg</td>
<td>0.21 mg</td>
<td>0.18 mg</td>
<td>0.15 mg</td>
<td>0.12 mg</td>
<td>0.09 mg</td>
<td>0.06 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4200</td>
<td>0.32 mg</td>
<td>0.28 mg</td>
<td>0.25 mg</td>
<td>0.22 mg</td>
<td>0.19 mg</td>
<td>0.16 mg</td>
<td>0.13 mg</td>
<td>0.10 mg</td>
<td>0.06 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4400</td>
<td>0.33 mg</td>
<td>0.29 mg</td>
<td>0.26 mg</td>
<td>0.23 mg</td>
<td>0.20 mg</td>
<td>0.16 mg</td>
<td>0.13 mg</td>
<td>0.10 mg</td>
<td>0.07 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4600</td>
<td>0.35 mg</td>
<td>0.31 mg</td>
<td>0.28 mg</td>
<td>0.24 mg</td>
<td>0.21 mg</td>
<td>0.17 mg</td>
<td>0.14 mg</td>
<td>0.11 mg</td>
<td>0.07 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4800</td>
<td>0.36 mg</td>
<td>0.32 mg</td>
<td>0.29 mg</td>
<td>0.25 mg</td>
<td>0.22 mg</td>
<td>0.18 mg</td>
<td>0.14 mg</td>
<td>0.11 mg</td>
<td>0.07 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5000</td>
<td>0.38 mg</td>
<td>0.34 mg</td>
<td>0.30 mg</td>
<td>0.27 mg</td>
<td>0.23 mg</td>
<td>0.19 mg</td>
<td>0.15 mg</td>
<td>0.12 mg</td>
<td>0.08 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Increase interval to q 6 dosing for at least 3 doses
- Increase interval to q 8 dosing for at least 3 doses
- Increase interval to q 12 dosing for at least 2 doses
- Increase interval to q 24 dosing for at least 2 days
Adjunctive Therapy for Neonatal Abstinence Syndrome

1. Predominant opioid exposure? Yes
   - If morphine alone is not controlling symptoms, consider Clonidine
   - Start 1mcg/kg/dose every 4-6 hours with morphine dosing
   - May be increased by 0.5-1mcg/kg/dose every 24 hours to a maximum of 12 mcg/kg/day

   Once morphine is weaned off
   - Wean Clonidine 0.5-1mcg/kg/dose everyday.
   - If infant has rebound hypertension (defined as an increase of blood pressure >95th percentile of age-specific norms), or tachycardia (>200bpm), resume previous dose for 24 hours and attempt to wean again.

2. Predominant opioid exposure? No

   If an infant has been exposed to multiple drug classes, or has significant CNS hyperirritability, oral phenobarbital may be added.
   - Starting 10-20mg/kg/dose followed by 2-5mg/kg/day QD or divided BID to begin 24 hours later.
   - Serum phenobarbital levels are not monitored unless use is for the management of seizures. Increases in dose are not recommended as infant gains weight. Infant is allowed to outgrow the dose as symptoms wane. This is usually achieved over the first 6-8 weeks of life.
Pharmacologic Treatment: Phenobarbital

• Does not control GI symptoms
• Sometimes works better for CNS/behavioral symptoms
• Loading dose 10-20 mg/kg/dose
• Maintenance dose 2-5 mg/kg/day QD or divided BID to start 24 hours after loading
• Allow infant to outgrow dose, no need to monitor levels unless use is for seizure management
Pharmacologic Treatment: Clonidine

- Alpha-2 adrenergic agonist: presynaptic inhibitor of norepinephrine/dopamine release
- Reduces signs/symptoms while neurons reverse their tolerance to opioids
- In combination with morphine, it shortens opioid treatment for NAS

Pediatrics 2009;123:e849-e856

- Clearance increases rapidly to 70% adult rate by 1 month

J Clin Pharmacol 2011;51:502

- Single drug treatment for NAS-limited experience

Pharmacologic Treatment: **Clonidine**

- Can cause hypotension (defined as blood pressure below the 5\textsuperscript{th} percentile) and bradycardia (<60bpm)
- Blood pressures and heart rates should be closely monitored prior to each dose for 24 hours after initiation or change in dosing
- Rebound hypertension and tachycardia upon weaning
- No published studies on the outpatient weaning of clonidine, therefore encourage weaning off clonidine prior to discharge
Length of hospitalization/treatment

Highly variable

Focus on length of sleeping periods, ability to gain weight, ability to be cared for by a “reasonable lay person”

Safety of the home environment
Breastfeeding

Check prenatal labs for infectious disease risk (HIV positivity is an absolute contraindication)

Check drug screens for poly-drug use (controversy currently exists about BF with marijuana-no consensus)

Safe to breastfeed with methadone/buprenorphine

Do not prevent NAS, but some studies have found it may help
Concentrations in breastmilk are low and not related to maternal dose

0.05 mg of methadone per day through the breast milk

McCarthy and Posey J Hum Lact 2000;16(2):115-120

Questions?

Feel free to reach out to me!
camille.fung@hsc.utah.edu
References


