Neonatal Abstinence Syndrome
How We Got Here and Where We Are Going

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Newborn Special Care Associates
Abington Jefferson Health
Disclosures

• I have no financial disclosures
• We will discuss the use of morphine in infants which is an off label use
Objectives

• Discuss the incidence/epidemiology of opioid use
• Discuss the incidence/epidemiology of Neonatal Abstinence Syndrome
• Discuss treatment strategies for Neonatal Abstinence Syndrome
• Discuss Quality Improvement Efforts for Neonatal Abstinence Syndrome
Opioids

• Natural, endogenous and synthetic
• Bind μ receptors in CNS
  – Supraspinal analgesia
  – Sedation, euphoria, miosis, respiratory depression and decreased GI motility
  – Prolonged use causes physical and psychological dependence
Opioids

• Natural
  – Morphine (extracted from opium)

• Synthetic
  – Codeine, heroin, hydromorphone, fentanyl, methadone

• Endogenous
  – Enkephalins, endorphins, endomorphins
The Problem

• Overdose death rate increased by 137% since 2000
  – 200% increased in death from opioid overdose
• Americans consume 80% of global opioid supply
  – 99% of hydrocodone supply
• Heroin overdoses have tripled in last 4 years
  – Past misuse of prescription opioids clearly linked

Manchinkati, et al
Increasing Death from Opioids

- **Sex:**
  - Males (7.6%)
  - Females (4.7%)

- **Age**
  - 25-34 year olds (10.5%)
  - 35-44 year olds (8.7%)
  - 55-64 year olds (5.7%)
  - ≥ 65 year olds (7.7%)

- **Race**
  - White, non hispanic (8%)
  - Black, non hispanic (8.2%)

- **Geography**
  - Northeast (8.8%)
  - Midwest (9.6%)
  - South (6.9%)

Rudd, R.A. et al
Increases in Drug and Opioid Overdose Deaths—United States, 2000–2014

- Drug overdose deaths involving opioids
- Natural and semisynthetic opioids
- Synthetic opioids excluding methadone
- Methadone
- Heroin

Deaths per 100,000 population

Year

American Journal of Transplantation
Volume 16, Issue 4, pages 1323-1327, 22 MAR 2016 DOI: 10.1111/ajt.13776
The Problem

1986
Publication that opioids can be used in people without cancer and pain

1996
Purdue Pharma releases oxycontin

1996
American Pain Society Trademarks pain as the 5th VS

1998
Federation of State Medical Boards- Drs can safely Rx narcotics

1998
VA/JCHAO make pain 5th VS
The Problem

2001
JCHAO issues standards urging hospitals to regularly ask patients about pain

2007
Purdue Pharma pleads guilty to misbranding of oxycontin

2012
259 million opioid Rx written $9 billion

2013
Opioid deaths surpass car accidents as leading cause of accidental death

2001
JCHAO publishes guide to address physician concerns about addiction and tolerance
The Problem

• Pregnant women do not escape the reach of opioid addiction
  – 4.5% of pregnant women report using illicit drugs

• Infants born to women on opioids are at risk of Neonatal Abstinence Syndrome (NAS)

• 300% increase in NAS (2000-2013)
  – 1.5 → 6 cases/1000 hospital births

https://www.cdc.gov/mmwr/volumes/65/wr/mm6531a2.htm
# The Problem

<table>
<thead>
<tr>
<th>US Census Division</th>
<th>NAS Rate per 1000 Births (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New England</td>
<td>13.7 (12.5-14.5)</td>
</tr>
<tr>
<td>Middle Atlantic</td>
<td>6.8 (5.9-7.6)</td>
</tr>
<tr>
<td>East North Central</td>
<td>6.9 (6.0-7.8)</td>
</tr>
<tr>
<td>West North Central</td>
<td>3.4 (3.0-3.8)</td>
</tr>
<tr>
<td>South Atlantic</td>
<td>6.9 (6.3-7.4)</td>
</tr>
<tr>
<td>East South Central</td>
<td>16.2 (12.4-18.9)</td>
</tr>
<tr>
<td>West South Central</td>
<td>2.6 (2.3-2.9)</td>
</tr>
<tr>
<td>Mountain</td>
<td>5.1</td>
</tr>
</tbody>
</table>

Dramatic Increases in Maternal Opioid Use and Neonatal Abstinence Syndrome

Every 25 minutes, a baby is born suffering from opioid withdrawal.

Average Length or Cost of Hospital Stay

- With NAS: 16.9
- Without NAS: 2.1

- With NAS: $3,500
- Without NAS: $66,700

NAS and Maternal Opioid Use on the Rise

Source: Patrick et al., JAMA 2017. Patrick et al., Journal of Perinatology 2015

National Institute on Drug Abuse

Source: Pennsylvania Healthcare Cost Containment Council
AVERAGE LENGTH OR COST OF HOSPITAL STAY

<table>
<thead>
<tr>
<th></th>
<th>DAYS</th>
<th>COST</th>
</tr>
</thead>
<tbody>
<tr>
<td>WITH NAS</td>
<td>16.9</td>
<td>$66,700</td>
</tr>
<tr>
<td>W/O NAS</td>
<td>2.1</td>
<td>$3,500</td>
</tr>
</tbody>
</table>

Source: Pennsylvania Healthcare Cost Containment Council
NAS AND MATERNAL OPIOID USE ON THE RISE

Source: Pennsylvania Healthcare Cost Containment Council
Pennsylvania Data

Substance-related Rate per 1,000 Neonatal Stays in FFY 2015

Source: Pennsylvania Healthcare Cost Containment Council
## Pennsylvania Data

<table>
<thead>
<tr>
<th>Condition</th>
<th>Substance-related Stays</th>
<th>All Other Stays</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low birth weight</td>
<td>15.3%</td>
<td>6.6%</td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>20.7%</td>
<td>9.9%</td>
</tr>
<tr>
<td>Difficulty feeding</td>
<td>12.3%</td>
<td>3.4%</td>
</tr>
<tr>
<td>Prematurity</td>
<td>16.4%</td>
<td>8.4%</td>
</tr>
</tbody>
</table>

### Average Length of Stay

<table>
<thead>
<tr>
<th>Condition</th>
<th>Substance-related Stays</th>
<th>All Other Stays</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average length of stay</td>
<td>14.1 days</td>
<td>3.8 days</td>
</tr>
<tr>
<td>Average Medicaid payment¹</td>
<td>$17,855</td>
<td>$10,316</td>
</tr>
</tbody>
</table>

¹ Includes both substance-related and all other stays.
The Problem

• Pennsylvania by the numbers (2000-2015)
  – Neonatal stays related to substance abuse
    • ↑ 250% (6.5 → 19.6/1000 neonatal stays)
  – Neonatal abstinence syndrome
    • ↑ 870% (1.6 → 16/1000 neonatal stays)
  – Cost
    • 28,000 days
    • $20 million
Neonatal Abstinence Syndrome

• Constellation of symptoms seen in infants who are exposed to opiates in utero

• Some variation in onset and severity of symptoms
  – Timing of most recent drug use prior to delivery
  – Maternal metabolism
  – Placental metabolism
  – Infant metabolism / excretion
  – Concomitant use of other drugs / substances
Neonatal Abstinence Syndrome

- 55-94% of infants exposed in utero exhibit symptoms
- Seldom effects infants < 34 weeks gestation
Opioid Receptors
Opioid use in Pregnancy

• Opioids are small, lipophilic, low molecular weight
  – Cross placental and blood brain barriers
• Detoxification associated with increased risk of fetal distress and loss
Neonatal Abstinence Syndrome

• CNS symptoms
  – Continuous and/or high-pitched crying
  – Difficulty sleeping
  – Hyperactive Moro Reflex
  – Tremors
  – Hypertonicity
  – Skin excoriation
  – Generalized convulsions / seizures
Neonatal Abstinence Syndrome

- Autonomic Symptoms
  - Temperature elevation
  - Sneezing / nasal stuffiness
  - Mottled skin
  - Tachypnea
  - Sweating
  - Yawning
Neonatal Abstinence Syndrome

- Gastrointestinal symptoms
  - Feeding difficulties
    - Unable to organize to feed
    - Biting nipple
    - Lack of coordination
  - Frequent watery / loose stools
    - Leads to skin breakdown
  - Regurgitation
  - Excessive sucking
  - Failure to thrive
### Neonatal Abstinence Syndrome

<table>
<thead>
<tr>
<th>Substance</th>
<th>Onset of Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heroin</td>
<td>Birth – 3 days</td>
</tr>
<tr>
<td>Methadone/buprenorphine</td>
<td>Birth – 7 days (subacute signs up to 6 months)</td>
</tr>
<tr>
<td>Benzodiazapene</td>
<td>Hours - 2 weeks</td>
</tr>
</tbody>
</table>
Non Narcotic Substance Exposure

• Cocaine
  – No withdrawal
    • NEC, abruption, fetal distress and IUGR

• Alcohol
  – Hyperactivity, tremors, poor suck, hyperphagia
  – Sx at birth

• Caffeine
  – Jitteriness, bradycardia, vomiting, tachypnea
  – Sx at birth and for 1-7 days
Non Narcotic Substance Exposure

• Barbiturates
  – Similar to opioids
  – Sx at birth up to 14 days

• SSRI’s
  – Irritability, tremors, poor suck, feeding difficulties, hypertonia, fever, hypoglycemia, seizures
  – Sx hours to days
Non Narcotic Substance Exposure

• Benzodiazapene
  – Similar to opioids
    • Hypo/hypertonia
    • Poor suck
    • Hypothermia
    • Apnea
    • Tremors
    • Vomiting
    • Tachypnea
  – Onset hours to weeks
Differential Diagnosis

- Sepsis
  - meningitis
- Electrolyte abnormality
- Hematologic irregularities
- Perinatal asphyxia
- Intracranial pathology
Diagnosis

• History, history, history
  – Maternal medical, family and social history
  – Pregnancy history
  – Birth history

• Labs
  – Cbc, bmp, +/- blood culture (if ill appearing)
  – Urine/meconium drug screens

• Risk/benefit evaluation
  – Rarely LP if history c/w NAS
Drug testing

- Ideally UDS from mother on admission
- Infant UDS (preferably first void)
- Infant Meconium drug screen
  - Reflects exposure from 20 weeks GA
  - Collect first two samples
- Infant hair
- Umbilical cord tissue
## Maternal Urine Toxicology

### Drug Detection Times (since last use):

<table>
<thead>
<tr>
<th>Drug or Class</th>
<th>Detection Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>6 - 12 hours</td>
</tr>
<tr>
<td>Amphetamine or methamphetamine</td>
<td>48 hours</td>
</tr>
<tr>
<td>Barbiturates, short acting</td>
<td>24 hours</td>
</tr>
<tr>
<td>Barbiturates, long acting</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Benzodiazepines, short acting</td>
<td>3 days</td>
</tr>
<tr>
<td>Benzodiazepines, long acting</td>
<td>30 days</td>
</tr>
<tr>
<td>Cocaine</td>
<td>2 – 4 days</td>
</tr>
<tr>
<td>Marijuana, single use</td>
<td>3 days</td>
</tr>
<tr>
<td>Marijuana, daily use</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Codeine</td>
<td>48 hours</td>
</tr>
<tr>
<td>Heroin</td>
<td>2 – 4 days</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>2 – 4 days</td>
</tr>
<tr>
<td>Methadone</td>
<td>3 days</td>
</tr>
<tr>
<td>Morphine</td>
<td>2 – 3 days</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>2 – 4 days</td>
</tr>
</tbody>
</table>

Source: PEDIATRICS Volume 129, Number 2, February 2012
## Potential False Positives

<table>
<thead>
<tr>
<th>Drug or Class</th>
<th>Drugs which Potentially Cause False Positive Readings on Screening Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamines</td>
<td>Amantadine, chlorpromazine, desipramine, ephedrine, fluoxetine, labetolol, phenetermine, phenylephrine, ranitidine, trazodone</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>Ibuprofen, naproxen</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Sertraline</td>
</tr>
<tr>
<td>Cannabinoids</td>
<td>Dronabinol, NSAIDS (ibuprofen, ketoprofen, naproxen, piroxicam, sulindac, tolmethin), promethazine, PPIs</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Amoxicillin, coca leaf teas, tonic water</td>
</tr>
<tr>
<td>Methadone</td>
<td>Chlorpromazine, diphenhydramine, ibuprofen, verapamil</td>
</tr>
<tr>
<td>Opiates</td>
<td>Dextromethorphan, diphenhydramine, poppy seeds, rifampin, quinine</td>
</tr>
<tr>
<td>Phencyclidine</td>
<td>Dextroamphetamine, dextromethorphan, diphenhydramine, ibuprofen, imipramine, tramadol, venlafaxine</td>
</tr>
</tbody>
</table>

Source: Partnership Health Plan of California, 2015
Physical Exam

• Hypertonicity
  – Global vs. extremities
  – Head lag
  – Ventral suspension
Physical Exam

• Skin
  – Mottling
  – Diaper area
  – Excoriation
Assessment

- Finnegan Scoring
  - Developed by Dr. Lorega Finnegan in 1975
  - Provides quantitative assessment of NAS
  - Predominant tool used in the United States
  - Used for term neonates < 3 weeks of age

### NEONATAL ABSTINENCE SCORING SYSTEM

<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>SIGNS AND SYMPTOMS</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Continuous High Pitched (or other) Cry</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Continuous High Pitched (or other) Cry</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Sleeps &lt;1 Hour After Feeding</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Sleeps &lt;2 Hours After Feeding</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Sleeps &lt;3 Hours After Feeding</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Hyperactive Moro Reflex</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Markedly Hyperactive Moro Reflex</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Mild Tremors Disturbed</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Moderate-Severe Tremors Disturbed</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Mild Tremors Undisturbed</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Moderate-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 (Specific Area)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Myoclonic Jerks</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Generalized Convulsions</td>
<td>5</td>
</tr>
</tbody>
</table>

**CENTRAL NERVOUS SYSTEM DISTURBANCES**

<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>SIGNS AND SYMPTOMS</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sweating</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Fever 100°F-101°F (38°C-38.3°C)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Fever &gt; 101°F (38.3°C)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Frequent Yawning (&gt;3-4 times/interval)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Mottling</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Nasal Stiffness</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Sneezing (&gt;3-4 times/interval)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Nasal Flaring</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>
</tbody>
</table>

**METABOLIC/VAUGHAN/RESPIRATORY DISTURBANCES**

<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>SIGNS AND SYMPTOMS</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td></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>

**GASTROINTESTINAL DISTURBANCES**

<table>
<thead>
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<th>SYSTEM</th>
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<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td></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>

**TOTAL SCORE**

**INITIALS OF SCORER**

---

**FIGURE 1**

Modified Finnegan’s Neonatal Abstinence Scoring Tool. Adapted from ref 101.
Using the Finnegane Score

• Begin scoring when infants show signs of withdrawal
  – Score q3-4 hours, after feeds when infant at best
• Start “treatment” when 3 scores ≥ 24 or 2 scores ≥ 24 or one score of ≥ 14
Treatment

• Nonpharmacologic
  – Swaddling
  – Holding, rocking, swaying
  – Quiet, dark, non stimulating environment
  – Encourage rooming in
    • Extended family
Breastfeeding and NAS?

• YES!!!
  – If mother is in a treatment program
  – UDS is positive only for methadone/buprenorphine

• Associated with less severe NAS that presents later and is less severe

• Less frequently requires pharmacologic intervention
Breastfeeding and NAS

- Small amounts methadone/buprenorphine secreted into breast milk
- Long term neurodevelopmental information not available
- Not enough data to discourage breastfeeding
- Frank discussion with mother about slow weaning
Pharmacologic Treatment

• 83% of clinicians in the United States use an opioid as the drug of first choice
  – Morphine or Methadone
• Phenobarbital is most typical second-line drug if opiate does not control symptoms
• Clonidine as adjunctive therapy also an option
• Also consider using methadone
Quality Improvement

• Recently multiple studies have surfaced looking at the care of NAS
• Focus on decreased LOS
  – Decreased cost
• Standardization of treatments
• NAS Education
• Rooming In
Act
- What changes are to be made?
- Next cycle?

Plan
- Objective.
- Questions and predictions.
- Plan to carry out the cycle (who, what, where, when).

Study
- Complete the data analysis.
- Compare data to predictions.
- Summarize what was learned.

Do
- Carry out the plan.
- Document problems and unexpected observations.
- Begin data analysis.
NAS at Abington Hospital

- Abington Hospital
  - 8 miles north of Philadelphia
  - Approximately 5000 deliveries/year
  - 34 bed; Level 3b NICU
- Increasing opioid exposed infants
- NAS task force formed in 2014
NAS at Abington Hospital

• Pre Data
  – June 2013- June 2015
  – 101 infants with positive UDS/MDS
  – 36 infants required treatment with morphine
  – LOS with NAS 22.4 days
  – LOS without NAS 4.1 days
Abington Hospital-
Positive Drug Screen

- Methadone: 37
- Cocaine: 2
- PCP: 2
- Oxycodone: 25
- Opiates: 25
- MJ: 9
- Benzo's: 8
- Barbiturates: 17

Newborn
special care associates, pc
Abington Hospital – Jefferson Health Protocol

Infant criteria for NAS scoring:

- NAS ≥ 24 (3 consecutive scores that total ≥ 24)
- Yes: Initiate Newborn/Pediatric Drug Exposed Protocols
- NO: Mom discharged?
  - NO: Continue scoring infant
  - YES: Transfer to Pediatrics or SCN
    - NAS ≥ 24 (3 consecutive scores that total ≥ 24)
      - Yes: Initiate TREATMENT
      - NO: Continue scoring infant

Reminders:
- Meconium (2 specimens, one cup) and urine should be sent on admission
- Scoring should occur when infant is at its “best” – after feeds, swaddled, and held
- Nonpharmacologic methods of NAS treatment are preferred

D/C home 3-7 days
Post Data

• July 2015-May 2016
  – 38 babies opioid exposed
  – 18 babies treated for NAS
  – LOS 16.8 days
An Initiative to In Syndrome

Matthew R. Grossman, A Matthew J. Bizzarro

- Yale New Haven Children’s Hospital
- Standardization of nonpharmacologic care
- Parental education
- Novel Assessment Approach
- Morphine prn
- Bypassing the NICU
An Initiative to Improve the Quality of Care of Infants With Neonatal Abstinence Syndrome


- Novel Approach to NAS
- Functional Assessment
  - Ability to eat
    - BF effectively or take >1oz/feed
  - Ability to sleep
    - Undisturbed > 1 hour
- Ability to be consoled
  - Within 10 minutes
An Initiative to Improve the Quality of Care of Infants With Neonatal Abstinence Syndrome


- Novel approach to Treatment
  - If on scheduled morphine
    - 10% wean TID
- After maximum nonpharmacologic interventions
  - 1 dose of morphine given (0.05mg/kg)
  - Reassesed 3 hours later
  - Eating, sleeping and consoling well
  - No further doses
An Initiative to Improve the Quality of Care of Infants With Neonatal Abstinence Syndrome


- 55 infants pre implementation
- 44 infants post implementation
  - LOS: 22.4 → 5.9 days
  - Pharmacologic Tx: 98% → 14%
  - Costs: $44,000 → $10,000
  - No readmissions, no adverse events
Summary

• Opioid addiction is currently an epidemic
• Pregnant women can be addicted
• Neonatal Abstinence Syndrome – treatment has been stable through the years
• Breast feed when able
• Assessment change has no ADRs
• Nonpharmacologic treatment is feasible
Acknowledgements

• NAS Task Force at Abington Hospital Jefferson Health
• Moira Winstanley, NNP- BC
• Andrew Loh, MD
Thank you!
References


References


Newborn
special care associates, pc
References


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