Neonatal Narcotic Abstinence Syndrome: A National Epidemic

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Ohio Childrens Hospitals Neonatal Research Consortium
Objectives

• Describe the opioid epidemic in the United States as well as on a local level
• Review the mechanism of action of opiates and what causes withdrawal symptoms
• Describe current treatment strategies for NAS and outcomes
NEONATAL ABSTINENCE SYNDROME: SCOPE OF THE PROBLEM
Pain

- 1995: studies showed cancer patients’ pain was undertreated.
- 2000: Joint Commission on Hospital Accreditation: Pain is the Fifth Vital Sign
Prescription Drug Use On the Rise

• Narcotic prescriptions in U.S increased 6-fold from 1997-2006
• Now account for more overdose deaths than cocaine and heroin combined
• More deaths than car accidents
• In 2010, enough opiate pain relievers were prescribed “to medicate every American adult with a standard pain treatment dose of 5mg hydrocodone q4hr for 1 month”
Deaths from Narcotic Overdoses in Young Women


* Deaths per 100,000 population; age-adjusted to the 2000 U.S. standard population using the bridge-race estimates.
This represents 1 infant born per hour in the US with signs of drug withdrawal.
Epidemic of Unintentional Drug Overdoses in Ohio 1979-2008

• Narcotic prescriptions in Ohio increased 6-fold from 1997 to 2006
Opiate-Related Admissions to Treatment Centers - 2001

Legend

Opiate Addicts (%)
- 0.0% - 3.0%
- 3.1% - 6.7%
- 6.8% - 14.3%

Map Information:
This map represents the percentage of clients in treatment with an opiate-related diagnosis (heroin and prescription opioid). The highest concentrations of opiate admissions are in Cuyahoga (14.3%), Montgomery (12.5%), Mahoning (12.2%), Summit (12.1%) and Franklin (10.1%) counties. Noble, Paulding, Putnam and Wyandot did not have any opiate-related admissions.
Epidemic is Spreading - 2005

Client Admissions for Opiate Abuse and Dependence
Ohio MACSIS Data - 2005

Legend
Opiate Addicts (%)
- 1.0% - 3.0%
- 3.1% - 6.7%
- 6.8% - 34.4%

Map Information:
This map represents the percentage of clients in treatment with an opiate-related diagnosis (heroin and prescription opioid). The highest concentrations for opiate admissions are in Scioto (34.4%), Clark (21.1%) and Jackson (20.9%) counties. The counties with the lowest concentrations of an opiate-related diagnosis are Holmes (1.0%), Morgan (1.0%) and Henry (1.1%).
Epidemic is Spreading- 2007

Client Admissions for Opiate Abuse and Dependence
Ohio MACSIS Data - 2007

Legend
Opiate Addicts (%)
- 0.0% - 3.0%
- 3.1% - 6.7%
- 6.8% - 31.4%

Map Information:
This map represents the percentage of clients in treatment with an opiate-related diagnosis (heroin and prescription opioid). The highest concentrations for opiate admissions are in Jackson (31.4%), Scioto (30.8%) and Lawrence (22.7%) counties. The counties with the lowest concentrations of an opiate-related diagnosis are Putnam (0.0%), Coshocton (1.9%) and Holmes (2.0%).

Data Source:
Data from Multi Agency Community Information Systems (MACSIS)
Map produced April 2013
Epidemic is Spreading-2009

Client Admissions for Opiate Abuse and Dependence
Ohio MACSIS Data - 2009

Legend
Opiate Addicts (%)
- 2.3% - 3.0%
- 3.1% - 6.7%
- 6.8% - 64.1%

Map Information:
This map represents the percentage of clients in treatment with an opiate-related diagnosis (heroin and prescription opioid). The highest concentrations for opiate admissions are in Scioto (64.1%), Lawrence (49.5%) and Jackson (35.7%) counties. The counties with the lowest concentrations of an opiate-related diagnosis are Allen (2.3%), Coshocton (2.4%) and Carroll (3.5%).
Epidemic is Spreading - 2011

Client Admissions for Opiate Abuse and Dependence
Ohio MACSIS Data - 2011

Legend
Opiate Addicts (%)
- 3.1% - 6.7%
- 6.8% - 70.2%

Map Information:
This map represents the percentage of clients in treatment with an opiate-related diagnosis (heroin and prescription opioid). The highest concentrations for opiate admissions are in Scioto (70.2%), Lawrence (56.2%) and Athens (41.9%) counties. The counties with the lowest concentrations of an opiate-related diagnosis are Tuscarawas (5.5%), Holmes (4.4%) and Morgan (3.1%).

Data Source:
Data from Multi Agency Community Information Systems (MACSIS)
Map produced April 2013
Newborn Hospitalizations for NAS In Ohio

Figure 1: NAS inpatient hospitalization rate per 10,000 live births, Ohio, 2004-2011

Source: Ohio Hospital Association
What Dose Illicit Substance Use Look Like in Georgia?

• ~7% Georgia residents used illicit drugs in past month

*Illicit Drug Use in the Past Month among Individuals Aged 12 or Older, by State: Percentages, Annual Averages Based on 2012 and 2013 NSDUHs*

Substance Abuse Treatment Admissions, 2005

Georgia Primary Drug Abuse Treatment Episodes in 2005 by Type of Drug

- Cocaine: highest number
- Marijuana
- Stimulants
- Other opiates
- Other/Unknown
- Heroin
- Tranquilizers
- Sedatives
- Inhalants
- Hallucinogens
- PCP

Source: ONDCP, Georgia Drug Control Update
Non-medical Use of Prescribed Opiates

*Nonmedical Use of Pain Relievers in the Past Year among Individuals Aged 12 or Older, by State: Percentages, Annual Averages Based on 2012 and 2013 NSDUHs*

Neonatal Abstinence Syndrome
Neonatal Abstinence Syndrome (NAS)

• A withdrawal syndrome experienced by drug exposed neonates
• Usually refers to symptoms from opiate exposure
  – Other drugs implicated
    • Benzodiazepines, SSRIs, Cocaine, Amphetamines, Alcohol
• Affects 55%-94% of exposed neonates
Diagnosis

• Universal screening of ALL pregnant women
• Testing of urine, meconium, hair or umbilical cord samples
• Urine may have fastest turnaround but only reflects recent exposure (<3 days)
• Other samples give information over longer period
• No large studies comparing different methods
• Symptoms
Presentation of Opioid Withdrawal

• Timing
  – Which opioid abused
    • May be delayed until 7 or more days
  – Last use by mom
  – Net transfer across placenta
  – Infant metabolism
  – Polysubstance use

• Opioid receptors concentrated within CNS and GI tract
Specific Signs

• CNS irritability
  – Inconsolable, hyperactive reflexes, poor sleep, seizures

• Autonomic over reactivity
  – Sneezing, temperature instability, sniffles

• Gastrointestinal Dysfunction
  – Loose stools, emesis/reflux
Origin of NAS Assessment Tools

- Circa 1975
- ID symptoms for tool from literature and clinical experience
- Symptoms ranked by pathological significance
- Initial tool composed of 32 weighted items
Impact of Tool

• Decreased need for pharmacological management (30% versus 46%) compared to no scoring system
• Decreased duration of treatment (6 versus 8 days)
• Reduced hospital stay by 25%
Modified Finnegan Tool - 1986

Modifications to Original Finnegan

- 21 original items
- Reorganized into 3 categories:
  - CNS, GI and metabolic
- Same scoring process and cut-off points for RX treatment

Validation Studies

- None found
- Used by significant majority of NICUs

How many other “modified” tools are out there?
Pharmacology of NAS
What Do Opioids Do?

- Opiate receptors (μ, δ, κ)
  - All found in brain
  - μ also in GI tract

- Activation of receptor modulates neurotransmitter release:
  - Norepinephrine
    - Acutely inhibits release at synaptic terminals
    - Rate of release over time increases towards normal with chronic use
  - Also: Serotonin, acetylcholine, dopamine and substance P
Clinical Manifestations of Opioid Use

• Analgesia
• Drowsiness
• Respiratory depression
• Decreased GI motility, nausea and vomiting
• Use → tolerance, physiologic dependence, addiction
What Happens When Exposure Ends?

• Abrupt discontinuation → supranormal norepinephrine release
  – Autonomic and behavioral signs associated with NAS
Pharmacologic Treatment of NAS

• Relieve moderate to severe symptoms of NAS
  – Finnegan scores >8
• Non-pharmacologic therapy exhausted
• Humanely but lowest possible exposure
  – Neuronal apoptosis
Current Neonatal Strategies

• First line: opiate - generally morphine
• Methadone: ? Concern for pharmacokinetics, and arrhythmia?

Osborn, et al Cochrane Database, 2010
Methadone

- May turn out to be better drug
- Reports of long QT syndrome
- If choose this drug, recommend babies be on CR monitor.
Buprenorphine

- Partial μ-opioid agonist, sublingual tablet
- 2 small randomized open-label trials, Kraft et al 2008 and 2011
  - Buprenorphine vs. tincture of opium
    - No difference
  - Buprenorphine (higher dose) vs. morphine
    - Decreased treatment days and hospital stay
- Limited safety data, varying serum concentrations
Second Line

• When “max” opiate dose reached

<table>
<thead>
<tr>
<th></th>
<th>Opiate + Pheno</th>
<th>Opiate alone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time Score&gt; 8(%)</strong></td>
<td>10%</td>
<td>15%</td>
</tr>
<tr>
<td><strong>Duration Hosp (d)</strong></td>
<td>35 ± 21</td>
<td>76 ± 22</td>
</tr>
<tr>
<td><strong>Max Dose</strong></td>
<td>4.7</td>
<td>16.8</td>
</tr>
<tr>
<td><strong>Costs ($US1000)</strong></td>
<td>33.3 ± 17.9</td>
<td>69.2 ± 19.7</td>
</tr>
</tbody>
</table>

Osborn, Cochrane Review, 2010
Phenobarbital

• Long-acting barbiturate → CNS depression
  – Enhancement of inhibitory neurotransmitter γ-aminobutyric acid

• Polypharmacy
Clonidine

• Central α-adrenergic receptor agonist
• Acts at parasympathetic receptors in midbrain and medulla → inhibit sympathetic outflow by decreasing central catecholamine release
  – Decreases vasomotor tone and heart rate
• Abrupt discontinuation → hypertension and sympathetic overactivity (tachycardia, agitation, sweating)
Clonidine, cont.

Kaplan-Meier curve effect of clonidine on days of DTO therapy

Effect of clonidine on amount of DTO needed to control NAS

Knowledge Gaps

• Size of epidemic
• Optimal treatment strategies, including drug, dose, safety, side effects due to differences in neonatal metabolism
• Impact of poly substance use on severity of NAS
• Differences in outcome for different maternal treatment strategies
• Safety of treatment as outpatient
• Long term outcomes of children exposed to narcotics in utero
Ohio Childrens Hospital
NAS Consortium

- Organized in Jan 2012
- Chartered by Gov Kasich to work together to improve care of children
- Neo Inaugural Project: NAS- launched Sept 2012
Descriptors: 553 neonates (2012 - 2013)

<table>
<thead>
<tr>
<th>Descriptor</th>
<th>Mean</th>
<th>Range</th>
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<tbody>
<tr>
<td>Maternal Age, y</td>
<td>26.7 y</td>
<td>17-44</td>
</tr>
<tr>
<td>Maternal Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White, Non-Hispanic (%)</td>
<td>92%</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>84%</td>
<td></td>
</tr>
<tr>
<td>Insurance,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Public</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>10%</td>
<td></td>
</tr>
</tbody>
</table>
## Perinatal Descriptors

<table>
<thead>
<tr>
<th>Descriptor</th>
<th>N= 553</th>
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<tbody>
<tr>
<td>Prenatal Care</td>
<td>89%</td>
</tr>
<tr>
<td>Pregnancy Complications</td>
<td>85%</td>
</tr>
<tr>
<td>Sexually Transmitted Disease</td>
<td>7%</td>
</tr>
<tr>
<td>HIV</td>
<td>0</td>
</tr>
<tr>
<td>Hep C</td>
<td>25.9%</td>
</tr>
<tr>
<td>Hep B</td>
<td>1.0%</td>
</tr>
</tbody>
</table>
Maternal Opiate Exposures

<table>
<thead>
<tr>
<th>Source</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Illegal</td>
<td>46%</td>
</tr>
<tr>
<td>Prescribed</td>
<td>34%</td>
</tr>
<tr>
<td>Unknown</td>
<td>20%</td>
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</table>
## Infant Treatment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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<tbody>
<tr>
<td>Symptoms Started (hours; Mean)</td>
<td>46</td>
</tr>
<tr>
<td>Treatment Length (days; Mean)</td>
<td>18.5</td>
</tr>
<tr>
<td>Hospital Stay (days; Mean)</td>
<td>22.2</td>
</tr>
<tr>
<td>Number of Drugs Used (Mean)</td>
<td>1.5</td>
</tr>
<tr>
<td>Drugs used</td>
<td></td>
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<tr>
<td>Morphine</td>
<td>50%</td>
</tr>
<tr>
<td>Methadone</td>
<td>49%</td>
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</table>
Differences by Site

Days

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
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</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>10</td>
<td>15</td>
<td>20</td>
<td>18</td>
<td>25</td>
<td>30</td>
</tr>
<tr>
<td>Stay</td>
<td>5</td>
<td>10</td>
<td>15</td>
<td>12</td>
<td>20</td>
<td>35</td>
</tr>
</tbody>
</table>

Centers:
- A
- B
- C
- D
- E
- F
Poly Exposures

Number with Co-Exposure

- Tobacco
- Marijuana
- Cocaine
- Alcohol
- Amphetamine
Multiple Simultaneous Withdrawals

82% Exposed to tobacco
- Average cotinine level by cord analysis 135 ng
- Maximum = 270
- Average US Adult Smoker = 100 ng

10% Exposed to SSRI or Benzodiazepine
- Known withdrawal syndromes
Differences by Drug

Days

CENTERS

A B C D E F

Morphine
Methadone
# Ohio Potentially Better Protocol

<table>
<thead>
<tr>
<th>Non-Pharmacologic</th>
<th>Swaddle, Comfort, MBM or 22 Calorie</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiate</td>
<td>NAS score ≥ 9 q3h two times</td>
</tr>
<tr>
<td></td>
<td>Drug: Morphine/ Methadone 0.05 mg/kg PO</td>
</tr>
<tr>
<td>Escalate</td>
<td>If ≥ 12, increase dose</td>
</tr>
<tr>
<td>Stabilize</td>
<td>No increase for 48 hrs</td>
</tr>
<tr>
<td>Wean</td>
<td>10% of max dose daily</td>
</tr>
<tr>
<td></td>
<td>Discharge 48 hours off drug</td>
</tr>
</tbody>
</table>
Impact of Protocol

![Graph showing the impact of a new protocol on treatment days over consecutive patients.](chart.png)
How Can We Spread What We’ve Learned?

• OPQC
• January 2014 started the NAS project
Who Is OPQC?

- Ohio Department of Job & Family Services
- Ohio Department of Health – Vital Stats
- Ohio Medicaid
- Ohio ACOG AAP
- **Peds + OB + Quality Improvement** Leaders
- “OPQC Central”
  - Secure Central De-identified Data Processing
- **Staff at Ohio Maternity & Children’s Hospitals**

Start up $$ from CMS → ODJFS → OPQC
Through collaborative use of improvement science methods, reduce preterm births and improve outcomes of preterm newborns in Ohio as quickly as possible.”
Approach

• Prevent preterm birth where possible
  – Avoid delivery before 39 weeks

• When premature birth occurs:
  – Reduce mortality
  – Reduce complications
  – Involve the families
  – Improve the outcomes

• All Families education on “Back to Sleep”, and smoking avoidance.
Success to Date

• Decreased the rates of scheduled inductions without an indication before 39 weeks gestation

• 23 NICUs across the state have:
  – Decreased the rates of late infection of infants born at 22-29 weeks gestation
  – Increased the rates of breast milk usage
    • Decreased NEC rates
    • Decreased rates of post-natal growth failure
OPQC has prevented 75 deaths

Together we have saved enough Babies to fill **TWO** School buses!
NAS Participating Sites 2014

1/2014 start Level 3 and Level 2 teams
4/2014 start Level 2 teams
GLOBAL AIM

To reduce the number of moms and babies with narcotic exposure, and reduce the need for treatment of NAS.

SMART AIM

By increasing identification of and compassionate withdrawal treatment for full-term infants born with Neonatal Abstinence Syndrome (NAS), we will reduce length of stay by 20% across participating sites by June 30, 2015.

KEY DRIVERS

- Prenatal Identification of Mom
- Improve recognition and non-judgmental support for Narcotic addicted women and infants
- Attain high reliability in NAS scoring by nursing staff
- Optimize Non-Pharmacologic Rx Bundle
- Standardize NAS Treatment Protocol
- Connect with outpatient support and treatment program prior to discharge
- Partner with Families to Establish Safety Plan for Infant
- Partner with other stakeholders to influence policy and primary prevention.

INTERVENTIONS

- All MD and RN staff to view “Nurture the Mother- Nurture the Child”
- Monthly education on addiction care
- Fulltime RN staff at Level 2 and 3 to complete D’Apolito NAS scoring training video and achieve 90% reliability.
- Swaddling, low stimulation.
- Encourage kangaroo care
- Feed on demand- MBM if appropriate or lactose free 22 cal formula
- Initiate Rx If NAS score > 8 twice.
- Stabilization/ Escalation Phase
- Wean when stable for 48 hrs by 10% daily.
- Establish agreement with outpatient program and/or Mental Health
- Utilize Early Intervention Services
- Engage families in Safety Planning.
- Provide primary prevention materials to sites.

Project Name: OPQC Neonatal NAS
Project Leader: Walsh
Revision Date: 12/30/13
OPQC NAS AIM Statement

• By increasing identification of and compassionate withdrawal treatment for full-term infants born with Neonatal Abstinence Syndrome (NAS), we will reduce length of stay by 20% across participating sites by June 30, 2015
How will we accomplish our AIM?

• Develop and implement a standardized process for the identification, evaluation, treatment and discharge management of an infant with neonatal abstinence syndrome.
  – Standardization of Scoring Tool; improve consistency in use of Modified Finnegan Tool with D’Apolito video
  – Standardization of protocol bundles
  – Small tests of change (PDSA’s) towards implementing standardized protocol into Ohio hospitals

• Create a culture of compassion, understanding, and healing for the mother infant dyad affected by the problem of neonatal abstinence syndrome.
  – Nurture the Mother-Nurture the Child video
# Moving Towards a Standardized Approach

<table>
<thead>
<tr>
<th></th>
<th><strong>OCHA Protocol</strong></th>
<th><strong>OPQC Aggregate</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Scoring Tool</strong></td>
<td>Modified Finnegan; with a 90% or greater inter-rater reliability</td>
<td>79% use a Modified Finnegan; 71% of the teams have trained their nursing staff (inter-rater)</td>
</tr>
<tr>
<td><strong>Non-Pharm Bundle</strong></td>
<td>Swaddle, Comfort, MBM or consider low lactose, 22 kcal</td>
<td>100% of teams do at least one element of the bundle</td>
</tr>
</tbody>
</table>
| **Initiate**             | NAS score:  
> 8 q3h x 2 (twice)  
> 12 x 1 (once) | 46% use the OCHA protocol guidelines to initiate pharmacological treatment     |
| **Pharmacologic Bundle** | Drug: Morphine/Methadone  
0.05 mg/kg PO                                                 | 92% use Morphine(58%) OR Methadone(33%) as their primary medication; 46% start 0.05 mg/kg |
| **Escalate**             | If ≥ 12, increase dose 0.02 mg/kg                           | 29% increase dose 0.02 mg/kg                                                      |
| **Stabilize**            | No increase for 48 hrs.                                     | 38% hold for 48 hrs.                                                              |
| **Wean**                 | 10% of max dose daily                                       | 38% weaned by 10% daily                                                           |
| **Discharge**            | 48 hours off Morphine; 72 hours off Methadone               | 46% discharged 48 hrs. off drug                                                   |
Model for Improvement

What are we trying to accomplish?

How will we know that a change is an improvement?

What change can we make that will result in improvement?

Act  Plan
Study  Do
OPQC NAS Project
Collaborative Aggregate
Percent Infants that Received ANY Non Pharmacologic Elements Before Drug Treatment

n=Denominator, Nm=Number of NICUs included in the denominator

Monthly Percent
Baseline (99.1%)
Goal (100%)
OPQC NAS Project
Collaborative Aggregate
Percent Non Pharmacologic Bundle Compliance
n=Denominator, Nm=Number of NICUs included in the denominator

Monthly Percent
- Baseline (37.1%)
- JUL14 Centerline (58.4%)
OPQC NAS Project
Collaborative Aggregate

Percent Infants that Received Pharmacologic Treatment

n=Denominator, Nm=Number of NICUs included in the denominator

Desired direction of change

Monthly Percent
Baseline (47.7%)
OPQC NAS Project
Collaborative Aggregate
Percent Pharmacologic Bundle Compliance

n=Denominator, Nm=Number of NICUs included in the denominator

Monthly Percent
Baseline (45.9%)
Goal (95%)
OPQC NAS Project
Collaborative Aggregate
Average Length of Opiate Treatment
n=Denominator, Nm=Number of NICUs included in the denominator

Average (Days)

- Monthly Average
- Baseline (16.3 days)
OPQC NAS Project
Collaborative Aggregate

Average Length of Stay for Pharmacologically Treated Babies

n=Denominator, Nm=Number of NICUs included in the denominator

Average (Days)

Monthly Average
Baseline (20.6 days)
Potential Public Health Implications:

• **ALL** narcotics cause neuronal apoptosis-programmed cell death.
• Goal is humane withdrawal without harm from treatment.
• If all Ohio centers could reduce their length of treatment to that of best performer
• Reduction of 2100 days of narcotic exposure and 2100 hospital days annually
• National spread…..?
We Have to Move Upstream!
Summary

• Prenatal opiate exposure is on the rise
• Little randomized trials exist to determine “best” therapy
• The Ohio protocol works
  – Decreases Opiate exposure
  – Decreases length of stay
  – Empowers parents in the care of their child
• Resources available on our website:
  – www.opqc.net
The OPQC NAS Project is funded by The Ohio Department of Medicaid
Questions/ Discussion
Thank you