Neonatal Abstinence Syndrome
Treatment Innovations

National and Local Trends
Objectives

1. Review the range of accepted pharmacologic treatments for the treatment of NAS.
2. Describe and discuss the environmental treatments for the treatment of NAS and its impact on medical treatment.
3. Review the latest literature describing reductions in the length of stay for patients with NAS.
NAS Epidemiology


- 2004 -> 2013: NICU NAS admissions increased from **7 to 19 per 1000 admissions**
- Median LOS increased from **13 days to 19 days**
- Percentage of NICU days attributed to NAS increased from **0.6% to 4%**
NAS Epidemiology

  - Kids’ Inpatient Database and Nationwide Inpatient Sample, 2009 vs. 2012
  - NAS in 3.4 -> 5.8 per 1000 hospital births
  - Hospital charges:
    - $732 million -> $1.5 billion
Why do we treat NAS?

• Allow for adequate feeding.
• Allow for maternal-child bonding
• Reduce suffering.
• Are there long-term sequelae of under-treated or un-treated withdrawal?
• Are we treating ourselves, our staffs?
Competing Goals of Treatment

- Shortest possible time on medications
- Shortest possible hospital stay?
- Least suffering, evidence of withdrawal?
- Achieving infant ADLs
  - Consoling, feeding, growing, sleeping, maternal-child bonding, development …
Drugs of abuse to which the neonate may be exposed

• Narcotics*
• Amphetamines*
• Cocaine*
• Nicotine
• Alcohol
• Barbiturates

• Hallucinogens
• Inhalants
• Marijuana*
• Meprobamate

* Substances for which studies have documented adverse effects on newborn behavior, development, EEGs, etc.
Non-narcotic drugs causing withdrawal-like behaviors

- Alcohol*
- Barbiturates
- Caffeine
- Chlordiazepoxide
- Clomipramine
- Benzodiazepines
- Ethchlorvynol
- Glutethimide
- Hydroxyzine
- Meprobamate
- SSRIs*
NAS Pathophysiology

- Opioids **inhibit the release of noradrenaline** at synaptic terminals.
- Withdrawal of opioids cause an increase in the release of noradrenaline with concomitant stimulatory effects in the areas where opioid receptors are concentrated – the **CNS and the gastrointestinal tract**.
- Timelines
  - Heroine withdrawal: within 24 hours
  - Methadone withdrawal: within 24-72 hours
  - Broad time range of withdrawal due to multiple exposures: alcohol, nicotine, SSRIs, marijuana, etc.
Methadone vs. Buprenorphine


- Double-blind, double-dummy, flexible-dosing, randomized, controlled study comparing buprenorphine and methadone in 175 women at eight international sites.
- 131 out of 175 neonates followed to end of the study.
- Primary outcomes: number requiring treatment, peak NAS score, total morphine treatment dose, LOS, neonatal head circumference.
Jones et al …

- Treatment discontinued by 18% of the methadone group versus 33% of the buprenorphine group.
- Buprenorphine group required significantly less morphine: 1.1 mg vs. 10.4 mg (p<0.00091).
- Buprenorphine group had a significantly shorter hospital stay: 10 vs. 17.5 days (p<0.0091).
- Buprenorphine group had significantly shorter medication duration: 4.1 vs. 9.9 days (p<0.003).
- No other significant differences in primary outcomes.
Evidence basis for treatment?


- Range of treatments studied/used: tincture of opium / paregoric, morphine sulfate, methadone, clonidine, phenobarbital, benzodiazepines, clonidine, phenothiazines.
Evidence basis for treatment?

• No real comparisons of morphine vs. methadone
  ○ NEJM:
    Morphine used in 74% (2004-5) to 87% (2012-13)
• Hopkins group: standard clonidine adjunct.
  ○ 8% nationally
• Kentucky group: morphine vs. clonidine.
TG-MB Approach

- Infant drug testing: urine, meconium
- Observe up to 96 hours for withdrawal
- Early transfer to MB / maternal orientation
- Rule of 24 = 2 scores of 12 or 3 scores of 8
- Standard order set
  - Pharmacy consult versus MD-controlled wean
  - Establish starting dose: morphine 50 mcg/kg
  - Begin wean within 48 hours
  - Consider methadone transition.
  - Clonidine for patients on > 200 mcg/kg morphine
  - Wean 10% of daily dose daily
  - Discharge after 24-48 hours off drug treatment
Non-Drug Supportive Care

• Maternal-child focus
• Rooming in
• Skin-to-skin
• Breastfeeding
  • Scant methadone in breast-milk
• Flexible Feeding Schedule

• 22 kcal formula
• Low-stimulation
• ‘Trauma-centered care’
• Parent contracts?
• Volunteers?
Modified Finnegan’s

- Hyperactive Moro
- Tremors
- Muscle tone
- Excoriation
- Myoclonus
- Convulsions
- Sweating
- Hyperthermia
- Tachypnea
- Poor feeding

- Duration and quality of cry
- Length of sleep after feeds
- Yawning
- Mottling
- Nasal stuffiness
- Sneezing
- Nasal flaring
- Excessive sucking
- Spit-ups vs. projectile
- Loose/watery stool
Finnegan’s Pit-falls

• Cross-over with normal newborn behaviors
• Staff-training / Inter-observer reliability
  • D’Apolito Reliability Training System
• Parental presence?
• Scoring before feeds?
• Increased scores after 3 weeks of age (add 2) (Zimmerman-Bauer et al. Finnegan neonatal abstinence scoring system: normal values for the first 3 days and weeks 5-6 in non-addicted infants. *Addiction*. 2010: 105: 524-38.)
## MB Weaning

<table>
<thead>
<tr>
<th>Site</th>
<th>Proceed with wean</th>
<th>No dose change</th>
<th>Backslide / Rescue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Ohio</td>
<td>all scores &lt; 9</td>
<td>rising trend, or any score &gt; 8</td>
<td>2 consecutive scores &gt; 8</td>
</tr>
<tr>
<td>Cincinatti</td>
<td>average score &lt; 8 in past 24 hours</td>
<td>average score 8-12 in past 24 hours</td>
<td>average score &gt; 12 in past 24 hours</td>
</tr>
<tr>
<td>Vermont</td>
<td></td>
<td></td>
<td>if score 9-12, repeat score after a feed before acting</td>
</tr>
<tr>
<td>Yale</td>
<td>Subjective success with infant being able to eat, sleep and console.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swedish</td>
<td>scores &lt; 8</td>
<td></td>
<td>2 consecutive scores &gt; 7 and no response to calming</td>
</tr>
<tr>
<td>DOH</td>
<td>scores &lt; 8</td>
<td></td>
<td>2 scores &gt; 8 within 2 hours</td>
</tr>
<tr>
<td>PICC</td>
<td>stable scores &lt; 9 and no scores &gt; 12 in past 12 hours</td>
<td></td>
<td>2 consecutive scores &gt; 9, or 2 scores &gt; 12 in 12 hours</td>
</tr>
<tr>
<td>Mary Bridge</td>
<td>average score &lt; 9 in past 24 hours</td>
<td>average score 9-11 in past 24 hours</td>
<td>average score 9-11 AND single core &gt; 11</td>
</tr>
</tbody>
</table>
MB Data - VON

- February → August, 2014
  - LOS: 29 days → 16 days
  - NICU LOS: 25 days → 2 days
  - Treatment Duration: 25 days → 10 days
  - Breastmilk use: 25% → 50%
Early Discharge / Home Medication

- VON: Up to 33% discharged on medications – mostly phenobarbital
- Initial MB plan: discharge on methadone similar to many infants and children who are PICU graduates
- Barriers to home methadone:
  - Opposition from pharmacies and state foster system
  - Care delay during methadone to morphine transition
Evidence-Based Treatment?

- WA state survey / regional standard of care
- Vermont-Oxford Network VON
  - 21% cared for on med-surg floor (vs. nursery/NICU)
- Innovations to reduce LOS
  - MB and elsewhere = get patients out of NICU
  - Ohio = Finnegan’s coaching
  - Yale = ADLs over Finnegan’s
  - A few centers … narcotics at discharge
  - Use of non-narcotics medications - Kentucky
  - Use of adjunctive medications - Hopkins

- 80 newborns studied at two Hopkins / Baltimore hospitals
- Oral opium tincture given to all infants per protocol after 2 Finnegan’s scores ≥ 9
- In addition to narcotic, 40 infants also given placebo versus 40 infants also given clonidine
Agthe et al...  

- **Twice as many infants (40% vs. 20%)** in the placebo group required higher opium doses compared with the clonidine group.  

- **‘Treatment failure’ occurred in 12.5%** of infants in the placebo group compared with no failures in the clonidine group.  

- Median LOS in the clonidine group was **27% shorter**: 11 days (95% CI 8-15 days) versus 15 days (95% CI 12-17 days) in the placebo group.

- 31 newborns from a Lexington NICU, 15 treated with morphine and 16 treated with clonidine.
- **Morphine median LOS = 39 days.**
- **Clonidine median LOS = 28 days.**
- **Critique:** Both groups’ LOS significantly longer than ours and most other recent studies
Ohio NAS Performance Improvement


- Nationwide Children’s Hospital, Columbus, OH
- Standardized protocol, improved staff communication, D’Apolito training system
- 92 infants studied 2007-2012, 23 of those from a baseline period 2007-2009
Ohio NAS QI Timeline

• 2004-2008 baseline: LOS 36 days
  o Six-fold increase in NAS diagnoses
• 2009 methadone protocol: LOS ↓ 31 days
• 2009 NAS Taskforce convened
• 2009 Oral morphine protocol: LOS ↓ 27 days
• 2012 nursing re-training: LOS ↓ 18 days
Yale Approach (un-published)

- LOS decreased from 29 to 7.5 days
- Buprenorphine-exposed infants rarely need meds
- Clonidine per Hopkins model
- ADLs over Finnegans
  - Feeding adequately (working towards growth)
  - Sleep for 1 hour (score = 2 on Finnegans)
  - Console-able
  - Use of volunteers?
- Aggressive weaning, up to BID
- Rapid weaning of clonidine after morphine
# MB Financials: 2013 – 6/2015

<table>
<thead>
<tr>
<th>Year</th>
<th>Site</th>
<th>Encounters</th>
<th>ALOS</th>
<th>Avg. direct cost</th>
<th>Avg. RN cost</th>
<th>Avg. Rx cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>TG</td>
<td>95</td>
<td>10.8</td>
<td>$12,500</td>
<td>$27,437</td>
<td>$1,000</td>
</tr>
<tr>
<td></td>
<td>IPS</td>
<td>9</td>
<td>9.0</td>
<td>$29,412</td>
<td>$13,675</td>
<td>$839</td>
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<tr>
<td></td>
<td>GS</td>
<td>59</td>
<td>12.1</td>
<td>$13,045</td>
<td>$8,549</td>
<td>$242</td>
</tr>
<tr>
<td>2014</td>
<td>TG</td>
<td>119</td>
<td>8.9</td>
<td>$10,518</td>
<td>$21,883</td>
<td>$902</td>
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<tr>
<td></td>
<td>IPS</td>
<td>24</td>
<td>10.7</td>
<td>$11,232</td>
<td>$10,528</td>
<td>$331</td>
</tr>
<tr>
<td></td>
<td>GS</td>
<td>68</td>
<td>15.9</td>
<td>$16,972</td>
<td>$19,955</td>
<td>$453</td>
</tr>
<tr>
<td>2015</td>
<td>TG</td>
<td>52</td>
<td>7.4</td>
<td>$10,822</td>
<td>$23,254</td>
<td>$802</td>
</tr>
<tr>
<td>YTD</td>
<td>IPS</td>
<td>18</td>
<td>12.9</td>
<td>$15,283</td>
<td>$13,765</td>
<td>$382</td>
</tr>
<tr>
<td></td>
<td>GS</td>
<td>27</td>
<td>15.3</td>
<td>$16,026</td>
<td>$14,098</td>
<td>$461</td>
</tr>
</tbody>
</table>
**TG-MB Transfers – All NAS**

<table>
<thead>
<tr>
<th>Mary Bridge transfers from Tacoma General</th>
<th>2013</th>
<th>2014</th>
<th>Variance from 2013</th>
<th>June 2015 YTD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encounters</td>
<td>MB</td>
<td>TG</td>
<td>Total</td>
<td>MB</td>
</tr>
<tr>
<td>ALOS (days)</td>
<td>5.0</td>
<td>6.6</td>
<td>11.5</td>
<td>11.5</td>
</tr>
</tbody>
</table>

**TG-MB Transfers – Primary NAS**

<table>
<thead>
<tr>
<th>Mary Bridge transfers from Tacoma General</th>
<th>2013</th>
<th>2014</th>
<th>Variance from 2013</th>
<th>June 2015 YTD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encounters</td>
<td>MB</td>
<td>TG</td>
<td>Total</td>
<td>MB</td>
</tr>
<tr>
<td>ALOS (days)</td>
<td>5.0</td>
<td>6.6</td>
<td>11.5</td>
<td>12.2</td>
</tr>
</tbody>
</table>
LOS trends

2013 2014 2015 YTD

TG
MB
GS
TG+MB
Un-realized Goals / Next Steps

- Increased use of clonidine.
- Simplifying the score versus improving Finnegan’s inter-observer reliability
- Separating data by type of maternal drug uses.
- A sane marijuana policy? Suggestions?
- Better use of volunteers?
- Steady Reduction in length of stay
  - Nature of maternal drug use?
  - Institutional issues: scoring, pharmacy consult, staff fatigue?
Take Home Points

• NAS is on the rise, and hopefully we can ultimately reverse that trend
• The literature on the most optimal treatment for NAS is limited, but potentially increasing.
• Length of stay varies widely, with many confounding variables, but a number of centers have been able to reduce it.
Bibliography


• Zimmerman-Bauer et al. Finnegan neonatal abstinence scoring system: normal values for he first 3 days and weeks 5-6 in non-addicted infants. Addiction. 2010: 105: 524-38.)
Bibliography

• Agthe et al. **Clonidine as an Adjunct Therapy to Opioids for Neonatal Abstinence Syndrome: A Randomized Controlled Trial.** *Pediatrics* 2009; 123(5): e849-56.


Questions

• For which non-narcotic medication is there evidence that its use reduces length of stay for NAS?
  a) Phenobarbital
  b) Diazepam
  c) Clonidine
  d) Ativan

• All of the following non-pharmacologic interventions are used to treat NAS, EXCEPT:
  a) Kangaroo / skin to skin maternal contact
  b) A strict q2-3 hour feeding schedule
  c) Breastfeeding
  d) Low-stimulation environment
Therapeutic Considerations in Caring for Infants Born Substance-Exposed

Alta Kendall, ARNP NNP-BC
Pediatric Medical Group of Washington
In service to Multicare Tacoma General Neonatal Intensive Care Unit
Objectives

• Identify terminology related to substance-exposed newborns.
• Discuss assessment, symptomology, and therapeutic approaches in care of exposed infants.
• Describe components of withdrawal management.
• NAS – Neonatal Abstinence Syndrome
• SEN - Substance Exposed Newborn
• CDN - Chemically Dependent Newborn
• FAS - Fetal Alcohol Syndrome
• FASD – Fetal Alcohol Spectrum Disorder
Nuanced Terminology

• **State Regulation**: ability of the substance exposed infant to accommodate or adapt to external or environmental inputs/stimulation.

• **Feeding Intolerance**: beyond physical tolerance and retention of feedings, the inability to organize functional sucking and swallowing.
Please Refrain

• These infants are not born *addicted* to drugs: avoid inaccurate hyperbole, the reality is bad enough!
Accuracy in Description

• Exposed early to substances, these infants are drug and substance AFFECTED,

they are experiencing symptoms of substance withdrawal.
Assessment

• Infants demonstrate individualized behaviors and responses based on exposures and tolerance.

• Common patterns are recognizable.
Assessment

• Strong assessment skills include decoding macro and micro manifestations:

  high-pitched cries, seizures
  yawning, only brief periods at rest
Symptomology

• CNS – inability to regulate state:
  common presentation

  tolerates only minimal stimulation  with rapid escalation

  high-pitched or continuous crying
Symptomology

- Central nervous system: hyperreflexia – often Moro
  increased muscle tone
tremor, jittery, myoclonic jerking
excoriation from surface contact
seizures, convulsions
Symptomology

- Metabolic, vasomotor, respiratory:
  - sweating, fevers
  - excessive yawning, sneezing
  - nasal congestion/stuffiness
  - mottled skin
  - increased RR, nasal flaring
Symptomology

• Gastrointestinal:

  excessive, disorganized sucking
  inability to complete a feeding
  regurgitation, projectile vomiting
  abnormal stooling, flatus
Therapeutic Caregiving

• Individualized to infant’s presentation
• Provided by trained caregivers
• Recognizes symptoms related to type of drug exposure presents
• Adapt basic principles of handling
Therapeutic Touch

• Assist infant to gain body control:
  space: swaddling
  motion: slow, rhythmic swaying
  avoid rocking
Therapeutic Touch

• Assist infant to gain body *control*:
  
  vertical rocking: infant facing away
cupped patting: rhythmic
Therapeutic Mindfulness

• Be aware of your state regulation!

• Monitor for rising anxiety levels.

• Avoid unnecessary motion/activity.
Therapeutic Environment

• Minimize distractions.

• Voices soft/low.

• Reduce background noise volumes

• Dim lighting.
Therapeutic Feeding

• Provide setting of low stimulus

• Minimize interruptions

• Swaddle infant for feeding session
Therapeutic Feeding

- Avoid attempting to feed while infant is frantic
  assist infant to achieve state regulation

monitor for disorganized sucking
Considerations

• Substance-affected infants:
  
  are difficult to care for
  
  are at increased risk for abuse
Fragile – Handle with Care
Webviewer Instructions

Successful completion of post test is required to obtain a certificate of participation.

Cut and paste this link into your browser to access the post test.

http://www.surveygizmo.com/s3/2360369/WCGR1015