Children’s Specialized Hospital

Neonatal Abstinence Syndrome (NAS)

A Pharmacologic and Rehabilitation Program that Promotes Narcotic Weaning and Autonomic Regulation Necessary for Infant Development

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Objectives

- Define Neonatal Abstinence Syndrome
- Identify some of the signs and symptoms of withdrawal
- List the medical management for an opiate exposed infant
- Discuss the rationale for therapeutic intervention for a drug exposed infant
Setting the Stage for High Risk Newborns

- Infections
- Diabetes, Obesity
- IVF (superovulation) (10-15%)
- Pregnancy Induced Hypertension
- Maternal age: <17yrs and >35yrs
- Previous history of prematurity
- Uterine and Placental Indicators
- Illegal Drugs
- Prescription Medication
- Drinking, Smoking
Epidemiology: Public Health Issue

• 2009: Rate of NAS in the United States – 3.9/1,000 (out of 4.1 million live births per year)

• > 41% of pregnant women report illicit drug use.
• > 71% of pregnant women report use of prescribed pain medications
• > 10% of pregnant women report use of prescribed psychoactive medications

• Withdrawal signs develop in 55-94% of exposed newborns.

• 8% of teens, ages 12-17 years, use prescription drugs.
  • Pain medication: Vicodin, Oxycontin
  • Antidepressant: Prozac, Zoloft
  • Anti-Anxiety: Xanax
  • Stimulants: Adderal, Converta

* 2010: National Institute on Drug Abuse
Cost of Care

• National Aggregate: 2009
  • Mean Hospital Charges in 2009: $53,400 ($1,780/day)
  • 78% of cost covered by Medicaid*

* 2010: National Institute on Drug Abuse
• Constellation of behavioral and physiological signs and symptoms that occur in the newborn after the abrupt cessation of substances, most notably, Opioids.

  • NAS due to prenatal maternal drug use that results in withdrawal symptoms in the newborn.

  • NAS due to discontinuation of medications, such as Fentanyl or Morphine, used for pain therapy in the newborn.

* Neonatal Drug Withdrawal, AAP 2012
Drugs Frequently Associated with NAS / Withdrawal

• Opiates and Narcotics
  • Fentanyl, Morphine, Hydromorphone, Buprenorphine, Heroin, Methadone (Half-Life 24-72 Hours)
  • Codeine, Oxycodone, Pentazocine, Propoxyphene

• Other Drugs
  • Barbituates (Half-Life 36-96 Hours)
  • Cocaine, Amphetamines (Half-Life <24 Hours)

• SSRI’s, Antihistamines
Pathophysiology

• Illicit drugs can cause addiction in mother and physical dependence in the newborn, with passage of drugs across placental and CNS barrier.

• Drugs such as opiates cross maternal to fetal circulation quite readily, where they quickly accumulate due to immature liver metabolism and renal excretion.

• Abrupt discontinuation of drug at birth results in withdrawal in the newborn mitigated by increased Adenylyl cyclase activity with an abrupt rise in norepinephrine and subsequent autonomic symptomatology.

• Withdrawal is a function of half life: the longer the half life, the later onset of withdrawal.
• Urine toxicity: Only provides maternal drug use history a few days prior to delivery up to 72 hours after birth.

• Meconium analysis: Can be used to detect maternal opioids and cocaine exposure after 1st trimester up to 72 hours after birth. (Collected before contamination with formula).

• Hair analysis: Can indicate maternal use in the last trimester and up to 3 months postnatal life (Research laboratories).

• Umbilical cord tissue (immunoassay): Easy and rapid collection may foster its use.
Proposed Hypothesis for Expression of NAS Symptoms

• Methadone affects maternal vagal tone responsiveness.

• Fetal adaptation within the uterine environment to methadone induced changes in maternal vagal tone correlate with later newborn dysregulation of autonomic nervous system.

• Newborn autonomic instability may be moderated by both genetic and epigenetic factors. (Jansson, 2007)
**Clinical Presentation of Autonomic Dysregulation**

- **CNS**
  - High pitched cry, restlessness, sleeps <1-3 hours.
  - Hyperactive reflexes, tremors, myoclonic jerks.
  - Hypertonia, convulsions, frequent sneezing, yawning.

- **Vasomotor**
  - Sweating, mottling, temperature instability, apnea, fever, excoriation of skin.

- **GI Disturbances**
  - Poor feeding, excessive sucking or rooting,
Finnegan Scale

• Scale assesses 21 signs of withdrawal, based on the following domains:
  • CNS
  • Vasomotor
  • GI Disturbances
• Start pharmacotherapy for 3 scores of $>8$
• Wean medications for 3 scores of $<4$
• Score of 1 for least adverse effect.
• Score of 3 for most adverse effect.
Pharmacotherapy

- No optimum, absolute treatment established. Treat with medications in same drug class causing withdrawal.

- Opiate related and polydrug withdrawal.
  - Morphine: full mu receptor agonist (0.03mg/kg q 4); shorter acting
  - Methadone - full mu receptor agonist, longer acting, less fluctuation in levels at less frequent intervals; 0.05mg/kg q 6
  - Buprenorphine - Buprenorphine-partial mu receptor agonist; shorter duration of treatment but potential ceiling effect in patients that may require adjunct therapy.
  - Phenobarbital, -poly substance use; prolonged half life; adjunct therapy rather than primary treatment.
  - Benzodiazepines for alcohol withdrawal, adjunct for calming.
  - Clonidine as primary or adjunct therapy; reduces global sympathetic tone. less efficacious than opioids, 1 report SVT,3 Myocarditis,1 SIDS (Leikin Clinic Toxicol, 2009)
  - NOTE: Tincture of opiate (0.1ml / kg q 4) and paregoric no longer recommended (due to additives, camphor, ethanol - 46%; benzoic acid.

• Long term mortality rate is low.

• Increased risk of SIDS:
  
  • 3.7 fold increase risk in methadone exposed infants.
  
  • 2.3 fold increase in cocaine exposed infants.

• Seizures

  • 2-11% incidence of seizures in infants withdrawing from opioids. (Lacroix. Addiction, 2004)

• Breastfeeding encouraged except with Buprenorphine (buprenorphine and
Children’s Specialized Hospital: Infant Rehabilitation Program for therapy based interventions for infant withdrawal.
• Confounding variables such as withdrawal of opioids, genetic dysmorphisms (adult addiction) and environmental factors may all play a role in the pathogenesis of Neonatal Abstinence Syndrome and subsequent developmental issues.

• Fetal adaptation to unfavorable uterine environment may present as maladaptive or inappropriate physiologic and/or behavioral responses to extra uterine life. (Jansson)

• That is, vulnerable prenatal experiences may shape / moderate post natal autonomic and developmental outcome.

Lester, 2011
Pathophysiology of Developing Systems: Rationale for Rehabilitation

- Developing Neuronal Systems, especially opioid exposed, need experienced assessment, stimulation and interventional therapy to positively impact on development of the newborn beyond the pharmacologic treatment.
  - Sensory recruitment of muscles
  - Motor patterns
  - Motor planning
  - Cognitive processing
  - Social interaction and integration
  - Guidelines for opioid addiction in adults recommend comprehensive modalities: pharmacotherapy, behavioral modifications and psychosocial therapy. (Amer Soc Addiction Medicine, 2001)
Healing – it comes from the heart
Healing Environment
A Place Where Moms Can Relax
Aquatics for Tots: Soothing sensory input for calming, tone management and awareness.
Motor Patterns: Vital Stimulation

• Program to enhance feeding outcomes in medically fragile infants.
Motor Planning: Computer Mediated Learning

• Interactive modality stimulates infant motor response to sensory input.
Cognitive re-enforcement: Computer Based Learning
Sensory Recruitment of Muscles: Infant Massage
Social Interaction and Integration: Group Therapy
Self-calming strategies, music and positioning aids
Sensory stimulation for cognitive processing
Nutrition

- Small, frequent feedings to provide 150-220 kcal/kg
- Monitor growth velocity
- NAS exacerbates symptoms of GER
- Consider high calorie formulas when infant irritability or fatigue interferes with feeding
- Consider tube supplementation in infants with dysphasia
- Feeding specialist: When required
- WIC Program registration.

- Breastfeeding is not contra-indicated in mothers on Methadone, but not recommended in mothers on Suboxone by the manufacturer.
Coordination of Home Services

- Physician services (PMD, Specialists, Apnea Testing)
- Nursing (CPR and Formula Training)
- Home Nursing Services or Medical Day Car
- Medical or Positioning equipment
- Car seat safety check
- WIC referral and registration
- Provide medications prior to discharge
**NAS Program Outcomes: 2010 – 2012**

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Positive Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opiates</td>
<td>14/33</td>
<td>42% of patients</td>
</tr>
<tr>
<td>Methadone</td>
<td>17/33</td>
<td>52% of patients</td>
</tr>
<tr>
<td>Cocaine</td>
<td>4/33</td>
<td>12% of patients</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>4/33</td>
<td>12% of patients</td>
</tr>
<tr>
<td>Polypharmacy including Subutex</td>
<td>6/33</td>
<td>20% of patients</td>
</tr>
</tbody>
</table>

- Infant Drug Screen: 32/33 97% Positive
<table>
<thead>
<tr>
<th>Medication on Admission:</th>
<th>33/33</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone:</td>
<td>17/33</td>
<td>52% of patients</td>
</tr>
<tr>
<td>Morphine:</td>
<td>7/33</td>
<td>21% of patients</td>
</tr>
<tr>
<td>Morphine and Ativan:</td>
<td>7/33</td>
<td>21% of patients</td>
</tr>
<tr>
<td>Ativan:</td>
<td>1/33</td>
<td>6% of patients</td>
</tr>
<tr>
<td>Phenobarbitol:</td>
<td>1/33</td>
<td>3.4% of patients</td>
</tr>
</tbody>
</table>

• No Medication at Discharge: 32/33 97%

• Outpatient therapy programs have shorter hospital stay, but longer
### NAS Program Outcomes: 2010 - 2012

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Pneumogram</td>
<td>32/33</td>
<td>97%</td>
</tr>
<tr>
<td>Age appropriate weight gain</td>
<td>33/33</td>
<td>100%</td>
</tr>
<tr>
<td>Calorie dense formula</td>
<td>14/33</td>
<td>34%</td>
</tr>
<tr>
<td>Discharge Disposition</td>
<td>ALOS</td>
<td>4-6 weeks</td>
</tr>
<tr>
<td>Home</td>
<td>25/33</td>
<td>72%</td>
</tr>
<tr>
<td>Foster</td>
<td>5/33</td>
<td>17%</td>
</tr>
<tr>
<td>Adoption</td>
<td>1/33</td>
<td>3.4%</td>
</tr>
<tr>
<td>Other facility</td>
<td>1/33</td>
<td>3.4%</td>
</tr>
</tbody>
</table>

*Note- average duration of treatment in adult- 6 mos-2 years (Nicholls. 2010)*
- Total Motor Composite: 20% low average – Refer to EIP
- Cognition: 15% low average range – Refer to EIP
- Language: 40% low average range – Refer to EIP
  10% significantly delayed – Refer to EIP
- Feeding: 5-7% refer to Outpatient Feeding Therapy

* Gestational age > 36 weeks
** Mean age: 55 days of life
Outcomes: Program Services to Keep the Gains

- CSH Developmental Specialty Clinic and Follow-up
- Bayley Assessment at regular intervals
- EIP services for therapy
- 11 sites for OP therapy
- DCP&P to monitor family environment
- VNA - continued evaluation of patient
- CSH Pediatric Practice for patient and sibling
- CSH Medical Day Care
Outcomes: Press Ganey Parent Satisfaction

• PT, OT, Speech and Recreational Therapies all scored higher than the 94\textsuperscript{th} percentile with respect to parent satisfaction, compared to other pediatric facilities.

• \textbf{100} percent of parents were confident with their training and could independently render their child’s care.
Children’s Specialized Hospital: Extra Care. Extraordinary Results
References


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