The Impact of Maternal Opioid Use on Pregnancy, Infant Withdrawal and Developmental Outcomes

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Objectives

- Define Neonatal Abstinence Syndrome and Infant Withdrawal
- Understand the Changing Demographics of Maternal Substance Use
- Describe Benefits of an Inpatient Neonatal Program: Detoxification and Rehabilitation
- Discuss Infant Developmental Outcome Measures
- Future areas of research
Setting the Stage for High Risk Pregnancies

- Infections
- Diabetes, Obesity
- IVF (superovulation) (10-15%)
- Pregnancy Induced Hypertension
- Maternal age; <17 yrs and >35 yrs
- Previous history of prematurity
- Uterine and Placental Indicators
- Alcohol, cigarettes, marijuana
- Illicit Drugs
- Prescription meds
Public Health Issue: Mother and Child

- 300% increase in overall sales of prescription painkillers
- 33% increase use of prescription analgesics in pregnant women
- Opioid exposure in high risk pregnancy called for guidelines among national agencies that protect the pregnant mother, fetus and newborn with NAS.*
- MAT with methadone or buprenorphine was recognized as safe and necessary to prevent maternal relapse and infant demise or IUGR.**
- Overarching principles developed for identification and treatment of pregnant women with SU and their newborns as well as protection against discrimination, stigmatization and criminalization.***

Sources:
* 2012 — NCSACW
** 2012 — Committee Opinion ACOG;ASAM,AAP
*** 2014 — World Health Organization
2009 — National Survey on Drug Use. US Dept. of Health and Human Services
Identification of Maternal Substance Use

- Interview Screening such as the 4P’s
- SU should be routine part of interview
- Develop trust, respect, nonjudgmental environment
- Education of risk during pregnancy and to fetus
- Lab testing, urine tox as follow up to interview screen (notify woman ahead of time)
- Refer to treatment centers; offer MAT; make appt in office

Source: 2012—Committee Opinion ACOG
Epidemic Rise of Neonatal Drug Withdrawal

- Rate: 4.4/1000 live births (ICD 9 CM code 779.5)*
- 71% report use of prescription pain medication
- 15.6% pregnant women report illicit drug use
- 10% pregnant women report use of prescription psychoactive meds
- 8% teens age 14-17 report use of prescription medications:
  - Pain meds – Vicodin, Oxycontin
  - Antidepressant – Prozac, Zoloft
  - Anti-anxiety – Xanax
  - Stimulants – Adderal, Concerta

Source: * Patrick et al., 2012
Hospital Care Expenditures

- National Aggregate 2012; hospital costs increased from $253 to $595 million since 2006
- Increase maternal hospital stays related to SU – 7.9/1000
- Increase neonatal hospital stays related to withdrawal increased by 71%
- Infants Mean LOT methadone vs. morphine – 17.4 vs. 22.2 days
- Infants Mean LOS methadone vs. morphine – 21 vs. 25 days**
- 20% neonatal stays related to withdrawal also had low birth weight
- 79.9% cost covered by Medicaid*


Source:  
** Patrick, 2014  
* Patrick et al., 2012
Neonatal Abstinence Syndrome

- Constellation of signs and symptoms that occur in newborns involving the central, autonomic and gastrointestinal systems after abrupt cessation of in-utero exposure to substances, especially opioids.*
- 55-94% exposed infants develop signs of withdrawal
- Not all infants will require treatment with pharmacotherapy; but all should receive non-pharmacologic interventions**

Pathophysiology of Opioid Withdrawal

Opiates and Narcotics — (naturally occurring) morphine; (synthetic agonists) like heroin, methadone, Fentanyl, Oxycontin; (partial agonist), buprenorphine, (endogenous) endorphins

- activate Mu receptors in the noradrenergic nucleus of the pons in the CNS to produce analgesia and state of euphoria; altered GI motility or autonomic hypersecretory phase
- blocks action of glutamate — primary excitatory neurotransmitter; by inhibiting release of norepinephrine
- abrupt discontinuation of maternal opioids at birth causes supernormal release of norepinephrine with autonomic, GI, and behavioral symptoms of withdrawal; sleep disturbances related to serotonin expression**

Source: Curr. Drug Safety. 2006
** Kocherlakota, 2014
Preterm Infants and Risk of NAS and Withdrawal

- Incidence and severity less extensive in preterm infants:
  - Decreased receptor development and decreased receptor sensitivity
  - Decreased cumulative exposure
  - Decreased transmission across placenta during early gestation
  - Decreased fatty tissue stores
Pharmacokinetics: Opioids*

- Withdrawal is a function of half life (neonatal liver metabolism and renal clearance); longer than adults
- Morphine-withdrawal may present 24 hours after birth, but usually 24-48 hours
- Methadone—24-72 hours after birth
- Buprenorphine—(partial agonist) 40-72 hours after birth; NAS less severe following maternal Buprenorphine (Jansson,2012)
- Benzodiazepines and barbiturates may delay withdrawal
- Poly-drug and alcohol exposure—prone to severe and prolonged withdrawal
- Symptoms of withdrawal may be delayed at least 7 days after birth
- NAS and withdrawal may be bi-phasic; initial phase lasting up to 2 weeks; followed by a relapsing course for weeks (Kocherlakota)

Source: * Kocherlakota, 2014
Cocaine and amphetamines — “EFFECT”

» Short half-life, symptoms can appear before half-life.

» Stimulate the release and block re-uptake of neuro-transmitters (norepi, serotonin, dopamine).

» CNS stimulant, rapidly crosses placenta.

» Some studies suggest exposed infants exhibit hyperactive Moro, jitteriness and sucking.

» Unresolved if cocaine limits head growth or brain development.

Studies do not support withdrawal or toxicity syndrome.
SSRI—Selective Serotonin Reuptake Inhibitors; onset 24-48 hrs

Antidepressants, Mood disorder (Prozac, Zoloft, Lexapro, Celexa)

Third trimester use linked to neonatal signs: crying, jitteriness, hypertonia, respiratory distress, feeding and sleep disturbances, hypoglycemia, seizures (toxicity)

Serotonin syndrome in adults: change in mental status, Autonomic hyperactivity, neuromuscular abnormalities

SSRI may prolong severity of infant withdrawal in Opioid using mothers

Recent reviews are inconclusive as to adverse Neurodevelopmental outcomes in newborns born to women treated with SSRI’s.

Source: De la Cuevas-Curr. Drug Saf. 2006
Toxicology

- **Urine Tox** — 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 last trimester and up to 3 months postnatal life. (Research laboratories)

- **Umbilical cord tissue (immunoassay)** — easy and rapid collection may foster its use.
Finnegan Scale to Assess Withdrawal

- CNS: seizures (11%), tremors, high pitched crying, hyper tonicity, hyperreflexia, yawning, sneezing
- Autonomic (Vasomotor): fever, sweating, nasal stuffiness or rhinorrhea, mottling, hypertension, excoriation of skin
- GI: poor sucking or feeding, vomiting, diarrhea, poor weight gain

Score of 1 for least adverse effect
Score of 3 for most adverse effect usually 3-4 hours after a feeding

Finnegan Scoring and Pharmacotherapy

- Infant scored q 2 hours after birth, then q 4
- If severity score >8 for two or more consecutive scores consider pharmacotherapy.
- Consider weaning medication every 24-48 hrs for two consecutive scores < 8; dose may be decreased by 10-20%
- Medication my be discontinued when morphine dose is < 0.04mg/kg/day or methadone <0.05mg/kg/day

| SYSTEMS | SIGNS AND SYMPTOMS | SCORE | AM 2 | 4 | 6 | 8 | 10 | 12 | PM 2 | 4 | 6 | 8 | 10 | 12 | DAILY WT. |
|---------|-------------------|-------|-----|---|---|---|----|----|-----|---|---|---|----|----|---|---------|
|         |                   |       |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
| CENTRAL NERVOUS SYSTEM DISTURBANCES | High Pitched Cry | 2     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Continuous High Pitched Cry | 3     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Sleeps < 1 Hour After Feeding | 3     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Sleeps < 2 Hours After Feeding | 2     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Hyperactive Moro Reflex | 2     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Markedly Hyperactive Moro Reflex | 3     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Mild Tremors Disturbed | 2     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Moderate Severe Tremors Disturbed | 3     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Mild Tremors Undisturbed | 1     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Moderate Severe Tremors Undisturbed | 2     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Increased Muscle Tone | 2     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Excoriation (specify area): | 1     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Myoclonic Jerks | 3     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Generalized Convulsions | 3     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Sweating | 1     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Fever < 101°F (39.3°C) | 1     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Fever > 101°F (39.3°C) | 2     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Frequent Yawning (> 3-4 times/interval) | 1     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Mottling | 1     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Nasal Stuffyness | 1     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Sneezing (> 3-4 times/interval) | 1     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Nasal Flaring | 2     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Respiratory Rate > 60/min | 1     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Respiratory Rate > 60/min with Retractions | 2     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Excessive Sucking | 1     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Poor Feeding | 2     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Regurgitation | 2     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Projectile Vomiting | 3     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Loose Stools | 2     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |
|        | Watery Stools | 3     |     |   |   |   |    |    |     |   |   |   |    |    |   |         |

<table>
<thead>
<tr>
<th>SUMMARY</th>
<th>TOTAL SCORE</th>
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<th>SCORER'S INITIALS</th>
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<th>STATUS OF THERAPY</th>
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Pharmacotherapy

No optimum, absolute treatment, though treatment with same class of drug used by mother is preferred:

- Morphine — short acting; start 0.04mg/kg/dose q 3-4 hr
- Methadone — longer acting; start 0.05 to 0.1mg/kg/dose q 6 hr
- Phenobarbital — adjunct therapy. Load 15-20mg/kg and maintenance of 3-4mg/kg/day. Monitor levels.
- Benzodiazepines — adjunct therapy for polysubstance and alcohol though not preferred for single opioid use. Dose-0.5mg/kg
- Paregoric and Tincture of Opium not recommended due to neurotoxic agents.
- Clonidine, buprenorphine isolated reports — need more studies. Naloxone precipitates seizures.

AAP Policy Statement: Neonatal Drug Withdrawal 2012; aids in self-regulatory control
Supportive Interventions and Services

- Environmental modifications; calming strategies such as gentle rocking, swaddling, therapeutic bath
- Appropriate sensory stimulation such as infant massage, lullaby, low lighting
- Parent training and handling
- Therapy to improve tolerance to handling, and developmental positions, sensory responses, improve feeding techniques
- Maximize nutritional support due to hyper metabolic state with high calorie density formula; fortified breast milk for optimum weight gain; consider gas, reflux, dysmotility
- DCPP protective agencies; WIC, EI, OP, VNA, Prescriptions, car seat
Long Term Outcomes

- Long term mortality rate is low
- Increased risk for SIDS:
  - 3.7 fold increased risk in methadone exposed infants.
  - 2.3 fold increased risk in cocaine exposed infants.
- Seizures
  - 2-11% incidence myoclonic seizures in infants withdrawing from opioids. (Lacroix. Addiction, 2004)
  - Developmental morbidity: cognitive and receptive language**

Source: Substance use during pregnancy, 2005
** Beckwith & Burke, 2014
Children Specialized Hospital

- Largest Pediatric Acute Rehab Hospital in US
- 68 inpatient beds; over 23,000 outpatient visits
- Teams - Infant Toddler; Brain injury; Spinal Cord, Chronic Illness; Pain management, Orthopedic
- More than 200 admissions to IT; 17 NAS to date
- Specialty hospital; member of Children’s Hospital Association
- Referrals from tri-state area
- Recognized by Leap Frog 2014
- 1st Pediatric rehab hospital to be named Top Hospital Awards 2014
Poor fetal adaptation to changes in maternal vagal tone in response to opioids; basis for newborn physiologic and neurobehavioral dysregulation **

Chronic Opioid exposure leads to fetal hypoxia and placental insufficiency

Treatment is aimed at moderating both physiologic and epigenetic factors.***

Sources: ** Jansson, Dipetro, Elko, & Velez, 2007
*** Lester, 2011
Components of Program for Infant Withdrawal

- Non-pharmacologic interventions
- Staff competency with administration of Finnegan
- Standardized protocol for initiation of a MAT for detoxification and weaning process
- Maternal/Caregiver teaching and home simulation testing
- Identify barriers to discharge
- Withdrawal process is complex; be certain infant is stable in environments prior to discharge
- Assess infants for need for Early Intervention
- Provide ongoing support for mother and infant upon discharge
- Continue Multispecialty follow-up
Therapy Interventions that Impact Developing Newborn Neuronal Systems

- Sensory recruitment of muscles (posture); Infant Massage; Aquatic therapy; adaptive tactile input
- Neuronal Conditioning for Motor patterns (eg. swallowing, breathing) Vital Stim, kinesiotaping
- Motor planning (rattle, hands to mouth, toy/switch activation, contingency learning)
- Cognitive processing (interaction with environment and caregivers for learning)
- Social interaction (calming, play)
**CSH: NAS Program and Protocol**

**Day of Admission**
- Review Transfer information
- Physical Assessment
- Medication Reconciliation
- Family Orientation to Program

**Medication Assisted Treatment**
- On admission continue with same medication and dose upon transfer
- Decrease dose by 10% every 24-48 for 3 consecutive scores < 8 or average <24 or 2<12
- If scores > 8 increase dose by 10%
- Discontinue morphine when Dose < 0.04mg/kg/day or methadone<0.05mg/kg/da
- CBC, lytes bilirubin as needed

**Nursing Plan of Care**
- Finnegan scores q 4 hr
- Daily Weights, weekly HC and monthly height
- VSS q shift and pox prn
- Monitor skin integrity
- Carryover therapeutic calming interventions
- Family training on CPR, medications, FTV
- RHC
- Immunizations prn

**Nutrition Consult**
- Daily assessment
- Consider high calories and or increase in volume
- Consider formula change for intolerance
- Confer with MD/APN for management of reflux, gastritis, poor motility, stooling or constipation
- Maintain growth velocity curves

**Discharge Criteria**
- Discontinuation of all medications used for detox
- Finnegan scores < 8 off medications for minimum of 72- hours
- Demonstrate age appropriate weight gain
- Bayley III Developmental Assessment
- DCPP identification of family caregivers and involvement post discharge
- Referral for VNA, WIC, EIP, OP referral; car seat safety check
- Obtain medications for reflux etc prior to discharge
- Schedule PMD and subspecialty discharge appointments

**Therapy Interventions**
- Team evaluation
- Positioning aids for developmental postures and skills
- Calming strategies: rocking, swaddling, therapeutic bath, music therapy, visual stimulation, infant massage, aquatic therapy
- Graded sensory input
- Feeding techniques and strategies
Program Highlights

- MAT by experienced physician—steady taper off narcotics while encouraging weight gain; management of withdrawal seizures and tone
- Breastfeeding where appropriate
- Nutritional support for age appropriate weight gain; high caloric requirements and supplementation
- Medical treatment of acute gastritis, dysmotility, reflux, constipation
- Cardiorespiratory evaluation; CXR, PCG
- Nursing competency and administration of Finnegan
- Parent teaching, support and education; daily and weekend instruction and 8-12 hour independent provision of care
- NB counseling center for MAT; counseling
- WIC office nearby; onsite pharmacy for infant meds PTD
- Car service; bedside accommodations, Ronald McDonald House
- Coordination of services for discharge; collaboration with DCPP, referrals made to EI, OP, VNA, VGO (telemedicine) visits, MD, Neurodev.
Foundations for Developmental Milestones

- Feeding specialist available for diagnosis and treatment strategies of swallowing disorders (including vital stimulation)
- Gross motor therapist to identify and treat maladaptive positioning, increased muscle tone, tolerance to handling and GM millstones for age (including aquatic therapy)
- Occupational therapists to identify and treat poor self calming and focus; poor visual and auditory attention (including music therapy) and recreation and cuddlers for ongoing support
- Child Life Specialist for infant massage, parenting classes
Model for Inpatient Therapy

- Speech — 6-12 sessions per week
- PT — 5-6 sessions per week
- OT — 5-6 sessions per week
- Infant Massage — 1-2 sessions per week
- Therapeutic bath — 3-5 sessions per week
- Aquatic therapy — 1-2 sessions per week
- Cuddler — 1-3 sessions per week
- Parent instruction daily and weekends
Aquatic Therapy
Neuromuscular Electrical Stimulation
(Vital Stim)
Contingency Learning
Infant Massage
Environmental and Positioning Modifications
Outcomes 2009-2013

- N=42; Bayley=28
- Length of stay: 18-35 days
- Discharge: 75% mother; 25% foster
- MAT—50% morphine, 50% methadone
- Weaned off meds—100%
- Finnegan scores at discharge <6(100%)
- Achieved age appr weight gain—100%
- Normal pneumogram—98%
- Caregiver confidence and successful FTV—100%
- DCPP,VNA involvement—100%
Research Question: Are Developmental Outcomes In NAS Patients Significantly Different than Non-Exposed Peers?

Goal: Compare Bayley-III scores for NAS patients to peers without NAS history.

Hypothesis: Infants diagnosed with NAS demonstrate developmental delays compared to infants without NAS history.

Method: Administration of Bayley-III at discharge; comparison and analysis with historical normative data.

Exclusion criteria:

» Premature (less than 37 weeks gestation)
» Medically fragile (congenital heart/lung disease, known chromosomonal anomaly)

Protocol # 20130884, approved by Western IRB May 2013.

» Retrospective chart view
» Waiver of consent granted
Prior to discharge, the Bayley-III is completed.

» Designed for use between 1 and 42 months of age.

» Standardized tool derived from assessment of 1700 children, with classification derived from a normative curve.
### Bayley-III descriptive classifications

<table>
<thead>
<tr>
<th>Composite or Composite Score Equivalent</th>
<th>Classification</th>
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<tbody>
<tr>
<td>130 and above</td>
<td>Very Superior</td>
</tr>
<tr>
<td>120-129</td>
<td>Superior</td>
</tr>
<tr>
<td>110-119</td>
<td>High Average</td>
</tr>
<tr>
<td>90-109</td>
<td>Average</td>
</tr>
<tr>
<td>80-89</td>
<td>Low Average</td>
</tr>
<tr>
<td>70-79</td>
<td>Borderline</td>
</tr>
<tr>
<td>69 and below</td>
<td>Extremely Low</td>
</tr>
</tbody>
</table>
Percent of infants in each Bayley-III descriptive category: Study group vs. normative group
Percent of infants in each Bayley-III descriptive category for motor function vs. normative curve.
Percent of infants in each Bayley-III descriptive category for cognition vs. normative curve

Extremely Low
Borderline
Low Average
Average
High Average
Superior
Very Superior

Normal curve
NAS- Cognitive
Percent of infants in each Bayley-III descriptive category for language vs. normative curve
Bayley Outcomes at Discharge
N=28/42 (2009-2013)

- **Cognition:** (14% BR, ELR)
  - 7% scored in the borderline range (scores 70-79)
  - 7% scored in the extremely low range (scores at or below 69)

- **Total motor (fine and gross motor):** (4% BR)
  - 4% of infants scored in the borderline range.

- **Total language (expressive and receptive):** (40% BR, ELR)
  - 29% scored in the borderline range
  - 11% scored in the extremely low range.

- **Mean age testing:** 58 days study group (21-98 days)
Key Points

- Bayley-III established as a historical control using normative population who were evaluated for the development of the Bayley-III
- One group of 1700 infants age 1 month to 42 months (entire standard population of the Bayley-III)
- Second smaller control group of 300 infants matched more closely in age to our group, 30-90 days (mean age – 60 days)
- Standard sample two sets of analyses were performed:
  1) Two-sample T-tests comparing mean composite scores for NAS infants to controls
     - T-tests: used to determine if the means of two sets of data are significantly different from each other
  2) Chi square test comparing descriptive categories for NAS infants and controls
     - Chi square: to investigate whether distributions of categorical variables differ from one another.
     - Only language and motor available.
### T-test comparing composite scores

Bayley standard N=1700; mean of 100 and SD of 15

<table>
<thead>
<tr>
<th>Composite Score</th>
<th>Cognition</th>
<th>Language</th>
<th>Motor</th>
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<tbody>
<tr>
<td>Mean</td>
<td>90</td>
<td>82</td>
<td>96.3</td>
</tr>
<tr>
<td>SD</td>
<td>11.3</td>
<td>12.5</td>
<td>8.6</td>
</tr>
<tr>
<td>Median</td>
<td>95</td>
<td>84.5</td>
<td>97</td>
</tr>
<tr>
<td>Min, Max</td>
<td>65, 105</td>
<td>53, 103</td>
<td>73, 112</td>
</tr>
<tr>
<td>Diff vs. Bayley (T-Test)</td>
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</tr>
<tr>
<td>Mean</td>
<td>-10</td>
<td>-18</td>
<td>-3.7</td>
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<tr>
<td>T-Score</td>
<td>-4.48</td>
<td>-7.32</td>
<td>-2.07</td>
</tr>
<tr>
<td>P-value</td>
<td>$&lt;0.0001$</td>
<td>$&lt;0.0001$</td>
<td>0.047</td>
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</table>
### Language classification: Chi-squared test

*Chi-squared test = 38.15, P-value <0.001*

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<tr>
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<th>Bayley N=100 n(%)</th>
<th>Study Group N=28 n(%)</th>
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<tbody>
<tr>
<td><strong>&gt;=130</strong></td>
<td>34 (2)</td>
<td>0</td>
</tr>
<tr>
<td><strong>120-129</strong></td>
<td>134 (7.9)</td>
<td>0</td>
</tr>
<tr>
<td><strong>110-119</strong></td>
<td>241 (14.2)</td>
<td>0</td>
</tr>
<tr>
<td><strong>90-109</strong></td>
<td>874 (51.4)</td>
<td>8 (28.6)</td>
</tr>
<tr>
<td><strong>80-89</strong></td>
<td>245 (14.4)</td>
<td>9 (32.1)</td>
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<tr>
<td><strong>70-70</strong></td>
<td>129 (7.6)</td>
<td>8 (28.6)</td>
</tr>
<tr>
<td><strong>&lt;=69</strong></td>
<td>41 (2.4)</td>
<td>3 (10.7)</td>
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Motor classification: Chi-squared test

<table>
<thead>
<tr>
<th>Chi-squared test = 10.71, P-value = 0.0976</th>
<th>Bayley N=100 n (%)</th>
<th>Study Group N=28 n (%)</th>
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<tbody>
<tr>
<td>&gt;=130 Very superior</td>
<td>34 (2)</td>
<td>0</td>
</tr>
<tr>
<td>120-129 Superior</td>
<td>121 (7.1)</td>
<td>0</td>
</tr>
<tr>
<td>110-119 High average</td>
<td>318 (18.7)</td>
<td>1 (3.6)</td>
</tr>
<tr>
<td>90-109 Average</td>
<td>838 (49.3)</td>
<td>20 (71.4)</td>
</tr>
<tr>
<td>80-89 Low average</td>
<td>240 (14.1)</td>
<td>6 (21.4)</td>
</tr>
<tr>
<td>70-70 Borderline</td>
<td>104 (6.1)</td>
<td>1 (3.6)</td>
</tr>
<tr>
<td>&lt;=69 Extremely low</td>
<td>43 (2.5)</td>
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Mean Language and Cognition scores were significantly lower ($p<.001$) in NAS group compared to Bayley sample of 1700 and smaller group of age matched controls of 300.

No significance noted when comparing gender, Male=57%
Discussion

- Small sample size; need for continued data collection.
- Early developmental deficits identified in full term infants with in utero drug exposure and Neonatal abstinence syndrome; all treated with medication and aggressive therapeutic interventions.
- Significant scores in Domains of Language and Cognition when comparing NAS with historical normative group.
- Delay in discharge due to lack of caregiver identification.
Follow up Bayley Results
Jan 2014-June 2015

- N=12/16 of original 28
- 45% Cognitive Deficits (LA)
- 60% Total Language deficits (LA, BR, ELR) 2nd assessment*
- 36% lower scores as compared to 1st assessment*
- Persistence of language deficits
- 54% Fine Motor deficits (ELR) 2nd assessment*
- 1 patient with emerging oppositional behavior; 1 with ASD, nystagmus
- Emerging deficits in FM, in addition to Lang. and Cog. may be indicative of global delay vs. isolated deficits

* 1st assessment – 30-80 days (inpatient) 1-2 months
* 2nd assessment – 108-249 days 3.6-8.3 months
* 3rd assessment – 306-547 days 10.2-18.2 months
<table>
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<tbody>
<tr>
<td><strong>Cognition:</strong> (27% BR, ELR)</td>
<td><strong>Cognition:</strong> 45% LA</td>
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<td>» 20% scored in the borderline range (scores 70-79)</td>
<td><strong>Fine Motor deficits 54% (ELR) 2nd assessment</strong>*</td>
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<tr>
<td>» 7% scored in the extremely low range (scores at or below 69)</td>
<td>Emerging deficits in FM, in addition to Language and Cog. may be indicative of global delay rather than isolated deficits</td>
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<tr>
<td><strong>Total motor</strong> (fine and gross motor): (4% BR)</td>
<td><strong>Total Language deficits (64% LA,BR,ELR) 2nd assessment</strong>*</td>
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<td>» 4% of infants scored in the borderline range.</td>
<td><strong>Persistence of language deficits</strong></td>
</tr>
<tr>
<td><strong>Total language</strong> (expressive and receptive): (40% BR, ELR)</td>
<td><strong>1 patient noted with oppositional behavior emerging; 1 with fine nystagmus</strong></td>
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<tr>
<td>» 29% scored in the borderline range</td>
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<td>» 11% scored in the extremely low range.</td>
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**Mean age testing:** 58 days study group(25-98 days)

* *1st assessment- 30-80 days (inpatient) 1- 2 months |
* *2nd assessment- 108-249 days 3.6- 8.3 months |
* *3rd assessment – 306-547 days 10.2- 18.2 months |
Future Plans

- Stratify NAS group based on bi-phasic presentation of withdrawal: first 2 weeks vs. relapsing course and impact on Bayley scores
- Stratify infants based on severity of admission Finnegan scores into 2 groups; >8 and < 8 to determine impact on Bayley scores and developmental deficits
- Evaluate impact of MAT with morphine vs. methadone on Bayley scores and developmental deficits
- Impose standardized weaning protocol based on evidenced based literature
- Identify emerging patterns of difficult behavior in long-term follow up


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