Outcomes of Infants with Neonatal Abstinence Syndrome

Caroline O. Chua, MD, FAAP
Medical Director, Division of Neonatology
Director, Neonatal Follow Up Clinic
Nemours Children’s Hospital
Orlando, Florida
Disclosure

I have nothing to disclose in relation to this presentation
Objectives

- Describe the characteristics of neonatal abstinence syndrome
- Describe the long term consequences of prenatal opioid exposure on the neonate
Neonatal Abstinence Syndrome (NAS)

- Drug withdrawal syndrome that occurs primarily among opioid-exposed infants around 2-3 days after birth.

- Variable, complex, and incompletely understood spectrum of signs of neonatal behavioral dysregulation.

- Incidence rate increased dramatically over the last 10 years
  - Increased in maternal opioid use
    - Illicit drug use
    - Prescription drug use
  - Increased fetal drug exposure
Opioid Abuse and Dependence Among Pregnant Women
Overall and by Age (per 1,000) in the U.S., 1998 - 2011

Maternal opioid use inc from 1.19 to 5.63 per 1,000 hospital birth
NAS inc from 1.2 to 5.8 per 1,000 hospital birth

Patrick et al, J Perinatology. 2015; 35(8):650-655
Exposures Associated with NAS

- **Most commonly seen in infants exposed to opioids in utero**
  - Heroin
  - Fentanyl
  - Morphine
  - Codeine
  - Oxycodone
  - Methadone
  - Buprenorphine
  - Hydromorphone

- **Other implicated substances**
  - SSRIs
  - Nicotine
  - Benzodiazepines
  - Barbiturates
  - Cocaine
  - Amphetamines
Epidemiology: NAS

- 55-94% of exposed babies develop NAS
- ~27/1000 NICU admissions
- The number of babies requiring treatment
  - Varies between 42-94%

McQueen et al. NEJM. 2016; 375(25):2468-2479
Mechanism of Opioid Withdrawal in Neonates

- Corticotrophin
- Serotonin
- Dopamine
- Noradrenaline
- Acetylcholine
- Others
NAS: Signs and Symptoms

- Reflect dysfunction in 4 domains:
  - State control and attention
  - Motor and tone control
  - Sensory integration
  - Autonomic functioning

- Other findings:
  - Lower birth weight/SGA
  - Preterm birth
  - Seizures
    - Reported in 2-11%
  - Abnormal EEG changes
    - Reported in >30%
  - Associated neonatal complications
    - Respiratory complications
    - Feeding difficulties
    - Hypoglycemia
    - Failure to thrive
Clinical Manifestation of NAS

- Presentation is widely variable (onset, severity)
  - The variability is poorly understood

- Several factors that might affect variability:
  - Maternal exposure (substance used, polysubstance use, psychotropic drug use, timing of exposures, frequency and dose of drugs)
  - Maternal factors (nutrition, infections, stress, comorbid psychiatric conditions)
  - Placental opioid metabolism (metabolic rate)
  - Genetics and Epigenetics (mu-opioid receptor gene and promoter)
  - Infant factors (preterm, comorbid infections, medications)
  - Environmental factors (physical environment)
Drug Addiction And Babies: Long Term Effects

- Increased Anxiety
- Behavioral Issues
- Low Birth Weight
- Increased Risk Of Drug Abuse
NAS: Long Term Effects and Problems

- Neurodevelopment and motor development
- Behavior and cognition
- Vision and hearing
- Child abuse and neglect
- Risk of future drug use
- Sleep and risk of SIDS or SUID
- Pain management
- Psychosocial implications

Neurodevelopment and Motor Problems

- Multiple studies showing increased risk of neurodevelopmental delays

- Inconsistent evidence about development of methadone exposed infants
  - Bayley MDI and PDI at 3, 6 and 12 months of age showed comparable results (normal development) \(^1,2\)
  - Bayley MDI and PDI at 18, 24 and 36 months of age were lowered among methadone exposed infants \(^3,4\)

- Buprenorphine exposed infants tend to be delayed \(^5\)
  - Significant motor skills delay

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Behavior and Cognition

- **Heroin exposed infants have poor development**
  - Poor cognitive skills
  - Poor perceptual skills
  - Poor memory skills

- **Methadone exposed infants have ongoing problems**
  - Hyperactivity
  - Short attention span
  - Poor verbal and performance skills
  - Poor memory skills
  - Poor perceptual skills

- **Buprenorphine exposed infants have similar problems**
  - Hyperactivity
  - Impulsivity
  - Attention problems
Behavior and Cognition

- Adopted exposed children scored higher than exposed children with biological family, but still lower than non-exposed children.

- Environmental risks magnify weaknesses caused by exposure.
Vision and Hearing Problems

- Strabismus
- Reduced visual acuity
- Nystagmus
- Refractive errors
- Cerebral visual impairment
- Overall, visual development is delayed

- Otitis media is common with methadone
  - Severe or chronic otitis media
    - Hearing disabilities
    - Developmental disabilities
    - Learning disabilities
  - Recurrent otitis media
    - Hearing loss
    - Language delays

Child Abuse and Neglect

- Adverse childhood experiences (ACE) can cause
  - Obesity
  - Cardiovascular disease
  - Psychiatric illnesses

- Genetic, social and environmental factors
  - Complex interplay of outcomes

- Complex interpersonal trauma is common
  - Lack of responsiveness to infant
  - Unrealistic expectations of infant
  - Increased maternal aggression
  - Increased physical punishment
  - Intergenerational transmission
Child Abuse and Neglect

- Intergenerational trauma is commonly seen
  - Distorted thought patterns
  - Poor parenting interactions
  - Poor self-esteem and sense of worth
  - Heightened sensitivity to drug triggers

- The incidence of child abuse is tripled
  - With psychiatric illness
  - With drug using caregivers
  - With environmental stressors
Child Abuse and Neglect

- Child protective services considers parental drug abuse
  - A primary factor in child abuse
  - A primary factor in child neglect

- Rate ranging from 50-80% of all cases
Risk of Future Substance Abuse

- Studies show higher rate of drug use
  - With tobacco exposure
  - With marijuana exposure
- Studies have not shown these effects with opioids
- Large longitudinal studies are needed
Sleep and Risk of SIDS/SUID

- Brain opiate receptors and onset/regulation of sleep
- “Quiet sleep” significantly reduced, even 4-5 weeks after NAS treatment finished

Toddler sleep

**SIDS or SUID**
- A few studies have shown an increase in SIDS
  - All SIDS deaths reported tobacco using mothers
- More studies are needed before inferring an association
Pain Management

- Routine Life Events
- Response to pain medications
Psychosocial Implications

- Parenting
  - Infant Care
    - Decreased bonding due to NICU stay
    - Decreased parental presence in NICU
    - Parental guilt
    - Multi-disciplinary care
  - Preschool/School Age
    - Hyperactivity
    - Developmental delay
    - Aggressive conduct disorder
    - Learning disabilities
    - Sleep regulation
Psychosocial Implications

- **Biological Family**
  - Increased risk of neglect/abuse in addicted households
  - 20% increase in maltreatment in cocaine exposed infants with biological parents

- 60-90% of drug addicts may have mental, emotional or personality disorders, leading to poor parenting skills
Psychosocial Implications

- Family Caregivers
  - Grandparents

- Adolescence
  - More at risk to other type of addictions

- SES – socioeconomic status – lower income

- Australian population based linkage study of births, hospitalization and death from 2000-2011
  - NAS children are more likely to re-hospitalized for maltreatment, trauma, and mental/behavioral disorders
Infant/Child with NAS

- Impaired Parent Parenting
- Increased risk of Neglect and Abuse
- Difficult Child
- Attachment Issues
- Infant/Child
- Parenting
- Attachment Issues
- Increased risk of Neglect and Abuse
- Difficult Child
NAS Child Removed from Biological Family

- Infant/Child
- Attachment Problems
- Multiple Foster Homes
- Difficult Parenting
## Summary of Effects of Prenatal Drug Exposure

<table>
<thead>
<tr>
<th></th>
<th>Nicotine</th>
<th>Alcohol</th>
<th>Marijuana</th>
<th>Opiates</th>
<th>Cocaine</th>
<th>Methamphetamine</th>
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</thead>
<tbody>
<tr>
<td><strong>Short-term effects/birth outcome</strong></td>
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<tr>
<td>Fetal growth</td>
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<td>Strong effect</td>
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<tr>
<td>Anomalies</td>
<td>No consensus on effect</td>
<td>Strong effect</td>
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<td>Withdrawal</td>
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<tr>
<td><strong>Neurobehavior</strong></td>
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<td><strong>Long-term effects</strong></td>
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<td>Growth</td>
<td>No consensus on effect</td>
<td>Strong effect</td>
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<td><strong>Behavior</strong></td>
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</table>

* Limited or no data available.
Maternal opioid use is an increasing problem
More infants are being born exposed to opioids
More infants are requiring hospitalization and treatment
The short-term effects of NAS are well documented
The long-term effects are becoming known
Early intervention and environmental stability are important
Parent education and support is crucial
Ongoing intervention can optimize outcomes
Summary

- Role of primary care physician:
  - Prevention
  - Identification of exposure
  - Recognition of medical issues for the exposed newborn infant
  - Protection of the infant
  - Follow up care
Drug addiction is a disease of the brain and it’s **NOT** a moral failure

It does not discriminate  
It does not subside on its own  
But… it can be overcome.