Objectives

- Current context
- Opioid-dependent pregnant women
- Pathophysiology of NAS
- Signs and symptoms of NAS
- Factors affecting the incidence and severity of NAS/NOWS
- Management of NAS
- Outcomes
- UVM Experience

Disclosures:

- I will discuss off-label uses of medications
- I have no financial disclosures

However, I am a Canadian, eh?

Neonatal Abstinence Syndrome (NAS) or Neonatal Opioid Withdrawal Syndrome (NOWS) often results when a pregnant woman is on opioid agonist treatment with methadone or buprenorphine, prescribed opioid pain relievers, or uses opioids (e.g., heroin, oxycodone) during pregnancy.

Defined by alterations in the:

- Central nervous system
  - high-pitched crying, irritability
  - exaggerated reflexes, tremors and tight muscles
  - sleep disturbances

- Autonomic nervous system
  - sweating, fever, yawning, and sneezing

- Gut and gastrointestinal distress
  - poor feeding, vomiting and loose stools

- Signs of respiratory distress
  - nasal stuffiness and rapid breathing

NAS is not Fetal Alcohol Syndrome (FAS)

NAS is treatable

NAS / NOWS: Description

(Farquhar et al., Addict Dis. 1975; Desmond & Wilson, Addict Dis. 1975)
### Neonatal Abstinence Syndrome

<table>
<thead>
<tr>
<th>State</th>
<th>Incidence Rate</th>
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<tbody>
<tr>
<td>Maine</td>
<td>38.4</td>
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<tr>
<td>Vermont</td>
<td>33.3</td>
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<tr>
<td>W Virginia</td>
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</tbody>
</table>

Vermont had the highest annual rate increase of states surveyed.

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### NAS: Current Context

- **Issues facing substance-using pregnant women and their children**
  - Generational substance use
  - Legal involvement
  - Unstable housing
  - Unstable transportation

- **Limited parenting skills and resources**
- Exposure to trauma
- Lack of positive and supportive relationships

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### Vermont Headlines

- **Vt.'s top story: Toddlers' deaths, child protection**
  - By DAVE GRAM, December 26, 2014

  - Shumlin signs child protection reform bill into law June 15, 2015
  - Hundreds mourn death of Lara Sobel
  - DCF caseworker gunned down Friday night
  - WPTZ, August 12, 2015

  - Vt. takes custody of record number of children, September 15, 2015
Medication Assisted Treatment (MAT): Standard of Care for Pregnancy

• WHO 2014: “Pregnant women dependent on opioids should be encouraged to use opioid maintenance treatment... rather than... attempt opioid detoxification.”
• Facilitates retention of mothers/infants with decreased use of illicit substances when compared to no medication
• MAT results in NAS / NOWS which needs Rx in 50-60% patients (Jones et al, 2010)
• The severity of NAS does not appear to differ according to the dose of methadone maintenance therapy mothers received during pregnancy” (Cleary et al, 2010; Jones et al., 2013)

NAS ≠ NAS ≠ NAS

NAS Profile

3
Pathophysiology of Neonatal Opioid Withdrawal

NAS: Signs and Symptoms
- Signs of withdrawal typically start after 24-96 hours after birth depending upon the specific opioid exposure
- Central nervous system signs
  - Tremors
  - Irritability, high-pitched crying
  - Sleep difficulties
  - Tight muscles tone, hyperactive reflexes
  - Myoclonic jerks (sometimes mistaken as seizures), seizures - rare
- Autonomic signs
  - Sweating, fever, yawning and sneezing
  - Rapid breathing, nasal congestion

What would happen if NAS is untreated?
- Depends upon the severity
- There are many infants who do not receive medication for NOWS and their outcome is good
- However, an irritable, crying baby who does not sleep and cannot feed will be at risk for:
  - Dehydration
  - Abusive trauma
  - Interrupted attachment and maybe failure of attachment
  - Excessive irritability and dehydration are very likely to lead the caregiver to seek medical attention
- An infant may die without treatment – however in an extensive literature search, the only reported deaths occurred over 100 years ago.
- NAS does not lead to poor neurodevelopmental outcomes

Scoring tools for NAS
- Finnegan Neonatal Abstinence Scoring System
  - 31 items
  - Symptoms are weighted
  - Guidelines for pharmacologic treatment at score of 8 or greater
- MOTHER score (modified Finnegan score)
  - 19 items (which contribute to total score)
  - Items weighted differently
  - Some items eliminated and others added
  - Guidelines for treatment based on score rather than weight
- Lipsitz Neonatal Drug-Withdrawal Scoring System
  - 11 items
  - Items scored for severity and gives guidelines for treatment
- The Neonatal Withdrawal Inventory – 8 point checklist
- The Neonatal Narcotic Withdrawal Index – 6 signs plus others

NAS Assessment: MOTHER NAS Scale
- NAS score is not the sole determining factor in the decision to start starting Rx
- Score can be affected by:
  - State of infant
  - Painful stimuli
  - Order of score
  - "Motive" of scorer

Courtesy of H Jones
Factors affecting NAS

- Substances
  - Nicotine
  - Benzodiazepines
  - SSRIs
- Single gene polymorphisms
- Hospital protocols and education of the staff, breastfeeding support

NAS: Management

- Admit to Mother/Baby Unit – rooming-in if possible
- Minimum stay of 4-5 days to allow for symptoms to peak (onset of withdrawal in buprenorphine exposed infants is later than with methadone exposed infants)
- Utilize non-pharmacologic treatment as available
- Encourage breastfeeding
- Encourage mother to participate in the assessment of the newborn
- Role of drug testing in the infant (?)
- Crucial: excellent multidisciplinary communication

NAS: Non-pharmacologic Treatment

- Breastfeeding is associated with reduced severity of withdrawal, delayed onset, decreased need for Rx (Abdel-Latif et al, 2006)
- Rooming-in decreased the need for Rx, length of Rx, and LOS (Abrahams et al, 2007)
- Water beds decreased amount of medication needed (Oro et al, 1988)
- Acupuncture (Fippelli et al, 2012)
- Kangaroo therapy or skin to skin
- Decreased environmental stimuli
- Frequent small demand feeds
- Pacifiers
- Swaddling, containment, holding, vertical rocking
- Provider, nursing attitudes

NAS: Pharmacologic Treatment

- Short-acting opioids (morphine sulfate, dilute tincture of opium)
  - Inpatient treatment
  - Symptom-based versus weight-based
  - Endorsed by the AAP (2012)
- Methadone
  - Inpatient treatment and inpatient to outpatient treatment
  - Symptom versus weight based
  - Allows for shorter length of stay (with outpatient treatment)
  - Endorsed by the AAP (2012)
- (Several studies including MS Brown et al (2015) which revealed shortened duration of treatment with methadone)
- Dilute tincture of opium and phenobarbital (Cayle et al, 2002)
- Buprenorphine (Kraft et al, 2011)
  - Shorter length of stay in buprenorphine treated infants
  - Well tolerated
- Clonidine (Agthe et al, 2009)
  - Oral clonidine alone or as adjunct to short-acting opioids
  - Shortens the duration of therapy. No short-term cardiovascular side effects were observed
Outcomes: Baldacchino et al, BMC Psychiatry 2014

### Psychomotor in opioid and non-opioid exposed infants

<table>
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<tr>
<th>Study Name</th>
<th>Subgroup</th>
<th>Assessment</th>
</tr>
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<td>Hunt (2008)</td>
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<td>BSID (Psychomotor)</td>
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<tr>
<td>Burlowski (1998)</td>
<td>1 year old</td>
<td>GDS (Locomotor)</td>
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<tr>
<td>Moe (2002)</td>
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<td>BSID (Psychomotor)</td>
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<tr>
<td>Hans (2001)</td>
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</tr>
<tr>
<td>Hans (2001)</td>
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### Cognition in opioid and non-opioid exposed infants

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<td>Burlowski (1998)</td>
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<td>Ornoy (2001/2003)</td>
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<tr>
<td>Moe (2002)</td>
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<td>McCarthy Motor Scale</td>
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<tr>
<td>Walhord (2007)</td>
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<td>McCarthy Motor Scale</td>
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### Behaviour in opioid and non-opioid exposed infants

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<tr>
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<td>Vineland Social Maturity</td>
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<td>Ornoy (2001/2003)</td>
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<td>Achenbach</td>
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**Total Opioid-exposed Newborns Followed at UVM Children’s Hospital (1,332 newborns)**

**Children And Recovering Mothers (CHARM) Collaboration in Burlington, Vermont**

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UVM Children’s Hospital
Antenatal Visit With Neonatology

• Schedule 1 – 2 visits with NeoMed Clinic staff
• Written information (Care Notebook)
  • http://www.uvm.edu/medicine/vchip/?Page=ICONcarenotebook.html
• Promote breastfeeding

UVM Children’s Hospital
NeoMed Experience

Alleviation of fear
• Care Notebook
• You are not alone...
• Ask them for their stories
Respect
• Introductions to others on the team
  • “Tell me about yourself”
• “What are your dreams / goals”
Recognition of strengths
• Hearts

Why methadone for treatment of neonatal abstinence syndrome?

• Decreased frequency of dosing
• Less respiratory depression
• Less need for adjustment of dose
Benefits /risks of newborn outpatient treatment program with methadone

**Benefits**
- Length of stay reduced
- Slow wean of methadone reduces symptoms of withdrawal
- Allows for more breastfeeding success
- Empowers family

**Risks**
- Safety concerns – overdose to baby, use by others
- Long half-life may lead to “overmedication” in hospital
- Often prolonged course – are we treating normal baby irritability with methadone?

Infrastructure: what works in Vermont

- Clinic staff with ability to “track infants down”
- Close relationships with obstetrics, substance abuse treatment providers, WIC, child protective services and home health nursing
- Single pharmacy to dispense methadone

UVM Children’s Hospital
NeoMed Clinic

- First NeoMed clinic visit within 1 week of discharge
- Infants requiring medication for NAS are seen at least every 2 weeks
- Bayley III Scales at 8-10 months
- Hepatitis C antibody at 18 months for exposed infants
- Multidisciplinary approach involving primary care provider, home health, early intervention, CHARM team, and maternal substance abuse provider

UVM Children’s Hospital:
Infants born to opioid dependent women with substance abuse on methadone or buprenorphine at delivery (N = 970)
Timing of initiation of opioid agonist treatment (OAT)

- % Mothers on OAT prior to conception
- Average GA started OAT if not prior to conception

Why did pharmacologic treatment for NAS decrease?

- Better use of non-pharmacologic treatment
- Less subjectivity in NAS scoring
- Through participating in MOTHER study
- Decreased assumption of need for treatment
- Over time, the proportion of buprenorphine-treated pregnant women increased
UVM Children’s Hospital
Average length of outpatient treatment with methadone

- Average length of treatment: 2.05 months (2015)
- No infant deaths from methadone overdose
- From 2000 to 2015 there were 14 deaths/1332 opioid-exposed infants (deaths < 2 years of age)
  - Shared sleeping: 7
  - Motor vehicle accidents: 2
  - Extreme prematurity: 2
  - Remainder (1 each): SIDS, congenital heart malformation, abusive head trauma
Vermont Experience: Overall

- ChARM Team: Children and Recovering Mothers
- Monthly collaborative multidisciplinary meetings
- High risk factors:
  - Increased distance to treatment center
  - Discontinuation of methadone / buprenorphine
  - Actively using partner
  - Abusive relationship with partner
  - Women respond well to positive interactions with health care providers

Summary

- The incidence of NAS is increasing – does this represent increased identification of cases, increased access to care for pregnant opioid-dependent women?
- Behind every case of NAS, there is a mother suffering from the disease of addiction – this is where efforts need to be the greatest – need to decrease judgement, increase access to trauma-informed treatment.
- Community strategies that focus on punishment will result in increased morbidity and mortality for children and their families.
- Developmental / behavioral outcomes are overall not affected by opioid-exposure in utero on its own, unlike alcohol exposure.

Acknowledgements

We would like to thank the infants and families we have had the pleasure of caring for – we continue to learn from them daily.