Neonatal Abstinence Syndrome: Current Concepts and Management

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Objectives

- Recognize growing incidence of opioid abuse during pregnancy
- Recognize growing incidence of Neonatal Abstinence Syndrome
- Recognize common neonatal comorbidities
- Understand basic neonatal treatment principles

Headlines

- USA Today: April, 2012
  - "Number of pain-killer addicted newborns triples in ten years"
- New York Times: April, 2012
  - "Newly born and withdrawing from pain killers"
  - "Epidemic of Prescription Opiate Abuse and Neonatal Abstinence"

JAMA 2012;307 (18):1974-1975.

Neonatal abstinence syndrome (NAS) is a new problem, having just come of age since the early 2000's.

A. True

B. False

Neonatal Abstinence Syndrome: A“new” name for an old problem

- First case report 1875
- Congenital morphinism- most babies died
- 1903- First reported case of successful treatment with morphine

- **NAS was a leading cause for neonatal hospitalizations in the US in 2015**
- **Average length of stay ~ 17 days**
- **Increasing incidence 2003-2014**
  - **4x increase in urban settings**
  - **7x increase in rural settings**

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What is the incidence of NAS in the United States?

1. 2 / 1000 hospital births
2. 2 / 1000 hospital births
3. 4 / 1000 hospital births
4. 8 / 1000 hospital births
5. None of the above

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The most frequently prescribed opioids in women are:

1. Hydrocodone
2. Codeine
3. Oxycodone
4. Dilaudid

A. 1 & 3
B. 2& 4
C. 1, 2, & 3
D. 4 only
E. None of the above

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Opioid Pain Relievers

- Account for more overdose deaths than cocaine and heroin combined (CDC)
- More deaths than car accidents (CDC)
- 1.5 M U.S. Reproductive-age women and 50,000 pregnant women reported using prescription opioids for non-medical purposes.
- Use of opioid pain medications associated with increased likelihood of polysubstance abuse.
  - ETOH, THC

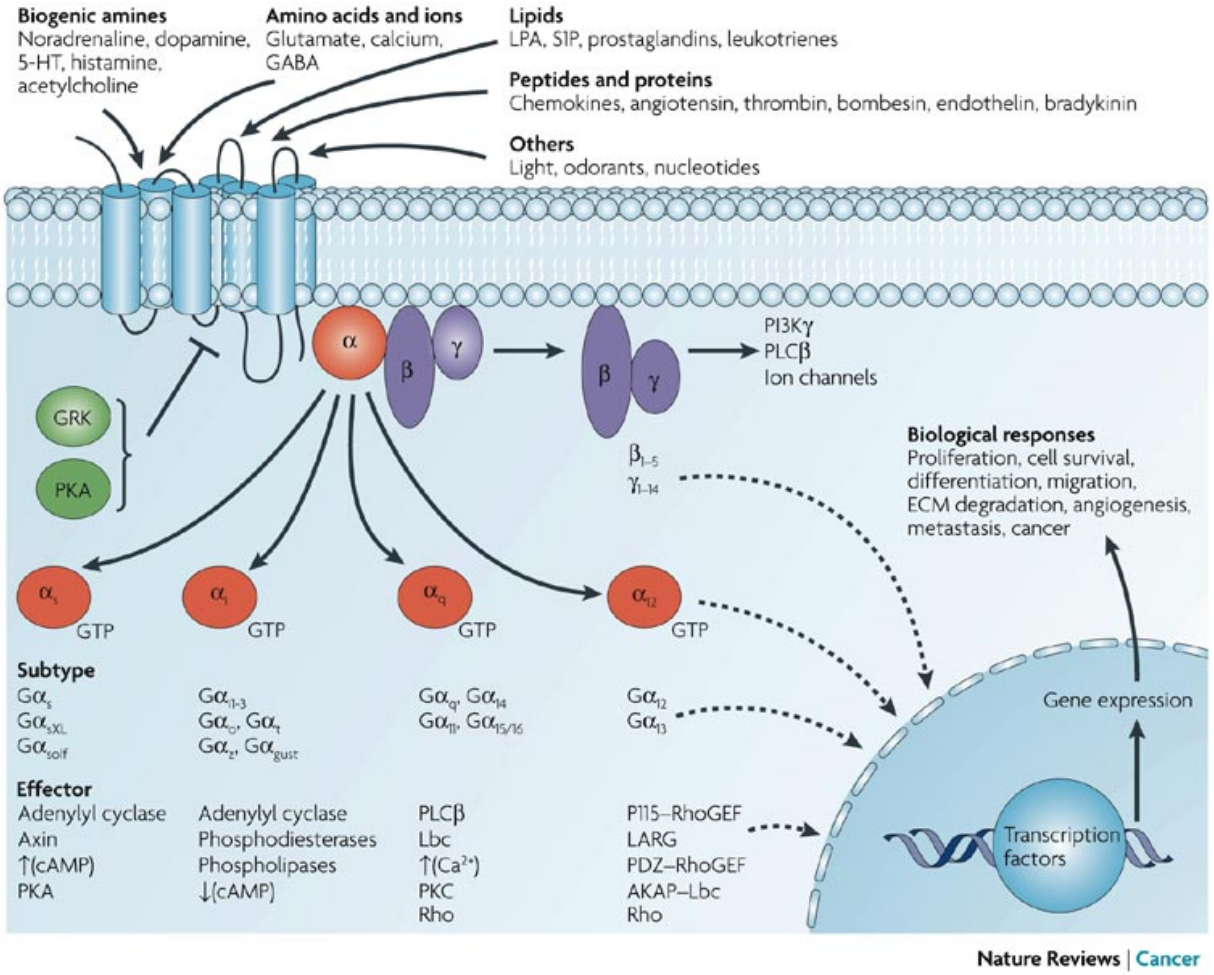
Kozhimannil, KE 2017

Endogenous Opioids-Endorphins

- Mediate complex behaviors involved in formation of stable, emotionally committed relationships

- Distribution: brain, spinal cord, digestive tract

Back to Basics- G coupled Receptors



4 types: delta, kappa, mu, nocicepti

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Does any of this help me take care of these babies?

Opioids

- Facts
  - Lipophilic- easily cross placenta
  - Transmission increases with gestation
- Abrupt discontinuation
  - Increased adenylyl cyclase activity
  - Ionic imbalance
  - Altered neurotransmitter activity
    - Supraphysiologic norepinephrine: *hyperthermia and tremors*
    - Decreased serotonin: *sleep deprivation*

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When talking to a mother about her opioid use during pregnancy, you can counsel her that other than an increased risk of neonatal withdrawal, infant exposed to opiates in-utero aren't expected to have any other problems.

1. True
2. False

Which co-morbidities are seen with NAS?

1. Prematurity and low birth weight
2. SIDS
3. RDS
4. Feeding intolerance

A. 1 and 3
B. 2 and 4
C. 1, 2 and 3
D. 4 only

E. All of the above

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Neonatal Co-Morbidities

- Prematurity
- Low birth weight 7 vs. **19%**
- Respiratory distress 8 vs. **31%**
- Feeding intolerance 3 vs. **18%**
- 74-fold increase in SIDS

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Neonatal Abstinence Syndrome

- Definition: Symptoms in newborns caused by abrupt discontinuation of trans-placental substances, usually opioids

- Symptoms
  - Neurological: tremors, irritability, increased wakefulness, seizures, frequent yawning/sneezing
  - Gastrointestinal: poor feeding, uncoordinated suck, vomiting, diarrhea, poor weight gain
  - Autonomic dysfunction: sweating, stuffiness, fever, temp instability

Drug Screening Options

- Urine
- Meconium
- Umbilical cord tissue or blood
- 50-60% of mothers who test positive for drugs deny their use
- Interviews underestimate users
- BOTTOM LINE: Have a policy for screening (universal vs. risk based)

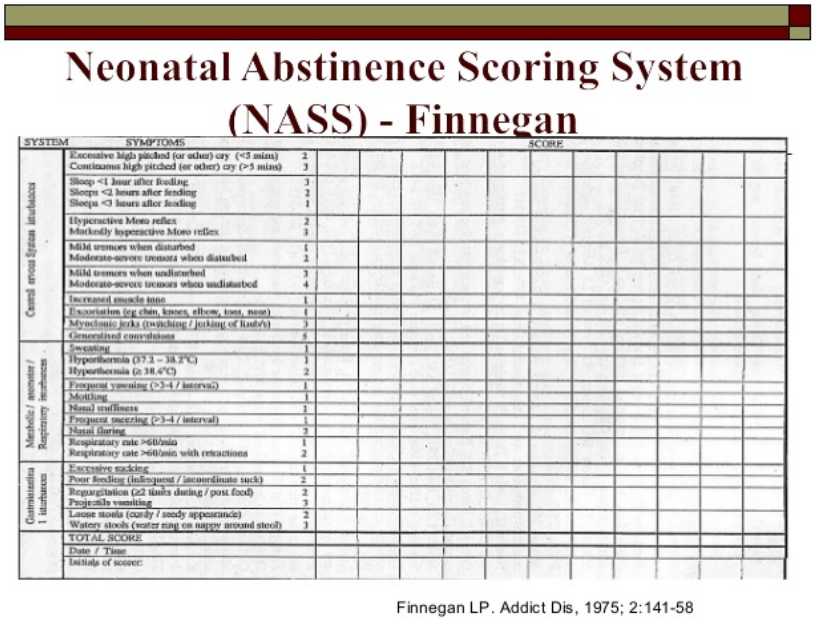
Neonates typically experience withdrawal symptoms in what time frame?

1. Heroin 4-25 hours
2. Methadone 48-72 hours
3. Buprenorphine 72-96 hours

AAP Recommendations- 2012

- 3-4 day observation for short-acting opiates
  - Oxycodone
  - Vicodin
  - Percocet, etc
  - Heroin
- 5-7 day observation for long-acting opiates
  - Methadone
  - Buprenorphine

ModifiedFinnegan Scores – objectively measuring withdrawal symptoms



Neonatal Abstinence Scoring System (NASS) - Finnegan

SYSTEM	SYMPTOMS		SCORE
Central nervous System disturbances	Excessive high pitched (or other) cry (<5 mins)	2	
	Continuous high pitched (or other) cry (>5 mins)	3	
	Sleeps <1 hour after feeding	3	
	Sleeps <2 hours after feeding	2	
	Sleeps <3 hours after feeding	1	
	Hyperactive Moro reflex	2	
	Markedly hyperactive Moro reflex	3	
	Mild tremors when disturbed	1	
	Moderate-severe tremors when disturbed	2	
	Mild tremors when undisturbed	3	
	Moderate-severe tremors when undisturbed	4	
	Increased muscle tone	1	
	Excoriation (eg chin, knees, elbow, toes, nose)	1	
	Myoclonic jerks (twitching / jerking of limbs)	3	
	Generalized convulsions	5	
Metabolic / vasomotor / Respiratory disturbances	Sweating	1	
	Hyperthermia (37.3 – 38.2°C)	1	
	Hyperthermia (≥ 38.4°C)	2	
	Frequent yawning (>3-4 / interval)	1	
	Mottling	1	
	Nasal stuffiness	1	
	Frequent sneezing (>3-4 / interval)	1	
	Nasal flaring	2	
	Respiratory rate >60/min	1	
	Respiratory rate >60/min with retractions	2	
Gastrointestinal disturbances	Excessive sucking	1	
	Poor feeding (infrequent / uncoordinate suck)	2	
	Regurgitation (≥2 times during / post feed)	2	
	Projectile vomiting	3	
	Loose stools (curdy / seedy appearance)	2	
	Watery stools (water ring on nappy around stool)	3	
	TOTAL SCORE		
	Date / Time		
	Initials of scorer:		

Finnegan LP. Addict Dis, 1975; 2:141-58

<7: Comfort

≥8: Treat (Rx)

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Treatment

- Non-pharmacologic
  - Maternal rooming in
  - Breast feeding
  - Skin to skin contact
  - Swaddling
  - Low stimulation environment
- Pharmacologic

Pharmacologic Treatment Goal

- Allow infant to withdraw without the excessive excitation that leads to withdrawal symptoms.
- Comprehensive Goals
  - Support vital functions: sleep, nutrition, social interaction
  - Initiate family bonding
  - Prevent complications: dehydration, weight loss, skin breakdown, seizures
  - Educate family and provide adequate medical and social resources

Which of the following drugs can be used to treat Neonatal Abstinence Syndrome?

1. Morphine
2. Methadone
3. Phenobarbitol
4. Clonidine
5. Buprenorphine (newer studies)
6. ✓ All of the above

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Compare and Contrast

	Morphine	Methadone
Pros	Years of Experience Stable formulation	Less frequent dosing Outpatient use
Cons	Frequent dosing	Limited data Limited clinical trial evidence Safety profile less defined 9% ethanol formulation
Data	Much	1 randomized control trial, 1997 Madden Few case series

Morphine vs. Methadone

Davis, JE et al. JAMA August 2018

- Improved short term outcomes in methadone group
  - 14% reduction in average LOS (2.9 days)
  - 16% reduction in average LOT (2.3 days)
- Long term outcomes need study

Why keep moms on methadone or buprenorphine during pregnancy?

- Pharmacotherapy and coordination of care are essential elements in the comprehensive care of pregnant patients with opioid addiction
- Comprehensive opioid maintenance treatment and prenatal care reduces the risk of obstetrical and fetal complications

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Benefits of Maternal Opioid Maintenance Therapy

- Improved prenatal care compliance
- Decreased STDs
- Improved nutrition
- Decreased risk of preeclampsia
- Less drug seeking and criminal behavior
- Less fetal exposure to rapid and unpredictable cycles of heroin-induced highs and withdrawal

Benefits of Maternal Opioid Maintenance Therapy

- Decreased preterm births
- Decreased intrauterine growth restriction
- Decreased low birth weight infants
- Decreased morbidity

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Predicting NAS

- Polydrug use: increased NAS
- No breast feeding: increased NAS
- Tobacco co-exposure increased length of stay by about 4 days
  - Nicotine withdrawal can mimic opioid withdrawal
- Maternal stress-
  - Prenatal maternal stress programs infant stress response (HPA axis)
  - Increased cortisol
  - Impaired maternal-infant interaction
  - Change infant neurobehavior

Inpatient vs. Outpatient Methadone Treatment for Infants with NAS

- Journal of Perinatology, 2012
- Combined inpatient/outpatient vs. inpatient weaning strategy
- Multidisciplinary group
- Retrospective analysis

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Inpatient vs. Outpatient Methadone Treatment

- Medical clearance
- Physician-Caregiver agreement
- Social Work clearance
- 67% mother/baby dyads met criteria for outpatient weaning
- Length of stay: 25 vs. 13 days
- Length of treatment: 14 vs. 37 days
- Cost: $27K vs. $13K

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Reality Check

- Outpatient methadone for neonates is not easy
  - Pharmacy restrictions- Children's, few others
  - Transportation to Children's weekly
  - Home nursing visits- Children's Home Care in Metro
  - Extra visits to primary MD
- It is hard to pull off without an invested multi-disciplinary outpatient team
- Requires dedicated family involvement

What happens to NAS babies when they grow up?

- Lack of evidence for long-term effects
- Inconsistent findings
- Confounders
  - Polysubstance use
  - Poverty, stress, nutrition

Thank You
Any Questions????

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