

OPIOID USE IN PREGNANCY

WHAT IS NEONATAL ABSTINENCE SYNDROME?

Neonatal Abstinence Syndrome (NAS) occurs when an infant is born with physical manifestations of opioid withdrawal, due to a mother's habitual use of opiates or their derivatives (heroin, methadone, morphine, merperidine, or codeine) during pregnancy. These infants suffer adverse effects at birth, including drug intoxication and drug withdrawal. Almost all infants regularly exposed to opiates in utero will be born with at least some of the symptoms of NAS.

CLINICAL PRESENTATION

The severity of presentation is based on the infant's level of exposure in utero. Of exposed infants, 60-80% will have moderate-to-severe symptoms requiring medical intervention. These symptoms are usually evident within the first 72-96 hours of the infant's life. Symptoms of withdrawal can be classified into three areas:

1. **Central Nervous System (CNS)**
2. **Autonomic Nervous System**
3. **Gastrointestinal (GI)**

SYMPTOM CLASSIFICATION		
CNS	Autonomic NS	GI
<ul style="list-style-type: none">▪ Irritability▪ Jitteriness▪ Tremors▪ Excessive crying▪ High-pitched cry▪ Hyperreflexia▪ Sleep disturbance▪ Seizures	<ul style="list-style-type: none">▪ Hyperthermia▪ Excessive sweating▪ Mottling▪ Tachypnea▪ Nasal congestion▪ Sneezing▪ Hiccapping▪ Yawning	<ul style="list-style-type: none">▪ Hyperphagia▪ Excessive sucking▪ Suck-swallow incoordination▪ Vomiting▪ Diarrhea▪ Poor weight gain

Severity and timing of onset of symptoms may vary, based on the type of opiate involved, the amount used, and the interval between last exposure to the drug and delivery. Infants exposed to codeine typically have mild symptoms, compared to those exposed to methadone or heroin.

Delayed NAS symptoms can occur with maternal polydrug use, especially with the combination of opiates and sedatives. This combination may mask the symptoms of NAS for up to two weeks after birth. A delay in withdrawal symptoms has also been observed with maternal use of high-dose methadone, due to the long half-life of the drug.

DIAGNOSIS AND EVALUATION

Differential Diagnosis: Infants less than 2 weeks who present with symptoms consistent with NAS should be evaluated for sepsis, electrolyte abnormalities neonatal hyperthyroidism, CNS hemorrhage, GI obstruction, colic, or congenital infections, such as toxoplasmosis and cytomegalovirus (CMV).

Evaluation

- Urine toxicology screen (mother and infant)
 - Helpful in detection of maternal polydrug use
 - Often required for child protective services investigation
- STI testing (if positive toxicology screen)
- If NAS suspected despite negative toxicology screens: CBC, C-RP, BMP, serum calcium and serum magnesium

MANAGEMENT AND TREATMENT

Women who become pregnant while addicted to opiates are advised to avoid acute withdrawal during pregnancy, due the increased risk of spontaneous abortion, intrauterine growth restriction, prematurity, and antepartum hemorrhage.

Non-pharmacologic (Supportive care)

- Contact social services to evaluate parenting behavior and safety of home environment (parents may need to complete a recovery program prior to release of infant)
 - Keep infant tightly swaddled in dimly lit, quiet environment with minimal interruptions between feedings
- Monitor weight of infant during and after initial hospital stay
- For drug-free mothers in a recovery program, breast-feeding is recommended (unless HIV infection)
 - May consider a hypercaloric formula (22-27 kcal/oz) in infants with continued inability to gain weight

Pharmacologic

- Pharmacologic treatment indicated for moderate to severe cases of NAS. Goals of pharmacologic therapy include:
 - Reduction of central/autonomic nervous system symptoms
 - Induce regular feeding and sleep cycles
 - Establish adequate weight gain (>15g/day)
 - Provide parental preparation and education

Finnegan Scoring System			
	MILD	MODERATE	SEVERE
Score	<8	8-16	>16
Treatment	<ul style="list-style-type: none"> ▪ Supportive care ▪ Social services 	<ul style="list-style-type: none"> ▪ Supportive care ▪ Neonatal opiate solution (NOS) 	<ul style="list-style-type: none"> ▪ Supportive care ▪ Neonatal opiate solution (NOS) ▪ Adjunctive therapy ▪ Social services
Outcome	<ul style="list-style-type: none"> ▪ Discharge after 72-96 hours ▪ Close outpatient monitoring 	<ul style="list-style-type: none"> ▪ Hospitalization for 1-3 weeks 	<ul style="list-style-type: none"> ▪ Hospitalization for >3 weeks ▪ Treatment of comorbidities (GERD/nosocomial infection)

Neonatal opiate solution (NOS) is an aqueous solution containing 0.4mg/mL of morphine sulfate. The starting dose for NOS is 0.2 to 0.5 mg/kg orally per day, divided into 6 to 8 doses, depending on the frequency of feedings. In order to stabilize the infant, the initial dose is continued for 48 to 72 hours. If the infant responds with improved feeding, sleeping and comfort, and a reduction in GI symptoms (equivalent to a NAS score consistently <8), the NOS dose may be decreased by 10% every 24 to 48 hours, as long as symptoms are controlled. If the infant's symptoms do NOT improve with the initial dosage, this dose may be increased by 10% until therapeutic goals are met. Although the maximum dose of NOS is 1 to 2 mg/kg per day, the addition of phenobarbital as adjunctive therapy should be considered in patients at an NOS dose of greater than 1mg/kg per day.

Phenobarbital is an alternative or adjunct therapy for treatment of NAS. It is not considered a first-line monotherapy, as it does not treat GI symptoms, such as vomiting and diarrhea. Additionally, there have been some concerns about the long-term adverse effects of phenobarbital on the newborn brain. In situations where phenobarbital is used, the infant should receive a loading dose of 15 to 20mg/kg (intramuscularly or orally), followed by 4 to 6 mg/kg per day divided in twice-daily dosing. Phenobarbital may be decreased by 10% in infants who are stabilized (similar to NOS), or increased by 10% until adequate control is achieved.

Methadone has not been adequately studied in NAS, however it is used frequently in newborn centers, at doses ranging from 0.5 to 0.1mg/kg orally every 6 hours. Subsequent dosing may be increased or decreased by increments of 0.05mg/kg as needed.

Even with successful medical management, NAS symptoms persist 4 to 6 months after birth. Sleep disturbances, hyperreflexia and GI disturbances tend to resolve later in the withdrawal process. There is also a higher incidence of Sudden Infant Death Syndrome (SIDS) in infants diagnosed with NAS.

TAKE-HOME POINTS

- Consider NAS in infants with neurologic, GI, or autonomic symptoms, even without a known history of maternal drug use
- Use an assessment and scoring system that staff have been trained to administer with consistency and low variability
- Involve social services early, and report patient to the appropriate child welfare agencies
- Provide NOS for all infants who present with moderate to severe symptoms
- Provide aggressive nutritional support if needed

Adapted from: McNett W. (2007). Neonatal Abstinence Syndrome. In Zaoutis LB, Chiang VW (Eds.), Comprehensive Pediatric Hospital Medicine (286-290). Philadelphia, PA: Mosby, Inc.