

Neonatal Abstinence Syndrome (NAS)

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THANK YOU

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Neonatal Abstinence Syndrome (NAS)

- ▶ Also referred to as *neonatal opioid withdrawal syndrome*, is defined by signs and symptoms of withdrawal that infants develop after in-utero exposure to opioids

Neonatal Abstinence Syndrome (NAS)

- ▶ Symptoms involve primarily the central nervous system, autonomic nervous system, as well as the GI system.
- ▶ Babies present with irritability, tremors, excessive fussiness (high pitched cry), diarrhea, vomiting, difficulty sleeping, agitation, feeding difficulties, temperature instability
- ▶ Severely affected neonates can have seizures (2-11%)

Neonatal Abstinence Syndrome (NAS)

Incidence

- ▶ ~ 1.2 per 1000 live births (2002)
- ▶ ~ 5.6 per 1000 live births (2012)
- ▶ ~ 20 per 1000 live births (2017)

Hiral et al; JAMA Peds 2020

Neonatal Abstinence Syndrome (NAS) Incidence

- ▶ One Study found 6.7 per 1000 in-hospital births with a NAS diagnosis in 2016, with total costs of \$572.7 million, represents a conservative estimate but one that demonstrates immediate effects of the opioid crisis on maternal and infant health.

Type of Drugs Matter

- ▶ Multiple factors can affect the timing and severity of presentation, like the type of drug exposure, type of opioids exposed in-utero, the timing of the last dose, cumulative dosage, and simultaneous exposure to other abuse drugs.
- ▶ Withdrawal from short-acting heroin presents on the first day of life (24 to 48 hours)
- ▶ Withdrawal from long-acting buprenorphine (36 to 60 hours)
- ▶ Withdrawal from methadone (48 to 72 hours) presents in the first three days of life

Screen and Confirmation

- ▶ Usual clinically confirmed but history may not be readily available, and hence, testing the infant may be necessary.
- ▶ Several methods are available to identify and/or confirm the in-utero drug exposure; the infant's urine, meconium, cord blood, or hair can be useful options.
- ▶ Testing the infant's urine or meconium for drugs is most commonly practiced because of its ease of collection and timely results.
 - ▶ Urine testing can identify drug exposure only a few days before delivery,
 - ▶ the maternal drugs may be identified in the infant's urine between 2 to 4 days.
 - ▶ If there is a delay in collecting neonatal urine, there is a high chance of false-negative results. **First void urine (preferred).**
- ▶ Meconium testing can identify drug exposure dating back to 20 weeks of gestation and hence, more sensitive than the urine test.
- ▶ Synthetic and semi-synthetic opioids, which require a specialized test to identify i.e fentanyl.
- ▶ Although these immunoassay screening tests are easy to perform in most hospitals, confirmatory mass spectroscopy tests are expensive and require advanced expertise.
- ▶ Hair and umbilical cord testing for drugs have also been evaluated but found to be less sensitive, with practical difficulties, and hence, its clinical utility is limited

Neonatal Abstinence Syndrome (NAS)

- ▶ Several scoring tools available
 - ▶ Recent trend is using the Eat, Sleep, Console tool (ESC)
 - ▶ Newer assessment tool that focuses on the baby's functionality; specifically, the infant's ability to eat, sleep, and be consoled
- ▶ Finnigan/Modified Finnigan tool
 - ▶ Used most commonly but it lacks internal consistency
 - ▶ There have been few studies of inter-rater reliability
 - ▶ Cumbersome (over 20 items)

Dodds et al; *Hospital Pediatrics* 2019

Wachman et al ; *JAMA* 2018

Modified Finnegan Score

Modified Finnegan Neonatal Abstinence Score Sheet			
System	Signs and Symptoms	Score	Comments
Central Nervous System Disturbances	Excessive high-pitched (or other) cry < 10 mins	2	The severity of crying should be assessed after the infant has discomforts and needs addressed- such as hunger, dirty diaper, or lost pacifier
	Continuous high-pitched (or other) cry > 10 mins	3	
	Sleeps < 1 hour after feeding	3	Score for the longest period of sleep during the scoring interval. Older infants will stay in a quiet awake state for longer- do not score them if they are awake but quiet
	Sleeps < 2 hours after feeding	2	
	Sleeps < 3 hours after feeding	1	
	Hyperactive Moro reflex	2	Hyperactive Moro Reflex:Arms stay up for 3-4 seconds Pronounced jitteriness of hands during or at end of Moro
	Markedly hyperactive Moro reflex	3	
	Mild tremors when disturbed	1	Mild tremors- Hands or feet only, lasts up to 3 seconds Moderate to severe tremors- Arms and legs as well, lasts more than 3 seconds Disturbed-seen when an infant is being touched, manipulated, or handled Undisturbed- when an infant is sleeping or at rest in their bassinet. There is no touch or manipulation involved.
	Moderate-severe tremors when disturbed	2	
	Mild tremors when undisturbed	3	
	Moderate-severe tremors when undisturbed	4	
	Increased muscle tone	2	Assess for head lag when the infant is gently lifted up by the arms Scores should only be given when the infant is at rest
	Excoriation (chin, knees, elbow, toes, nose)	1	Only score one time per abraded area- may score again if re-abraded
Myoclonic jerks (twitching/jerking of limbs)	3	Short quick contractions of muscle groups or an extremity. They tend to be one quick jerk, usually occur when the infant is sleeping	
Generalised convulsions- Seizure	5	Rhythmic movements that cannot be stopped, eye deviation, and lip smacking. A provider should be notified immediately and infant should be evaluated	
Metabolic/ Vasomotor/ Respiratory Disturbances	Sweating	1	Look for sweating is on the forehead or upper lip. Sweating on the back of neck may be from overheating due to bundling
	Hyperthermia 37.5-38.3C	1	Axillary temperature readings
	Hyperthermia- 38.4C and above	2	
	Frequent yawning (> 3-4 times/ scoring interval)	1	Approximately 15-20 second interval
	Mottling	1	Skin looks marbled with pink, white, and pale areas
	Nasal stuffiness	1	Nasal noises while breathing
	Sneezing (> 3-4 times/scoring interval)	1	Approximately 15-20 second interval
	Nasal flaring	2	An infant who is showing signs of respiratory distress should be carefully evaluated as this could be a sign of infection, metabolic disease, or lung problem in addition to NAS
	Respiratory rate > 60/min	1	The respiratory rate should be observed for full minute & the infant should not be crying while assessing. All needs should be met before assessing, it is okay to wait to count respirations until after a feeding if needed
	Respiratory rate > 60/min with retractions	2	
Gastrointestinal Disturbances	Excessive sucking	1	Increased rooting behavior and/ or if the infant rapidly wipes hands across mouth in an attempt to suck prior to or after a feeding
	Poor feeding	2	Any or all: Excessive sucking prior to feeding, infrequent while feeding, Takes in less than minimum amount needed for growth, Uncoordinated sucking reflex, Continuously gulps and stops frequently to breathe, Unable to close mouth around bottle or breast, Feedings take longer than 20-30 minutes
	Regurgitation	2	Regurgitates whole feed or regurgitates 2 or more times during a feed Not associated with burping
	Projectile vomiting	3	
	Loose stools	2	Stool is thinner than a peanut butter consistency with the presence of >50% water
	Watery stools (water ring on around stool)	3	Stool is more liquid than solid Presence of a WATER RING
	Total Score		
	Date/Time		
	Initials of Scorer		

The NAS score sheet lists 21 symptoms that are most frequently observed in opiate-exposed infants. Each symptom and its associated degree of severity are assigned a score and the total abstinence score is determined by totaling the score assigned to each symptom over the scoring period.

Key points • The first abstinence score should be recorded approximately within four after birth as needed (baseline score).

- Following the baseline score all infants should be scored at 3-4 hour intervals.
- Scoring is dynamic. All signs and symptoms observed during the scoring interval are included in the point-total for that period.
(8 points x 2 times scores start medication)
- Always score around feeding times, and do not wake an infant for scoring.
- Score the infant after all comfort measures have been met.

Eat, Sleep, Console Tool (ESC)

- ▶ A newer assessment tool that focuses on the baby's functionality; specifically the infant's ability to eat, sleep, and be consoled

Grossman et al; ESC CARE TOOL/Instructional Manual; 2018

Grossman et al; *Hospital Pediatrics* 2018

Dodds et al; *Hospital Pediatrics* 2019

Eat, Sleep, Console Tool (ESC)

- ▶ Short term data is promising
- ▶ Long term data lacking
- ▶ Reduction in need for pharmacologic treatment appears to be consistent along with decreasing length of stay and cost
- ▶ Research has not demonstrated increased rates of readmission or other complications (balancing measures)

Grossman et al; *Hospital Pediatrics* 2018

Dodds et al; *Hospital Pediatrics* 2019

Grisham et al; *Advan Neonatal Care* 2019

Improving Outcomes for Neonates with NAS (Neonatal Abstinence Syndrome)

Goals

- ▶ Optimize non-pharm (non-pharmacologic) measures
- ▶ Transition to new Eat, Sleep, Console Scoring tool from Modified Finnegan Tool (will take time)
- ▶ Decrease amount of pharmacologic treatment needed
- ▶ Decrease length of stay
- ▶ Implement new algorithm



Hosp Pediatr. 2019;9(8):632-638. doi:10.1542/hpeds.2019-0086

ESC Assessment										
<i>Give 1 point for each "yes" answer</i>										
Date										
Time										
Eating effectively (breastfeeds with effective suck, swallow, and/or latch and minimal regurgitation or able to eat the amount of prescribed formula)										
Sleeping effectively (able to sleep for 60 consecutive minutes)										
Console (able to console in 10 minutes or less)										
Total score										
RN initials										

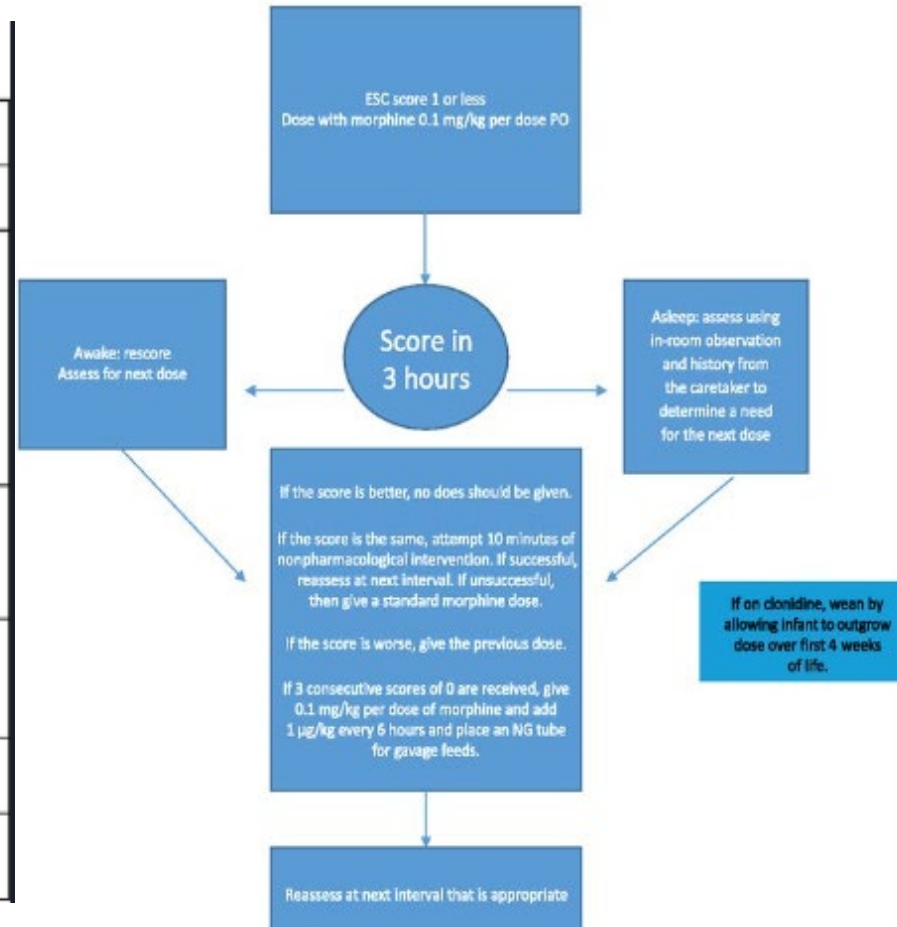


Figure Legend:

ESC scoring form and treatment pathway. NG, Nasogastric; PO, Per Os; RN, registered nurse.

Nonpharmacologic Measures

- ▶ The most clinically meaningful interventions in NAS management pertain to non-pharmacologic care
- ▶ Parental rooming-in *and* breastfeeding are considered the most important
- ▶ Wachman et al ; *JAMA* 2018

Nonpharmacologic Measures

- ▶ First-line treatment for infants with NAS
 - ▶ Significantly reduces an infant's likelihood of needing pharmacologic treatment
 - ▶ Reduces pharmacologic treatment duration when initiated

Nonpharmacologic Measures

- ▶ Rooming-in with parent throughout the hospital stay
- ▶ Ensuring parental presence at the bedside as often as possible during the hospital stay
 - ▶ Encouraging skin-to-skin contact
- ▶ Encouraging holding, gentle rocking, swaying by a caregiver or cuddler

Nonpharmacologic Measures

- ▶ Swaddling, flexed positioning
- ▶ Ensuring optimal feeding quality including encouraging breastfeeding
- ▶ Non-nutritive sucking with pacifier or finger (ensuring baby is well fed first)

Nonpharmacologic Measures

- ▶ Ensuring a quiet environment with low light stimulation in the room
- ▶ Limiting visitors to one at a time (and to those that will be quiet / supportive)
- ▶ Providing uninterrupted periods of sleep
 - ▶ Clustering infant's care

Pharmacologic Treatment For NAS

- ▶ Current inconclusive evidence to recommend one pharmacologic treatment regimen over another
- ▶ Although buprenorphine was consistently associated with shorter length of stay across 4 studies (1 RCT and 3 cohort studies) including a total of 258 buprenorphine-treated infants

Hall et al; *Am J Perinatol* 2018

Kraft et al; *New England Journal of Medicine*; 2017

Wachman et al ; *JAMA* 2018

Pharmacologic Treatment For NAS

- ▶ Methadone, morphine, and buprenorphine are the most commonly studied first-line pharmacologic agents
- ▶ Current evidence does not definitively favor one agent over another
- ▶ Clinical trials comparing these agents are ongoing

Pharmacologic Treatment For NAS

- ▶ For second-line therapy, phenobarbital or clonidine are the most commonly studied agents
 - ▶ Conflicting evidence as to which medication results in fewer opioid-treatment days

Wachman et al ; *JAMA* 2018

Akron Children's Updated Pharmacologic Protocol 2020

Based on the paper by Dodds et al ; *Hospital Pediatrics* 2019

- ▶ Used ESC approach (*our specific ESC tool is also based off of this paper*). There are many different ways to score ESC.
- ▶ Used prn morphine instead of scheduled dosing
 - ▶ Implemented clonidine more proactively for more severely affected neonates
- ▶ Their results demonstrated cost savings, decreased length of stay, and decreased medication use

Akron Children's Updated Pharmacologic Protocol 2020

Akron Children's Hospital Updated NAS Pharmacologic Protocol 2020

Does baby have an Eat, Sleep, Console score ≤ 1 despite optimization of non-pharmacologic measures?



Administer 0.1 mg/kg oral morphine



Rescore in 3-4 hours: If baby is asleep, assess using in-room observation and history from caretaker to determine ESC score



ESC score ≥ 2

No morphine dose should be given

Reassess in 3-4 hours



ESC score still ≤ 1



Attempt 10 minutes of non-pharm measures



Non-pharm measures *successful*

No morphine dose to be given

Reassess in 3-4 hours



Non-pharm measures *not successful*

Give 0.1 mg/kg oral morphine

Reassess in 3-4 hours

Akron Children's Updated Pharmacologic Protocol 2020



NICU Akron Children's Hospital Main Campus NAS Clinical Practice Guidelines- Updated July 2020

**If 3 consecutive ESC scores of 0 are received, start 1 mcg/kg/dose of oral clonidine every 6 hours (and continue with prn morphine dosing). Place an ng tube for gavage feeds. Clonidine will need to be weaned off over the next 2 – 4 weeks depending upon baby's NAS clinical status. **

Baby will need to be monitored for 48 hours after morphine and clonidine are discontinued prior to discharge home.

For neonates with severe NAS (requiring both morphine and clonidine) who also have a history of in-utero exposure to SSRIs, benzodiazepines, gabapentin (Neurontin), or anti-psychotic medications, consider adding phenobarbital as a 3rd agent if needed. (Phenobarbital dosing: 20 mg/kg load given as 10mg/kg/dose q12hrs for 2 doses with 5mg/kg/day maintenance given daily.) Some babies require phenobarbital levels in the mid-30s range for NAS stability and providers may need to increase dosage based on level and symptomatology. Neurology team should be consulted for NAS babies requiring phenobarbital and follow them after discharge for phenobarbital weaning.

If NAS baby is preterm, prescribers should order a lower morphine dose (0.05 mg/kg) to help prevent apnea or other issues. If preterm infants require clonidine, they should also be started on a lower dose of clonidine (0.5 mcg/kg/dose) every 6 hours.

Preterm neonates who are not feeding well solely due to prematurity should still be given a score of 1 for feeding. If the premature neonate is not feeding well due to severe withdrawal, they should be given a 0 for feeding.

If baby was exposed to in-utero buprenorphine (Subutex) or methadone and scores have remained consistently good without needing pharmacologic treatment or NICU transfer for concerning signs of NAS, provider may consider discharge home at day of life 5. Baby must also be demonstrating weight gain and not be more than 5% below birth weight, otherwise baby will need to stay for the full 7 days of evaluation.

Does Bup Does Affect Severity or Incidence of Neonatal Abstinence Syndrome?

- ▶ In Wong et al. NAS requiring morphine treatment occurred in neonates born to moms who dose was
 - ▶ ≤ 8 mg/d buprenorphine in 48.5%
 - ▶ > 8 mg/d buprenorphine in 41.4%
- ▶ No significant associations of maternal buprenorphine dose with peak NAS score, NAS severity requiring morphine, time to morphine start, peak morphine dose, or days on morphine.
- ▶ Among the other factors examined, only exclusive breastfeeding was significantly associated with neonatal outcomes, specifically lower odds of morphine treatment (odds ratio 0.24, $P = 0.003$).

Questions

