

Newborn Critical Care Center (NCCC) Clinical Guidelines

Guidelines for Management of Neonatal Abstinence Syndrome

BACKGROUND

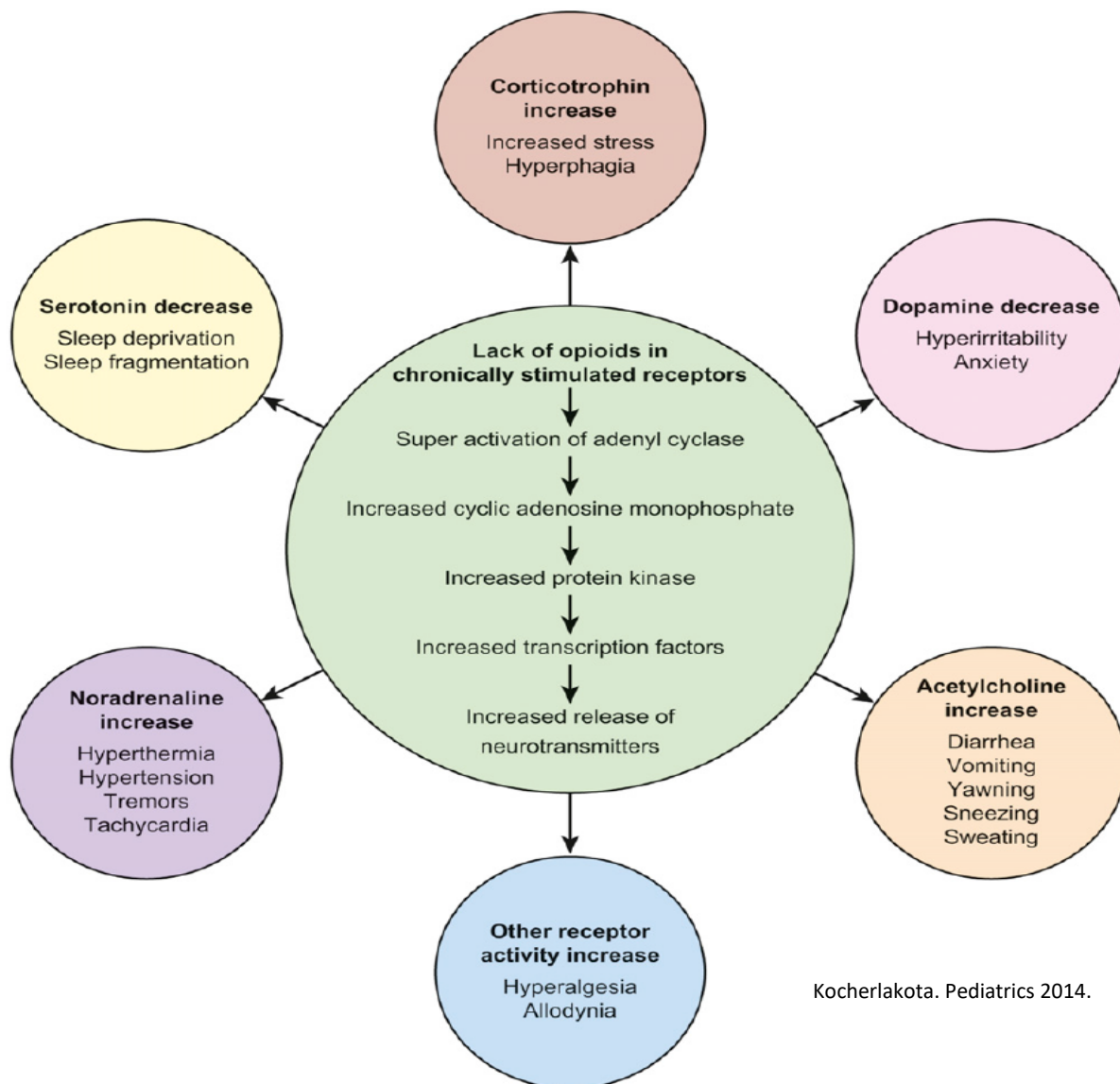
Neonatal abstinence syndrome (NAS) is a clinical spectrum of withdrawal that results from the abrupt cessation of chronic intrauterine exposure of the fetus to maternal drugs used via umbilical transfer. Historically, NAS secondary to short-acting opioids such as morphine or heroin was primarily described in the literature. More recently, NAS includes withdrawal from longer acting opioids such as methadone and buprenorphine as well as non-opioids such as antidepressants, anxiolytics, and other substances, alone or in combination. This results in a presentation that can vary widely in timing of onset, duration and symptomatology.

While the exact pathophysiology of opioid withdrawal in neonates is not known, it is understood that increased noradrenergic output from the locus coeruleus of the pons occurs as a result of upregulation cyclic adenosine monophosphate (cAMP) from chronic opioid agonism. This creates an environment for superactivation of cAMP-mediated processes once the opioid stimulus is withdrawn after birth, which increases various neurotransmitters and is thought to be largely responsible for the majority of signs and symptoms observed in NAS. Increased production of noradrenaline, acetylcholine, corticotropin and decreased production of serotonin and dopamine occur as a result. Accordingly, the central and autonomic nervous systems and gastrointestinal tract are predominantly affected.

In the last two decades in the United States, the percent of pregnant women using opioids quadrupled. While there is regional variation, recent data from 2016 showed an average rate of NAS of 20/1000 live births, up from 1.3/1000 live births in 2000. NAS often results in prolonged hospitalization and places an increasing strain on the healthcare system.

PRESENTATION

The onset, duration and severity of NAS depend on several characteristics of the drugs used by the mother, including their types, amounts, half-lives, receptor-binding capacities, receptor affinities, placental transferability and other pharmacologic properties.



The initial phase of NAS is often short but intense and can consist of tremors, seizures, irritability, feeding problems, vomiting, diarrhea, hyperthermia and lasts for 1-2 weeks. This can be followed by a chronic and relapsing course that includes hyperirritability, sleep disturbances, hyperphagia and other neurologic and autonomic signs that can last for a few weeks to a few months.

Although NAS is a clinical diagnosis, toxicological confirmation is necessary to identify the exact type of substance that the mother was using to confirm or rule out the use of other substances during pregnancy (see [NCCC Guidelines for In Utero Drug Exposure](#)) and [Appendix 1](#) for duration of detection in toxicological urine screens.

Additionally, NAS may be affected by the time of the last dose, the duration of exposure, the total accumulation of the exposure, and the multiplicity of substances the neonate was exposed to.

TABLE 1 Onset, Duration, and Frequency of NAS Caused by Various Substances

Drug	Onset, h	Frequency, %	Duration, d
Opioids			
Heroin	24–48	40–80 ²⁷	8–10
Methadone	48–72	13–94 ³⁷	Up to 30 or more
Buprenorphine	36–60	22–67 ^{46,48}	Up to 28 or more
Prescription opioid medications	36–72	5–20 ^{56,60}	10–30
Nonopioids			
SSRIs	24–48	20–30 ⁶⁴	2–6
TCAs	24–48	20–50 ⁶⁴	2–6
Methamphetamines	24	2–49 ¹⁰¹	7–10
Inhalants	24–48	48 ⁷⁰	2–7

Kocherlakota. Pediatrics 2014.

ASSESSMENT

Periodic assessment of the infant using validated tools is necessary to determine the severity of NAS, if and when pharmacologic intervention is necessary, and in monitoring, titrating and weaning from therapy. No scoring tool has been shown to be superior and all scoring tools available are subject to interobserver variability. Currently, the modified Finnegan scoring system (see [Appendix 2](#)) remains the most commonly used tool for assessing the severity of NAS in infants, and is used for opioid and nonopioid withdrawal assessment. Scoring should be initiated within 12 hours of birth, performed after feeds, at 3–4 hour intervals when the infant is awake. The score should represent the status of the infant both at the time of assessment and during the preceding time period. After 21 days of age, NAS scores can increase solely from normal developmental progression, thus all trigger thresholds should be increased by 2.

MANAGEMENT

While there is no one optimal model of care of NAS that has been established in the literature, the 2012 AAP Clinical Report on NAS recommends a 2-tiered approach to treatment of NAS, with first-line therapy focusing on nonpharmacologic interventions. Pharmacologic interventions should be considered only when nonpharmacologic measures fail. The long-term outcomes of NAS and success of interventions is poorly understood at this time, thus therapy is currently directed at short-term outcomes.

Nonpharmacologic Therapies

Nonpharmacologic therapy is the first-line therapy of NAS, and effective alone in many cases. It is also to be used as an adjunctive therapy, even when pharmacotherapy is required. It may be especially important to stay alert to early signs of irritability before they escalate. While active maternal participation is the best nonpharmacologic care, fathers, nurses and volunteers can help provide continuous excellent supportive care. Substance use disorder is a disease, and a caring, nonjudgmental approach may encourage maternal participation. As there is a spectrum

of NAS, the nonpharmacologic therapies that are useful in an individual infant varies. The NICU environment can be a challenging place to institute all of these measures, but should be attempted to the greatest extent feasible.

Environmental Control

- Continually quiet, dimly lit room, lower ambient temperature
- Gentle handling
- Sucking: pacifier use, feeding *ad lib*
- Swaddling: lessens stimulation, decreases crying times and promotes more sustained sleep. May be less helpful in neonates with fever
- Prone positioning (although caution to resume Safe to Sleep positioning prior to discharge with proper parental counseling)
- Vibrating Tranquilo mats may be placed under the baby – located in Pod G

Social Integration

- Kangaroo/skin-to-skin care
- Parental presence/rooming in
- Parent brochure (see [Appendix 3](#))

Feeding

- On demand with careful avoidance of waking infant
- Breastfeeding may decrease the incidence of NAS, the need for pharmacologic treatment, and the length of hospital stay. Breastfeeding is encouraged *if mother is active in a treatment program for 3 months prior to delivery with continued participation, with an otherwise negative urine toxicology screen on admission, and no other contraindications to breastfeeding*, (see [Breastfeeding Medications and Contraindications](#), [Academy of Breastfeeding Medicine Protocols: Substance Use and Breastfeeding](#) for reference). A lactation consult should be obtained. For infants receiving breast milk, additional powder of Similac Sensitive can be added to provide 22 kcal/oz if the infant demonstrates excessive weight loss or inadequate weight gain.
- Formula: When breastfeeding is contraindicated, or breast milk is not available, it is recommended that the infant be provided with Similac Sensitive 22 kcal/oz lactose-free formula. The higher calorie formula is designed to meet the exceptional caloric needs of infants with NAS, and may prevent the documented weight loss seen in these infants while allowing lower use of narcotics in treatment. The higher calorie formula is only needed at the onset of withdrawal- generally for a week or less. Discontinue when weight gain is firmly established. Discharge on the higher calorie formula will generally not be necessary.

Skin Care

- Diaper dermatitis is common due to diarrheal symptoms, and should be diligently attended to

Occupational / Physical / Speech Therapy

- Consult orders should be placed for neonates at risk for or with evidence of NAS

Pharmacologic Therapy

Pharmacotherapy to control withdrawal symptoms is required when nonpharmacologic therapy fails and withdrawal scores remain high, and/or serious signs, such as seizures or dehydration, are observed. While many medications are available to treat withdrawal, no single regimen is applicable to every patient, and appropriate therapy requires frequent, careful consideration and titration. Morphine and phenobarbital have been chosen for use in our protocol.

Opioid antagonists, such as naloxone (Narcan), are contraindicated in neonates because they may precipitate seizures. Any seizures should be controlled by usual seizure management in addition to management of NAS.

Overview of Stages of Treatment

NON-PHARMACOLOGIC BUNDLE	
Swaddle, skin-to-skin, decreased stimulation, breastfeed or 22kcal/oz formula	
PHARMACOLOGIC BUNDLE	
Initiate	<ul style="list-style-type: none">• Initiate morphine for Finnegan scores ≥ 8 THREE times in a row OR scores ≥ 12 TWO times in a row
Escalate	<ul style="list-style-type: none">• If Finnegan scores remain elevated, increase dosage based on infant's score
Stabilize	<ul style="list-style-type: none">• Maintain dose for 24 hours
Wean	<ul style="list-style-type: none">• Wean by 10% of stabilizing dose every 24 hours based on Finnegan scores
Discharge	<ul style="list-style-type: none">• Discharge once off morphine for 48 hours

Morphine

Morphine is the most commonly preferred medication to treat withdrawal and decreases the incidence of seizures, improves feeding, eliminates diarrhea, decreases agitation, and can control severe symptoms. Because it has a short half-life, it has to be administered every 3-4 hours. Dosing can be escalated rapidly for higher scores; however, weaning has to be gradual. When an optimal response has not been achieved with the maximal dose, an adjuvant medication should be considered.

- Morphine should be **initiated** at 0.05 mg/kg/dose every 3 hours PO for 3 consecutive scores ≥ 8 or 2 scores ≥ 12 within a 24 hour period.
- Dose of morphine should be **escalated** every 3 hours as needed after initiation by increasing dose by 0.02 mg/kg/dose for 2 scores in a row of 8-11 or by 0.04 mg/kg/dose for 2 scores in a row ≥ 12 .
- If total dose becomes ≥ 0.3 mg/kg/dose, consider phenobarbital therapy as an adjunct therapy.

Stabilization is achieved if all scores remain < 8 for a minimum of 48 hours.

- If infant has required above 0.4 mg/kg/dose of morphine or any phenobarbital for adjunctive therapy, use 72 hours of stabilization

Weaning should be initiated once the patient has stabilized on the same dose for 48 hours (or 72 hours for >0.4 mg/kg/dose of morphine use or any phenobarbital used), and may be continued as long as NAS scores remain < 8 . Begin weaning by 10% of the original stabilization dose every 24 hours. Morphine may be discontinued when a single dose is < 0.02 mg/kg/dose.

Backslide management is needed when score remains ≥ 8 after rescoring in 3-4 hours after optimizing nonpharmacologic options. You should then return to previous effective dose. Resume dose wean when average scores are < 8 for a minimum of 48 hours.

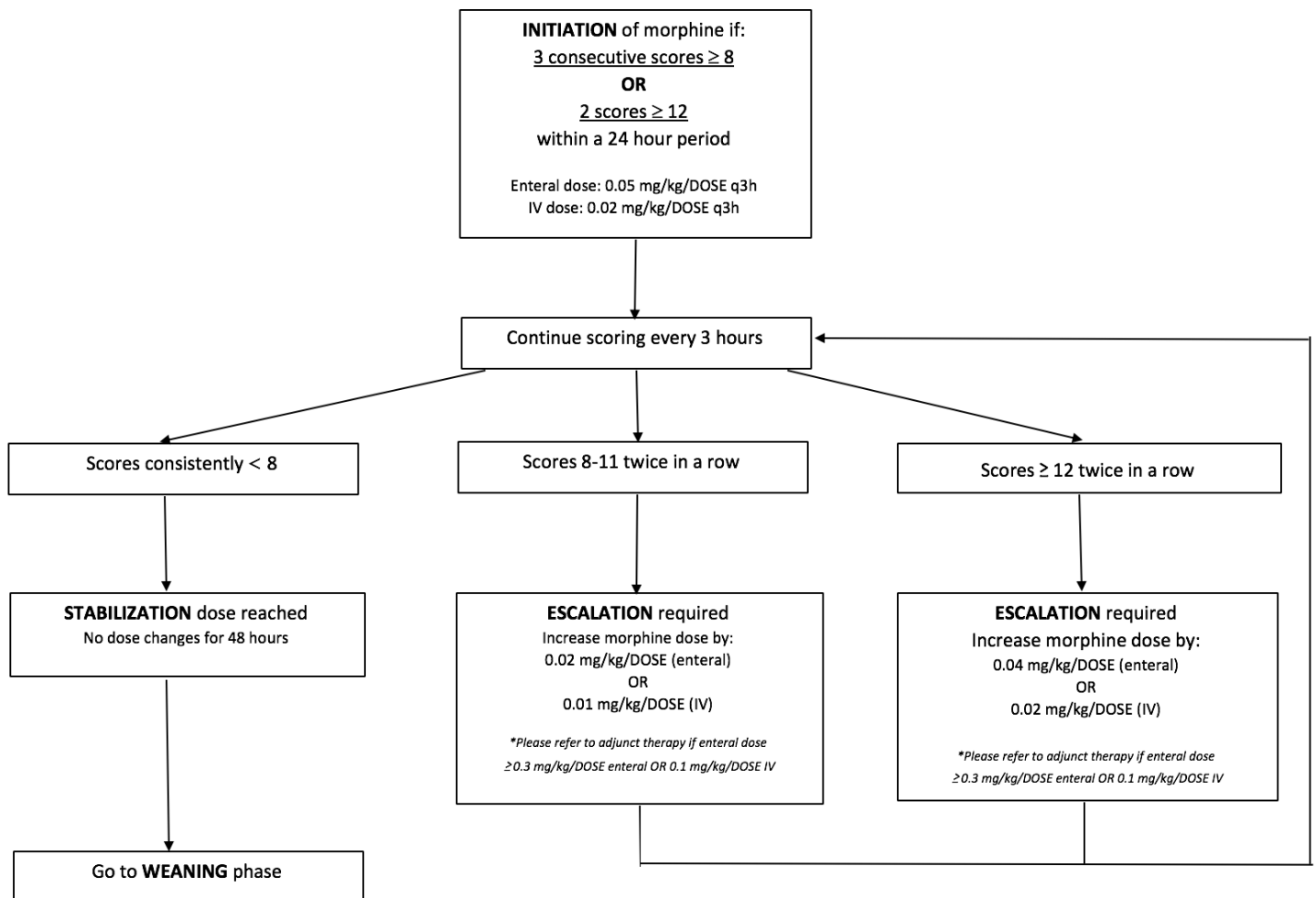
Consider:

- Adding phenobarbital if unable to wean dose for 2 consecutive days
- Weaning dose every 72 hours
- Weaning maintenance dose by 5% instead of 10% of stable dose

Discharge should be considered after 48 hours of hospital observation.

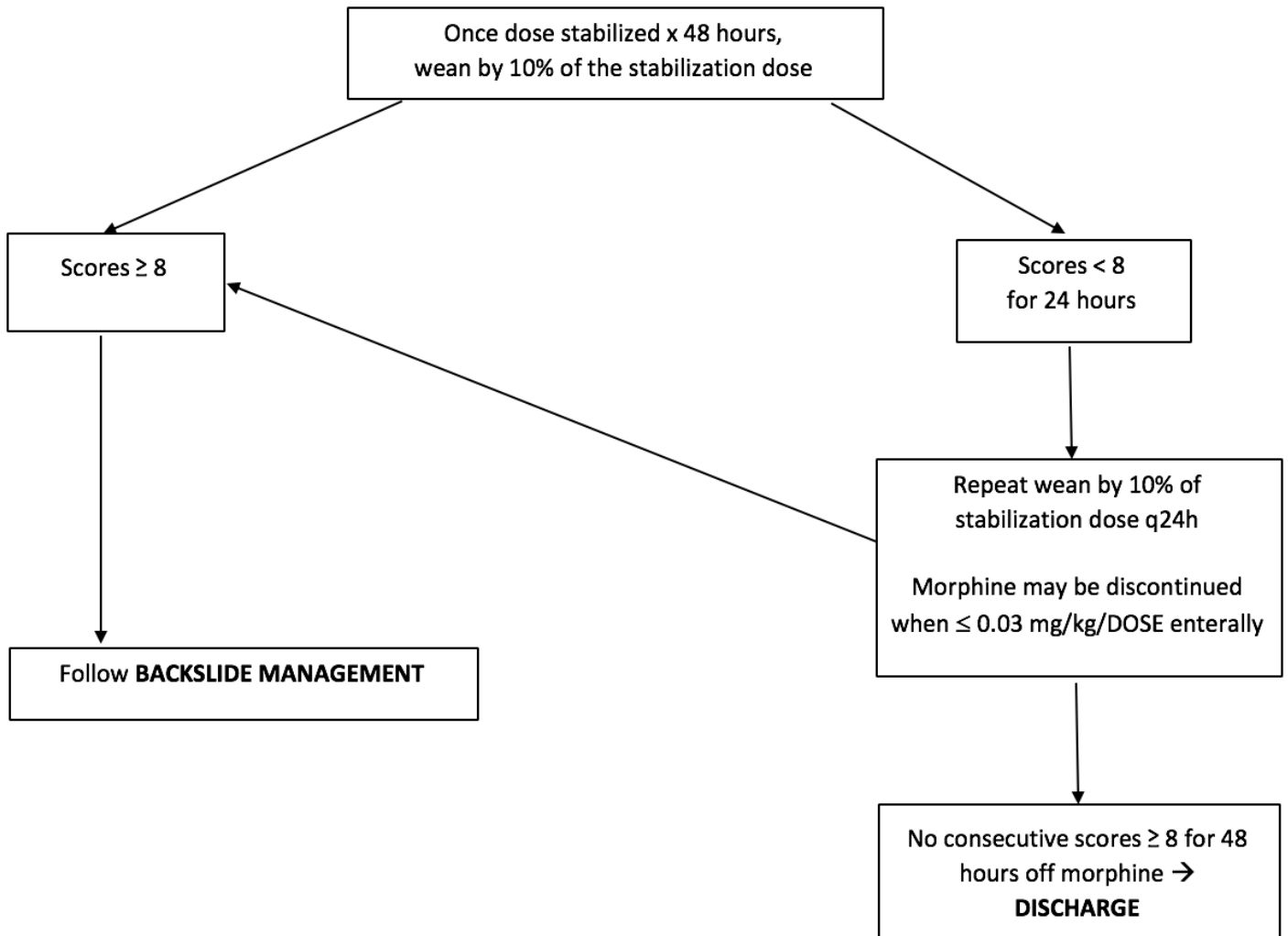
Enteral and intravenous morphine dosing are not equivalent. If an infant requires IV dosing, the initiation dose is 0.02 mg/kg/dose every 3 hours. If symptoms are not controlled, the IV dose may be increased by 0.01 mg/kg/dose every 3 hours until symptoms are controlled to a maximum of 0.1 mg/kg/dose IV, then consider addition of phenobarbital as adjunct therapy.*

Initiation, Escalation and Stabilization Phase



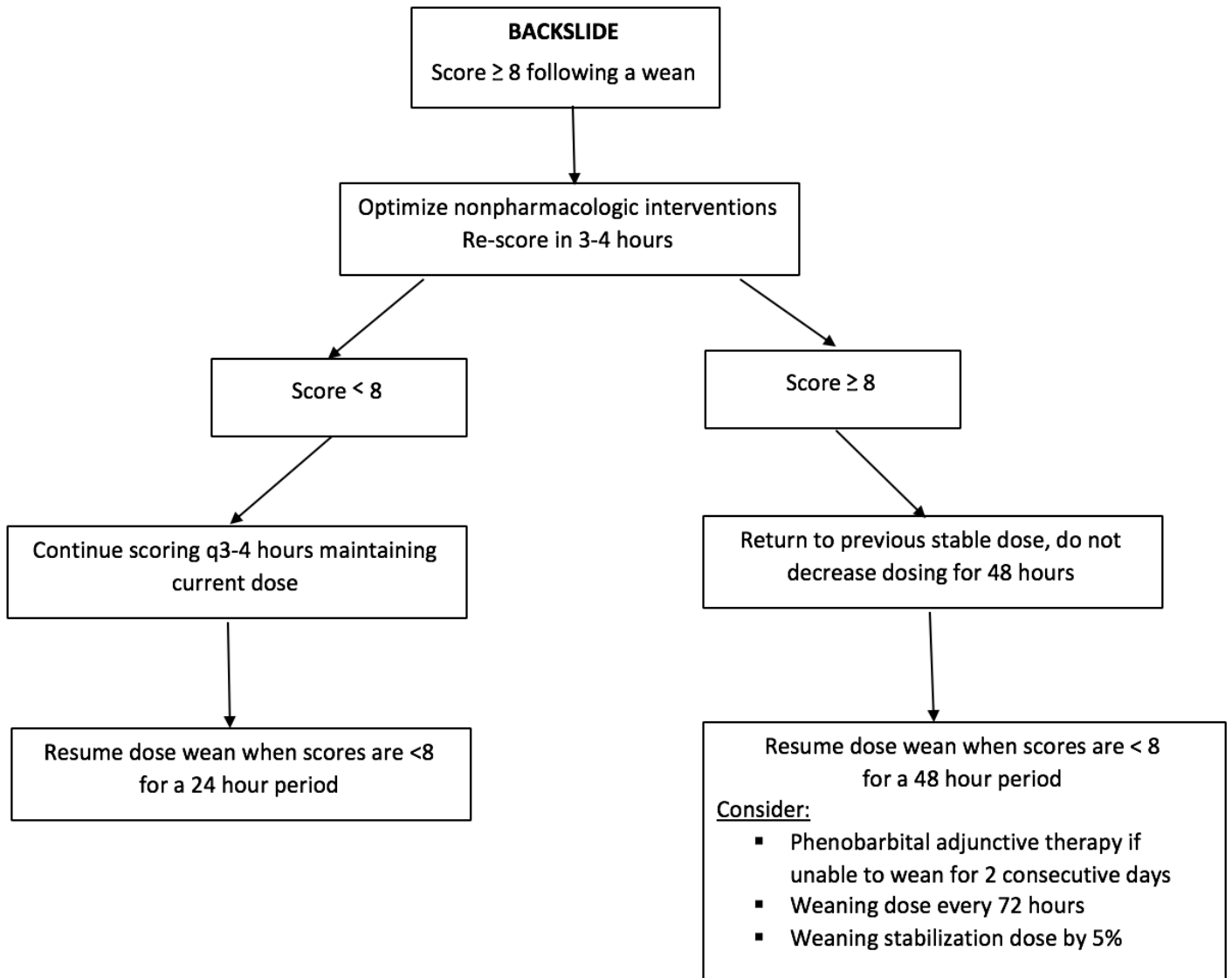
Adapted from:
Walsh, et al., Pediatrics, 2018.

Weaning Phase



Adapted from:
Walsh, et al., Pediatrics, 2018.

Backslide Management



Adapted from:
Walsh, et al., Pediatrics, 2018.

Phenobarbital

Phenobarbital is a drug of choice for non-opiate NAS or for infants suffering from polydrug withdrawal, and is often used as an adjunct to morphine therapy. Levels can be monitored. The doses used for withdrawal are not high enough to prevent seizures.

Consider using phenobarbital if polysubstance use is suspected/confirmed (including benzodiazepines, barbiturates, antipsychotics, antidepressants, other sedatives/hypnotics, tobacco) **AND**:

- CNS findings predominate (tremors, increased muscle tone, etc) rather than GI findings on NAS subscale
- Morphine dose exceeds 0.3 mg/kg/dose enteral or 0.1 mg/kg/dose IV with NAS score ≥ 8 **OR** unable to wean for 2 consecutive days

Loading dose of phenobarbital is 20 mg/kg/dose x 1 dose. Non-standard dosing of phenobarbital 10 mg/kg/dose every 12 hours x 2 doses as an alternative may be considered, as clinically appropriate.

- Enteral formula contains 10% alcohol
- Dividing the PO dose may decrease risk of emesis and/or sedation

Maintenance dose of phenobarbital is 5 mg/kg/dose PO once daily. **Do not weight adjust.**

Discontinue phenobarbital on second to last step of morphine wean to assess for tolerance of discontinuation. Given the long half-life of phenobarbital, this will wear off gradually over 4 days.

DISCHARGE, TRANSFER AND FOLLOW-UP CONSIDERATIONS

A social work consult should be obtained on all infants diagnosed with NAS upon admission. When the neonate shows no major signs of withdrawal and is feeding well, sleeping well, gaining weight and maintaining scores < 8 for at least 48-72 hours (see flowsheets), discharge can be considered. Please provide a weaning plan for all infants discharged to the floor or transferred out of our unit.

Infants with a history of NAS require neurodevelopmental follow up to identify motor deficits, cognitive delays or relative microcephaly, psychobehavioral assessments to identify hyperactivity, impulsivity and attention concerns in preschool age and beyond, and ophthalmologic assessment to identify nystagmus, strabismus, refractive errors and other visual defects, growth and nutritional assessment to identify failure to thrive and short stature, and family support assessments. This should be included in the discharge or transfer summary for pediatrician follow-up. If significant deficits are noted during admission, a SICC referral may be considered, but is not standard. Infants with NAS symptoms who required pharmacological intervention qualify for the Child Developmental Services Agency (CDSA) early intervention services. OT/PT/SLP will place consult orders when appropriate.

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Appendix 1

Urinary Screening and Approximate Duration of Detection

TABLE 3 Urinary Screening for Various Drugs and Approximate Duration of Detection in the Neonate^{116,118–120}

Substance	Compound/Metabolite/Usage	Duration of Detectability
Alcohol ¹²³	Ethanol	Few h
	Fatty acid ethyl esters	Up to 5 d
	Ethyl glucuronide	Up to 30 h
	Ethyl sulfate	
Amphetamines	Amphetamine	1–2 d
	Methamphetamine	1–2 d
Barbiturate	Short acting	<2 d
	Long acting	1–7 d
Benzodiazepines	Short acting	1–7 d
	Long acting	Up to 30 d
Cocaine	Cocaine	6–8 h
	Metabolites	2–5 d (up to 10–22 d with heavy use)
Marijuana	Single use	1–3 d
	Moderate use	5–7 d
	Heavy	up to 10 d
	Chronic heavy use	up to 30 d
Opiates	Heroin, morphine, codeine	1–2 d
	Hydromorphone, oxycodone	2–4 d
	Methadone	2–3 d
	Methadone metabolite	Up to 6 d
	Buprenorphine ¹²⁵	2–3 d
	Buprenorphine	2–3 d
	Norbuprenorphine	
Phencyclidine		1 to 8 d

Appendix 2
Finnegan Neonatal Abstinence Scoring System (FNASS)

SIGNS AND SYMPTOMS	SCORE	DEFINITION OF SIGNS AND SYMPTOMS
CENTRAL NERVOUS SYSTEM DISTURBANCES		
Excessive high-pitched (or other) cry < 5 mins	2	Score 2 if high-pitched at its peak, 3 if high-pitched throughout. Infant is scored if crying is prolonged, even if it is not high-pitched.
Continuous high-pitched (or other) cry > 5 mins	3	
Sleeps < 1 hour after feeding	3	Scale of increasing severity & a term infant should receive only one score from the three levels. A premature infant on 3 hourly feeds can sleep for 2½ hours at most. Scoring should thus be 1 if the baby sleeps less than 2 hours, 2 if less than 1 hour and 3 if the baby does not sleep between feeds.
Sleeps < 2 hours after feeding	2	
Sleeps < 3 hours after feeding	1	
Hyperactive Moro reflex	2	Moro (startle) reflex is normal reflex of young infants & occurs when sudden loud noise causes the child to stretch out the arms & flex the legs. Score if the infant exhibits pronounced jitteriness (rhythmic tremors that are symmetrical & involuntary) of the hands during/at end of a Moro reflex. Score 3 if jitteriness & clonus (repetitive involuntary jerks) of hands &/or arms present during/after the initiation of the reflex.
Markedly hyperactive Moro reflex	3	
Mild tremors when disturbed	1	Scale of increasing severity & an infant should only receive one score from the four levels. Undisturbed refers to the baby being asleep or at rest in the cot
Moderate-severe tremors when disturbed	2	
Mild tremors when undisturbed	3	
Moderate-severe tremors when undisturbed	4	
Increased muscle tone	2	Score if excessive/above-normal muscle tone/tension is observed -muscles become "stiff" or rigid & the infant shows marked resistance to passive movements, e.g. if the infant does not experience any head lag when being pulled to the sitting position; or if there is tight flexion of the infant's arms and legs (unable to slightly extend these when an attempt is made to extend and release the supine infant's arms and legs)
Excoriation (chin, knees, elbow, toes, nose)	1	Excoriations (skin abrasions resulting from constant rubbing against surface that is covered with fabric like bed linen). Score only when excoriations first appear, increase or appear in a new area.
Myoclonic jerks (twitching/jerking of limbs)	3	Score if involuntary muscular contractions which are irregular and exceedingly abrupt (usually involving a single group of muscles) are observed.
Generalized seizures	5	In the newborn generalized seizures often referred to as tonic seizures. Most commonly seen as generalized activity involving tonic extensions of all limbs, but sometimes limited to one/both limbs on one side. Unusual limb movements may accompany a seizure. In the upper limbs often resemble "swimming" or "rowing". In lower limbs, resembles "pedaling" or "bicycling." Other subtle signs may include eye staring, rapid involuntary eye movements, chewing, back arching, & fist clenching.

Sweating	1	Score if sweating is spontaneous and is not due to excessive clothing or high room temperature.				
Hyperthermia 37.2-38.3 °C	1	Temperature should be taken per axilla. Mild pyrexia (37.2-38.3°C) is an early indication of heat produced by increased muscle tone and tremors.				
Hyperthermia > 38.4 °C	2					
Frequent yawning (> 3-4 times/ scoring interval)	1	Score if more than 3 yawns observed within the scoring interval.				
Mottling	1	Score if marbled appearance of pink/pale or white areas present on the infant's chest, trunk, arms, or legs				
Nasal stuffiness	1	Score if infant sounds congested; mucous may be visible				
Sneezing (> 3-4 times/scoring interval)	1	Score if more than 3 sneezes observed within the scoring interval				
Nasal flaring	2	Score only if repeated dilation of the nostrils is observed without other evidence of lung or airways disease				
Respiratory rate > 60/min	1	Respirations counted for 1 minute. Score only if >60/min without other evidence of lung or airways disease. Score 2 if drawing in of the intercostal muscles (retractions).				
Respiratory rate > 60/min with retractions	2					
GASTROINTESTINAL DISTURBANCES						
Excessive sucking	1	Score if hyperactive/disorganized sucking, increased rooting reflex, or attempts to suck fists or thumbs (more than that of an average hungry infant) observed				
Poor feeding (infrequent/uncoordinated suck)	2	Score if infant demonstrates excessive sucking prior to feeding, yet sucks infrequently during a feeding taking a small amount of breast milk or formula, &/or an uncoordinated sucking reflex (difficulty sucking and swallowing). Premature infants may require tube feeding & should not be scored for poor feeding if tube feeding is expected at their gestation.				
Regurgitation (≥ 2 times during/post feeding)	2	Score if at least one episode of regurgitation is observed even if vomit is contained in the mouth.				
Projectile vomiting	3					
Loose stools (curds/seedy appearance)	2	Score if loose (curds/seedy appearance) or watery stools (water ring around a solid stool). Check the diaper after the exam is completed if not apparent during the exam.				
Watery stools (water ring around solid stool)	3					
TOTAL SCORE						
DATE/TIME						
SCORER'S INITIALS						

NEONATAL ABSTINENCE SCORING SYSTEM (NAS; MODIFIED FINNEGAN, 1990)

NOTE: ABSENCE OF BEHAVIOR SCORED '0' ON OWS, IS NOT SCORED WITH NAS.

Scoring (Modified Finnegan):

The modified Finnegan was designed for term babies on q 4 hour feeds and may need modification for preterm infants. In a term infant the scoring is performed 30-60 minutes after a feed, before the baby falls asleep.

1. Score infants at **4 hour intervals** unless when higher scores indicate more frequent scoring. Signs and symptoms that have occurred during that interval are part of the next score obtained.
2. If the **score is ≥ 8 , scoring frequency is increased to 2-hour intervals and continued for 24 hours** after the last total score of ≥ 8 was obtained. (Once the score has been ≤ 7 for 24 hours, resume 4-hour intervals for scoring).
3. If pharmacotherapy is not required, the infant is scored for the first 4 days of life at 4-hour intervals.
4. If pharmacotherapy is required, the infant is scored at 2-4 hour intervals, depending on the observed scores.
5. After cessation of pharmacotherapy, if the score is < 8 for the following 3 days, scoring may be discontinued. If the score is consistently 8 or more after stopping the medications, scoring should continue for the following 4 days (minimum) to ensure that the infant is not likely to develop late onset of withdrawal symptoms.

Scoring (OWS):

To be used with:

- **Infants who have received > 3 days of continuous or scheduled narcotics.**
 - **Infants who have received > 3 doses of narcotics per day for > 5 days.**
 - **Infants who have been prenatally exposed to narcotics and are at risk for developing withdrawal symptoms.**
1. Score **every 4 hours during weaning and for 48-72 hours after opioids have been weaned.**
 2. If **score is > 8 , change scoring frequency to every 2 hours** until the score is < 8 .
 3. Adjustment scores for individual signs may be subtracted from the total score if the sign is expected to occur independently of withdrawal due to an underlying disease or baseline condition of the infant. Adjustments to scores are only made after discussing with a Provider. Adjusted Score = Total Score – Adjustment(s).
 4. If the Adjusted Score is 8 for 3 intervals or > 12 for 2 intervals, the drug dose may need to be increased by 10% of the original dose. – Notify the Provider of the elevated scores.

What you and your Nurses can do to help:

All babies can and should:

- Be comforted in a quiet room with dim lights
- Have skin to skin contact with mother
- Be wrapped in a blanket (swaddled)
- Be held and cuddled
- Be in a room with dim lights

Doing these things can help the baby's withdrawal symptoms.

Breastfeeding:

If you are taking medication you may still be able to breastfeed, but talk with the doctor first to make sure it is safe for your baby. Bottle feeding is always an option.



How long will my baby need to stay in the hospital?

Your baby will stay in the hospital for at least 3-5 days to watch for signs of withdrawal. Babies that need morphine may stay in the hospital for 1-2 weeks.

Going Home:

Once your baby goes home, you will need to see your child's doctor within 24-48 hours.

During your first visit please tell your child's doctor about the medicine you were taking while you were pregnant.

Even after seeing your doctor, look for signs of withdrawal for a few more days. If you see any, call your child's doctor or UNC Pediatrics at (984) 974-6669.

*Approved by Pediatric Education
Committee
9/2017
Neonatal Abstinence Syndrome
Task Force*



**Neonatal
Abstinence
Syndrome (NAS)**

*Guide for parents and
family*

What is Newborn Abstinence Syndrome (NAS)?

NAS is a term for a group of signs a baby may have when he/she is withdrawing from prescribed or illegal drugs taken by the mother while she was pregnant.



What causes NAS?

Many types of medicine are passed from mother to baby while pregnant. Drugs like heroin or pain medicine can cause addiction in the mother. These drugs may cause the baby to become dependent on the drugs before birth. Once the baby is born, the baby is no longer getting these drugs so he/she can show withdrawal signs.

How is NAS diagnosed?

When your baby is born, a urine and stool (meconium) sample will be sent for a drug test. The nurses will watch your baby very closely for withdrawal symptoms. They will ask you if you have seen any signs of withdrawal in your baby. Every 4 hours they track your baby's "Opiates wean score" in the computer. These scores are closely monitored during your baby's stay. Higher scores mean that a baby is showing withdrawal signs and may need treatment.



When does NAS occur?

Not all babies who are exposed to opiates during pregnancy will have withdrawal. For infants who were exposed to methadone or suboxone, withdrawal signs happen 48-72 hours after birth.

Symptoms of NAS:

Fussy
Crying that will not stop
High Pitched crying
Jittery
Trouble sleeping
Tight muscle tone
Restless
Seizures
Frequent yawning, stuffy nose, and sneezing
Poor feeding or does not gain weight
Throwing up or loose, watery stools
Less than 8 wet diapers a day
Fever or unstable temperature

How is NAS treated?

Your infant may require treatment with morphine. Doses may be changed to fit your baby's needs.