Identifying Neonatal Abstinence Syndrome (NAS) and Treatment Guidelines

University of Iowa Children's Hospital -11/2014

What is Neonatal Abstinence Syndrome?

- Neonatal withdrawal after intrauterine exposure to certain drugs (illicit or prescription)
- Occurs with the abrupt cessation of the drug exposure at birth
- Most commonly seen with opioid exposure, but also seen after exposure to sedatives, selective serotonin reuptake inhibitors (SSRI), polysubstance abuse, and occasionally barbiturates and alcohol
- Develops in 55-94% of opioid drug-exposed infants and 28-30% of SSRI-exposed infants

Screening

- Maternal history
- Urine drug screen
- Meconium drug testing
- Umbilical cord testing

Clinical Signs of Withdrawal

Central Nervous System	Metabolism/Vasomotor/Respiratory	Gastrointestinal
• Irritability • Increased wakefulness • High-pitched cry • Tremor • Increased muscle tone • Hyperactive deep tendon reflexes • Frequent yawning • Sneezing • Seizures	• Diaphoresis • Nasal stuffiness • Fever • Mottling • Temperature instability • Piloerection • Mild elevations in respiratory rate and blood pressure	• Vomiting • Diarrhea • Dehydration • Poor weight gain • Poor feeding • Uncoordinated and constant sucking

Onset of withdrawal symptoms

- Onset of withdrawal depends on the half-life of the drug, duration of the addiction, and time of last maternal dose prior to delivery. On average, observation period for symptoms to appear is 3 days.

Drug	Approximate time to onset of withdrawal symptoms
Barbiturates	4-7 days but can range from 1-14 days
Cocaine	Usually no withdrawal signs but sometimes neurobehavioral abnormalities (decreased arousal and physiologic stress) occur at 48-60 hours
Alcohol	3-12 hours
Heroin	Within 24 hours
Marijuana	Usually no clinical withdrawal signs
Methadone	3 days but up to 5-7 days; rate of severity of withdraw cannot be correlated to dose of maternal methadone
Methamphetamines	Usually no withdrawal signs but sometimes neurobehavioral abnormalities (decreased arousal, increased physiologic stress, and poor quality of movement) occur at 48-60 hours
Opioids	24-36 hours but can be up to 5-7 days
Sedatives	1-3 days
SSRIs	Usually 2nd day of life—ranges from 5-48 hours

Preterm Infants and NAS

- Due to immaturity, less total body fat, and differences in total drug exposure, preterm infants may exhibit fewer signs of withdrawal than near-term and term infants.

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Treatment of Neonatal Abstinence Syndrome

Goal: stabilize clinical manifestations of withdrawal and restore normal newborn activity

Scoring of NAS

- Finnegan scoring (tool to quantify severity of NAS) *(See last page for Finnegan Scoring System)*
  - **Begin scoring within 3 hours of life**
  - **Continue scoring every 3-4 hours to coordinate with feedings and cares**
  - **Scoring should be done after feeding and nursing cares to eliminate irritability related to normal baby activities**
  - **Do not wake a sleeping baby to score**
- Used to determine initiation of pharmacologic therapy

Non-Pharmacologic Intervention

- Swaddling
- Rocking
- Minimal sensory or environmental stimulation
- Maintain temperature stability
- Feed (consider alternating bottle and pacifier during feed to compensate for excessive sucking and possibly prevent emesis)
- Breast milk feedings when appropriate can help reduce the need for pharmacological intervention

Pharmacologic Therapy

- **Begin when 3 consecutive Finnegan scores are ≥ 8 or when the average of two scores OR two consecutive scores is ≥ 12.**
- Morphine is the first-line agent and the mainstay of treatment.
- Phenobarbital is the first line additional therapy for polysubstance exposure and may be used in combination with opioid therapy for NAS secondary to opiate withdrawal.
- Opioid-dependency is likely seen after exposure to buprenorphine (Subutex), codeine, heroin, hydrocodone (Lortab, Vicodin), hydromorphone (Dilaudid), methadone, morphine, oxycodone (Percocet).
- Polysubstance-dependency is likely seen with the above drugs as well as barbiturates, sedatives, SSRIs.
- See next page for *Pharmacologic Management of NAS* guidelines.

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Pharmacologic Management of Neonatal Abstinence Syndrome in the NICU

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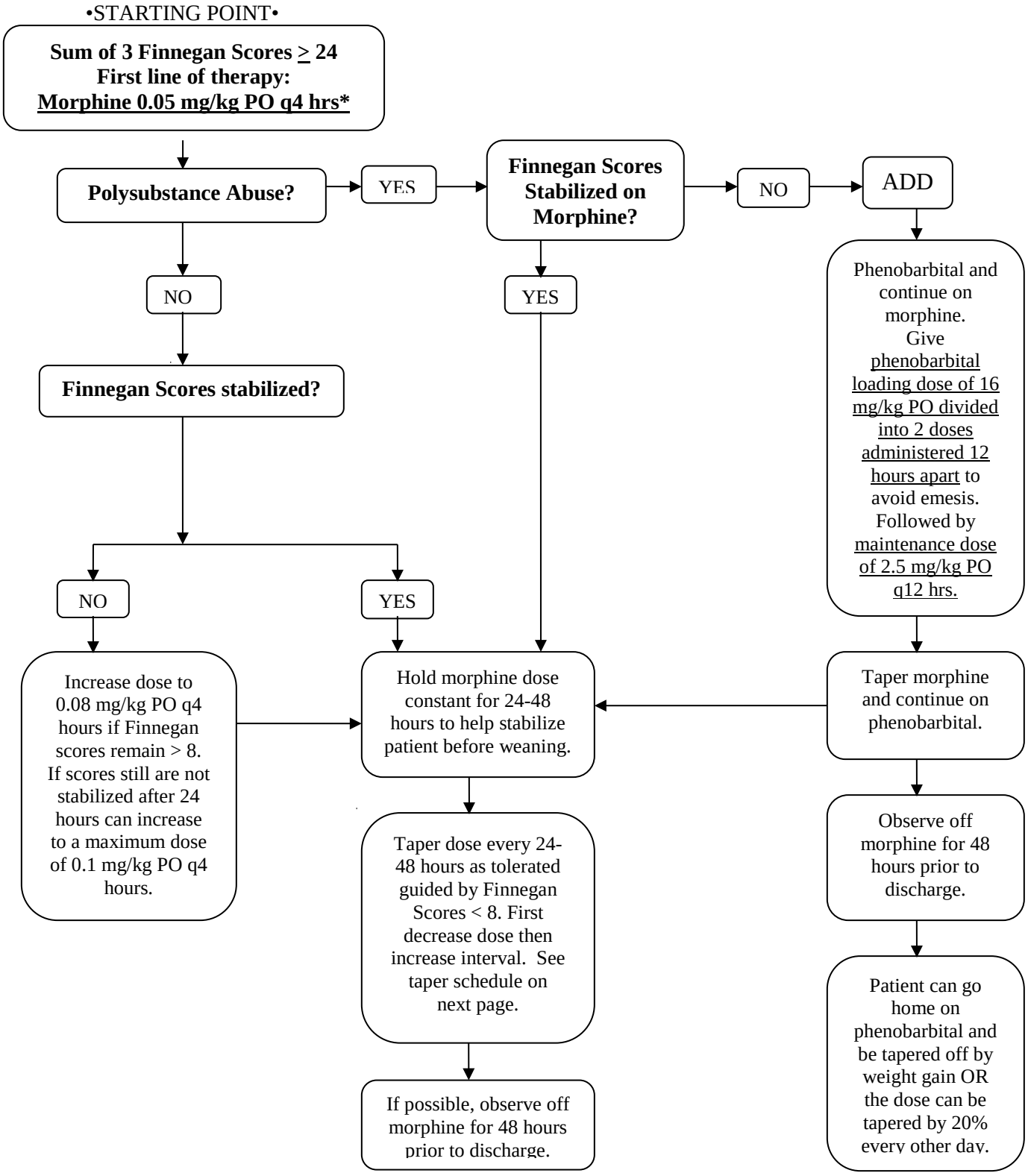

*0.05 mg/kg **PO** is recommended starting dose for NAS

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Tapering Schedule (Start this AFTER the patient is stabilized on a dose)

- Dosing on chart is in absolute mgs (NOT mg/kg)
- Find the dose on the chart that is closest to the dose the patient has been stabilized on and start there (this means you may not be starting at the top of the chart)
- Taper dose every 24-48 hours as tolerated, guided by Finnegan Scores of < 8

Recommended Tapering Schedule AFTER the infant is stabilized on a dose and ready to wean

Morphine TAPERING schedule (follow this side for infants > 3 kgs)	Morphine TAPERING schedule (follow this side for infants ≤ 3 kgs)
0.4 mg PO q 4 hrs	0.4 mg PO q 4 hrs
0.3 mg PO q 4 hrs	0.3 mg PO q 4 hrs
0.2 mg PO q 4 hrs	0.2 mg PO q 4 hrs
0.2 mg PO q 6 hrs	0.1 mg PO q 4 hrs
0.2 mg PO q 8 hrs	0.1 mg PO q 6 hrs
0.2 mg PO q 12 hrs	0.1 mg PO q 8 hrs
0.2 mg PO q 24 hrs	0.1 mg PO q 12 hrs
Discontinue	0.1 mg PO q 24 hrs
	Discontinue

Alternative pharmacological treatment *(not first-line at UIHC NICU)*

1) **Methadone** for opioid-dependency as an alternative to morphine. Dose 0.05 mg/kg PO every 12 hours. Increase by 0.05 mg/kg every 12 hours until NAS scores stabilize. Adverse effects include bradycardia and tachycardia and an ECG should be obtained to evaluate for QT-prolongation. Methadone has an extremely long half-life which can be up to 24 hours in a neonate. Methadone must be tapered by 10-20% per week over 4-6 weeks.
2) **Clonidine** as an alternative to phenobarbital. Clonidine is given in addition to morphine for polysubstance-dependency in term neonates with moderate to severe NAS uncontrolled by morphine alone. Dose 1 mcg/kg PO every 4 hours. Adverse effects include hypotension, rebound hypertension if clonidine is not tapered off over more than a week, AV-block, and bradycardia. MUST taper clonidine off over 10-14 days.

Outcomes

Alcohol	Acute ingestion: Hyperactivity, tremors for 72 hours followed by lethargy for 48 hours Chronic ingestion: abnormalities include CNS, growth deficiency, facial features, cardiac and musculoskeletal anomalies.
Amphetamines	IUGR, cardiac anomalies
Cocaine	Neurological complications (infarct, IVH, cystic lesions) Higher incidence of prematurity, low birth weight, placental abruption Associated with higher incidence of genitourinary tract and gastrointestinal anomalies Short and/or long term neurobehavioral abnormality
Heroin	Low birth weight
Marijuana	Higher incidence of tremors and altered visual responses
Methamphetamines	IUGR, prematurity, placental abruption, fetal distress, adverse long-term neurotoxic effects on behavior, cognitive skills, and physical dexterity.
Opioids	Active/passive detoxification results in fetal distress or fetal loss No other adverse outcomes identified so far
SSRIs	No adverse neurodevelopmental outcomes identified so far

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Modified Finnegan Scoring System[7]

System	Symptoms	Points	Score		
Central Nervous System	Excessive cry Excessive cry (inconsolable)	2 3			
	Sleep < 1 hour after feeding Sleep 1-2 hours after feeding Sleep 2-3 hours after feeding	3 2 1			
	Hyperactive Moro reflex Marked hyperactive Moro reflex	1 2			
	Mild tremors: disturbed Moderate-severe tremor: disturbed	1 2			
	Mild tremors: undisturbed Moderate-severe tremors when undisturbed	1 2			
	Increased muscle tone	1-2			
	Excoriation: skin red, intact Excoriation: skin broken	1 2			
	Generalized seizures	8			
Metabolism Vasomotor Respiratory	Hyperthermia: axilla temperature ≥ 37.3°C	1			
	Frequent yawning (≥ 4/interval)	1			
	Sweating	1			
	Nasal stuffiness	1			
	Sneezing (≥ 4/interval)	1			
	Tachypnea (rate > 60/min)	2			
Gastro-intestinal	Poor feeding	2			
	Vomiting	2			
	Loose stools	2			
	Weight loss/Failure to thrive	2			
	Excessive irritability	1-3			
Scoring	**TOTAL SCORE**				
	Initials of Scorer				

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