

**Ohio Children's' Hospitals Neonatal Research Consortium**  
**Enteral Morphine or Methadone Protocol for**  
**Neonatal Abstinence Syndrome (NAS) from Maternal Exposure**

**Introduction:**

The protocols are a synthesis of the best available, although limited evidence, and an analysis of practice variation across the state of Ohio in a cohort of 553 term infants with maternal narcotic exposure. These are viewed as potentially better protocols that humanely and safely wean infants off narcotics over a 2-3 week period.

**Each center should pick either Morphine or Methadone as their standard and use this for ALL NAS infants treated in that center.**

**Overview of Stages of treatment**

Potentially Better Protocol

<b>Non-Pharmacologic</b>	Swaddle, Comfort, 22 Calorie
<b>Initiate</b>	NAS score > 8 q3h two times
	Drug: Morphine/ Methadone 0.05 mg/kg PO
<b>Escalate</b>	If > 12, increase by 0.02 mg/kg/dose
<b>Stabilize</b>	Maintain dose for 48 hrs
<b>Wean</b>	10% of stabilization dose daily Discharge 48 hours off drug



**1. Scoring:** All Infants will be scored every 3 hours prior to a feeding with the modified Finnegan Scoring System. Begin scoring at every 3 hrs, when weaning phase begins, if not waking to feed until 4 hrs may score every 4 hrs.

1a. Some experts recommend using the *average* of NAS scores over a 24 hour period in the stabilization and weaning phase to minimize the impact of minor variations on dosing.

1b. **Adjust trigger scores when > 3 weeks old:** Research has shown that NAS scores increase over time as the infant matures so > 21 days all Trigger thresholds should be increased by 2. (For example: now would wean if average of scores in 24 hours are < 11),(REF: Zimmerman-Bauer U et al. Finnegan neonatal abstinence scoring system: normal values for the first 3 days and weeks 5-6 in non-addicted infants. Addiction 2010 March. 105: 524-528.)

1c. Centers should develop a plan for periodic refresher training for all nurses on NAS modified scoring system using the D'Apolito Reliability Training system, and a training system for on-boarding new nursing staff.

**2. Non-Pharmacologic Treatments:**

- a. All infants with NAS will be treated with a bundle of non-pharmacologic interventions including decreased stimulation, swaddling, and continuous holding and frequent feeds.
- b. Feedings: Each institution should develop a policy for the use of Mother's Own Milk. Consideration of supporting breast feeding may be given if the mother is active in a treatment program and mother's addiction specialist supports breast feeding. If MBM is not used, consider frequent feeds with an increased caloric density non-lactose containing formula at 22cal/oz. The higher calorie formula is designed to meet the exceptional caloric needs and combat the documented weight loss seen in NAS infants. Additional calories may not be needed once the infant is a week or more into the course and weight loss is < 10% of birthweight. 22 Calorie formula may be discontinued when weight gain is established firmly.
- c. See references at end for resources on Non-pharmacologic interventions.

### **3. Pharmacologic Treatment - Morphine:** (see page 6 for Methadone)

Treatment should be initiated if an infant has 2 consecutive scores > 8 OR 1 score  $\geq$  12.

Treatment is divided into the following phases: Initiation, Escalation, Stabilization, Wean

**a. Initiation Phase- most infants can be treated with oral medication.:**

	Morphine**
PO	0.05mg/kg/dose q3h
IV	0.02 mg/kg/dose q3h

(\*\*IV morphine and enteral morphine doses are not equivalent)

**b. Escalation Phase:**

	Morphine
PO	0.03mg/kg/dose q3h
IV	0.01 mg/kg/dose q3h

**Increase dose every 3 hrs until controlled (average NAS  $\leq$  8 in 24 hours)**

**\*Rescue Dose\*:** If infant has 1 score of  $\geq$  12, double the previous dose given (enteral or IV) x 1 and then adjust accordingly:

- If NAS score now < 12: make the scheduled maintenance dose (MD) the same as the rescue dose that was just administered. The first higher MD should be given at the next scheduled care/feed.
- If NAS score still  $\geq$  12: increase next dose by 50% of the prior dose. Continue to do so until score is < 12.

**Second Drug: Phenobarbital**

Consider starting phenobarbital if:

- **Polysubstance exposure** (benzodiazepines, barbiturates, antipsychotics, antidepressants, other sedatives/hypnotics, tobacco) is suspected/confirmed
- **AND CNS findings** (tremors, increased muscle tone, etc) rather than GI findings predominate on NAS sub scale score
- **AND Morphine dose** exceeds 0.3 mg/kg/dose with score remaining > 8; **OR** unable to wean for 2 consecutive days.

**Loading dose:** 10 mg/kg/dose po q12hr x 2 doses PO OR

20 mg/kg/ dose IV x1. (Enteral formulation contains 10% alcohol. Dividing dose PO may decrease risk of emesis and/or sedation.)

**Maintenance dose:** 5 mg/kg/dose po once daily (do not weight adjust)

**Phenobarbital Wean:** Two approaches may be used. (Neither has been directly studied.) Each center should pick one method.

- A. Discontinue when on second to last step of morphine wean to assess for tolerance of discontinuation. Given long half life of phenobarbital this will wear off gradually over 4 days.
- B. Discharging infant home on phenobarbital with subsequent weaning to be done either in Neo Clinic or by infant's PCP.  
(Given the high alcohol concentration limiting exposure may be the best practice. Hypnotic or nicotine withdrawal occurs rapidly and generally is completed by day 5- thus longer phenobarbital exposure may not be needed.)

**c. Stabilization:**

All scores remain  $\leq 8$  for minimum 48 hours. 72 hours of stabilization may be used if infant has had to increase above 0.4 mg/kg dose or if phenobarbital added.

**d. Morphine Weaning Phase:** Once stabilized on same dose for 48 hours, use this dose as the starting point of the wean. Begin weaning the dose by 10% (of the original dose when the first wean was started) every 24 hours. Drug may be discontinued when a single dose is  $< 0.02$  mg/kg/dose. Please see below for example.

**\*Ad lib infants\*:** Given the shorter duration of action of enteral morphine, it is best suited to be dosed on a q3hr schedule. Infants should be allowed to ad lib feed but kept on a q3hr drug schedule.

**\*Backslide\*:** If infant has 2 consecutive NAS scores  $>8$ , during the weaning process, assure that non-pharmacological measures are optimized (i.e.: swaddling, holding, decreased stimuli, etc) before going back to previous dose at which patient was stable. If infant's scores continue to be elevated (even after physical exam to ensure nothing else is wrong/bothering the infant), either weight adjust medication and/or continue to back up in a stepwise fashion until patient's scores are  $\leq 8$ . Once stabilized on new dose for minimum 48 hrs, resume 10% wean but consider weaning at less frequent intervals.

**e. Discharge:** Observe in-house x 48 hours off of morphine before discharge.

**Example:**

Infant X (wt: 3.2 kg) required 2 dose increases of his morphine to get his NAS scores consistently  $\leq 8$ . He has now been on the dose of 0.32 mg (0.1 mg/kg/dose) po q3hr for 72 hours. Team would like to begin weaning. As long as his scores remain consistently  $\leq 8$ , please decrease by 10% every 24hrs.

Day 1: 0.29 mg q3hr (0.09 mg/kg)  
Day 2: 0.26 mg q3hr (0.08 mg/kg)  
Day 3: 0.22 mg q3hr (0.07 mg/kg)  
Day 4: 0.19 mg q3hr (0.06 mg/kg)  
Day 5: 0.16 mg q3hr (0.05 mg/kg)  
Day 6: 0.13 mg q3hr (0.04 mg/kg)

Day 7: 0.1 mg q3hr (0.03 mg/kg)  
Day 8: 0.06 mg q3hr (0.02 mg/kg) x 24hr  
and then stop

Monitor in-house for minimum of 48hrs prior to discharge.

Ohio Childrens Hosp Protocol

# **METHADONE**

## **3. Pharmacologic Treatment with Methadone (see page 3 for Morphine):**

Treatment should be initiated if an infant has 2 consecutive scores > 8 OR 1 score  $\geq$  12

Treatment is divided into the following phases: Initiation, Escalation, Stabilization, Wean

### **A. Initiation Phase- all treatments are with oral medication.**

	<b>Methadone</b>
<b>PO</b>	0.05mg/kg/dose q6h

### **B. Escalation Phase:**

#### **1. Increase dose if NAS still > 8 after 3 doses of methadone**

	<b>Methadone</b>
<b>PO</b>	0.1mg/kg/dose q6h

#### **2. If 3 doses later NAS still > 8 increase to 0.15 mg/kg/dose q6h**

#### **3. Second Drug: Phenobarbital**

Consider starting phenobarbital if:

- **Polysubstance exposure** (benzodiazepines, barbiturates, antipsychotics, antidepressants, other sedatives/hypnotics, tobacco) is suspected/confirmed
- **AND CNS findings** (tremors, increased muscle tone, etc) rather than GI findings predominate on NAS sub scale score
- **AND Methadone dose** exceeds 0.2 mg/kg/dose with score remaining > 8; **OR** unable to wean for 2 consecutive days.

**Loading dose:** 10 mg/kg/dose po q12hr x 2 doses PO OR

20 mg/kg/ dose IV x1. (Enteral formulation contains 10% alcohol. Dividing dose PO may decrease risk of emesis and/or sedation.)

**Maintenance dose:** 5 mg/kg/dose po once daily (do not weight adjust)

**Phenobarbital Wean:** Two approaches may be used. (Neither has been directly studied.)

A. Discontinue when on second to last step of methadone wean to assess for tolerance of discontinuation. Given long half life of phenobarbital this will wear off gradually over 4 days.

B. Discharging infant home on phenobarbital for 30 days with subsequent weaning to be done either in Neo Clinic or by infant's PCP.

*(Given the high alcohol concentration limiting exposure may be the best practice. Hypnotic or nicotine withdrawal occurs rapidly and generally is completed by day 5- thus longer phenobarbital exposure may not be needed.)*

**C. Stabilization:**

All scores remain < 8 for minimum 48 hours. 72 hours of stabilization may be used if infant has had to increase above 0.4 mg/kg dose or if phenobarbital added.

**D. Weaning Phase:** Once stabilized on same dose for 48 hours, use this dose as the starting point of the wean. Begin weaning the dose by 10% (of the original dose when the first wean was started) every 24 hours. Drug may be discontinued when a single dose is < 0.02 mg/kg/dose. Please see below for example.

**\*Ad lib infants\*:** Infants should be allowed to ad lib feed but kept on a q6hr drug schedule.

**\*Backslide\*:** If infant has 2 consecutive NAS scores for >8, during the weaning process, assure that non-pharmacological measures are optimized (i.e.: swaddling, holding, decreased stimuli, etc) before going back to previous dose at which patient was stable. If infant's scores continue to be elevated (even after physical exam to ensure nothing else is wrong/bothering the infant), either weight adjust medication and/or continue to back up in a stepwise fashion until patient's scores are <8. Once stabilized on new dose for minimum 48 hrs, resume 10% weans but consider weaning at less frequent intervals.

**e. Discharge:** Observe in-house x 72 hours off of methadone before discharge.

**EXAMPLE:**

<u>Step</u>	<u>Dose/kg</u>	<u>Interval</u>
1	0.05 mg/kg	q 6 hrs * 4
1a- escalate to obtain NAS score <8. Once stable for 24 hrs, begin wean back to 0.05mg/kg by weaning daily by 0.025 mg/kg/dose.		
2	0.04 mg/kg	q 6 hrs * 4
3	0.03 mg/kg	q 6 hrs * 4
4	0.02 mg/kg	q 6 hrs * 4
5	0.02 mg/kg	q 8 hrs * 4
6	0.02 mg/kg	q 12 hrs * 4
7	0.01 mg/kg	q 12 hrs * 4
8	0.01 mg/kg	q 24 hrs * 4

Observe for 72 hours off methadone before discharge.

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