

## Neonatal Opioid Withdrawal Syndrome

Neonatal opioid withdrawal syndrome (NOWS), a specific type of neonatal abstinence syndrome (NAS), occurs when a baby withdraws from opiates the mother took or used chronically during pregnancy.<sup>2,13</sup> The chart below answers common questions about NOWS.

Question	Answer/Pertinent Information
What are the <b>signs and symptoms</b> of neonatal opioid withdrawal syndrome?	<ul style="list-style-type: none"> <li>• Symptoms typically occur within 24 to 72 hours of delivery.<sup>1</sup> <ul style="list-style-type: none"> <li>○ Symptoms may be delayed until up to seven days or longer after delivery with exposure to longer-acting meds (e.g., buprenorphine, methadone).<sup>1,2,13</sup></li> <li>○ Common symptoms include:<sup>2,13</sup> <ul style="list-style-type: none"> <li>▪ central nervous system (e.g., high-pitched crying, sleep disturbances, tremors)</li> <li>▪ gastrointestinal (e.g., diarrhea, poor feeding, regurgitation)</li> <li>▪ autonomic (e.g., nasal flaring or stuffiness, sneezing, yawning, tachypnea [rapid breathing], sweating)</li> </ul> </li> <li>○ Symptoms can progress to dehydration, weight loss, seizures, or death.<sup>1,2</sup></li> </ul> </li> </ul>
How should newborns be <b>screened</b> for neonatal opioid withdrawal syndrome?	<ul style="list-style-type: none"> <li>• Take a thorough history about maternal drug use, including prescription and non-prescription products.<sup>1</sup> <ul style="list-style-type: none"> <li>○ Use non-judgmental, open-ended questions to encourage honest responses regarding substance use.<sup>7</sup></li> </ul> </li> <li>• Urine (collected within hours of delivery) or meconium (newborn’s first stool) can be tested for opiates.<sup>2,13</sup> <ul style="list-style-type: none"> <li>○ Natural opiates show up on opiate screening (e.g., codeine, heroin, morphine).<sup>2</sup></li> <li>○ Synthetic opiates may not be detected on opiate screenings and need to be tested for separately (e.g., methadone, oxycodone).<sup>2</sup></li> </ul> </li> <li>• Several screening tools are available to assess the baby’s symptoms. Use a screening tool to assist with facility NOWS treatment, titration, and weaning protocol parameters. Examples include:<sup>2</sup> <ul style="list-style-type: none"> <li>○ <b>Modified Finnegan Scoring System</b> (also called the “MOTHER score”)                             <ul style="list-style-type: none"> <li>▪ most commonly used screening tool.<sup>28</sup> Focused on pharmacologic symptom management.<sup>5</sup></li> <li>▪ can be found at: <a href="https://www.universityhealth.com/~media/files/clinical-pathways/modified-finnegans-nas-scoring-tool-pt-approved-0615.pdf">https://www.universityhealth.com/~media/files/clinical-pathways/modified-finnegans-nas-scoring-tool-pt-approved-0615.pdf</a></li> </ul> </li> <li>○ <b>Eat Sleep Console (ESC)</b>. Focused on nonpharmacologic symptom management.<sup>5</sup> <ul style="list-style-type: none"> <li>▪ An example algorithm using ESC can be found at <a href="https://ilpqc.org/wp-content/docs/toolkits/MNO-Neo/Sample-Decision-Tree-Flowchart-ESC.pdf">https://ilpqc.org/wp-content/docs/toolkits/MNO-Neo/Sample-Decision-Tree-Flowchart-ESC.pdf</a></li> </ul> </li> <li>○ <b>Lipsitz Scoring Tool</b></li> <li>○ <b>Neonatal Withdrawal Inventory</b></li> </ul> </li> </ul>

Question	Answer/Pertinent Information
<p>How is the <b>Modified Finnegan Scoring System</b> used?</p>	<ul style="list-style-type: none"><li>• Scoring typically begins within two hours of birth and is re-evaluated every three to four hours.<sup>4,28</sup><ul style="list-style-type: none"><li>○ Follow-up scores may be measured sooner based on scores (e.g., within 30 minutes of a score &gt;8).<sup>4</sup></li></ul></li><li>• Most institutions and studies define neonatal withdrawal as a score of <math>\geq 8</math>, but evidence to inform a cutoff is lacking.<sup>1,2,28</sup></li><li>• The Modified Finnegan Scoring System evaluates signs and symptoms in the following areas:<sup>13</sup><ul style="list-style-type: none"><li>○ central nervous system (e.g., high-pitched crying, hyperactive startle reflex, tremors)</li><li>○ autonomic (e.g., sweating, nasal flaring, increased respiratory rate)</li><li>○ gastrointestinal (e.g., feeding problems, regurgitation, loose stool)</li></ul></li><li>• Facility protocols determine interventions based on individual, average, or consecutive scores.<sup>1,2</sup></li><li>• Examples of existing protocols can be found at:<ul style="list-style-type: none"><li>○ Provincial Council for Maternal and Child Health: <a href="https://www.pcmch.on.ca/wp-content/uploads/2022/02/NAS-Clinical-Guideline-Update-2016Nov25.pdf">https://www.pcmch.on.ca/wp-content/uploads/2022/02/NAS-Clinical-Guideline-Update-2016Nov25.pdf</a></li><li>○ Indiana government: <a href="https://www.in.gov/health/mch/files/ipqic/NAS-Pharmacologic-Therapy-Protocol-rev.pdf">https://www.in.gov/health/mch/files/ipqic/NAS-Pharmacologic-Therapy-Protocol-rev.pdf</a></li><li>○ University Health: <a href="https://www.universityhealth.com/~media/files/clinical-pathways/modified-finnegans-nas-scoring-tool-pt-approved-0615.pdf">https://www.universityhealth.com/~media/files/clinical-pathways/modified-finnegans-nas-scoring-tool-pt-approved-0615.pdf</a></li></ul></li></ul>
<p>What <b>supportive measures</b> are recommended?</p>	<ul style="list-style-type: none"><li>• The “eat, sleep, console” or ESC method is a strategy used in the management of NOWS. The ESC method involves assessing if babies can eat well, sleep undisturbed, or be consoled within ten minutes before using medications.<sup>29</sup> In addition, facilities may encourage the use of prn medications instead of using scheduled doses.<sup>30</sup> Using ESC instead of traditional scoring methods may reduce length of stay and need for opioid treatment [Evidence level B-1].<sup>18</sup></li><li>• The nonpharmacologic suggestions below are included as part of ESC, but also encouraged even if other scoring methods are used instead of the ESC method at your facility.<sup>6,10,13,18</sup><ul style="list-style-type: none"><li>○ Encourage <b>breastfeeding</b> unless contraindicated (e.g., active substance abuse, HIV).<sup>10,13,24,29</sup> Breastfeeding:<ul style="list-style-type: none"><li>▪ delays onset, and decreases severity, length of stay, and need for medication treatment of NOWS.<sup>10,24,27</sup></li><li>▪ promotes mother-infant bonding and provides optimal nutrition<sup>24,26</sup></li><li>▪ is compatible with buprenorphine and methadone.<sup>24</sup><ul style="list-style-type: none"><li>• only about 3% of maternal methadone dose reaches milk.<sup>24</sup></li><li>• monitor infant for sedation and respiratory depression if methadone is being titrated, especially if the dose is &gt;100 mg<sup>24</sup></li></ul></li></ul></li><li>○ Utilize <b>supportive measures</b>, such as:<ul style="list-style-type: none"><li>▪ comforting techniques (e.g., holding skin to skin, swaying, rocking, swaddling, offering a pacifier)<sup>10,18,28</sup></li><li>▪ frequent, small volume, high-calorie feedings<sup>10</sup></li><li>▪ minimizing environmental stimuli (e.g., limit exposure to light or noise)<sup>10,18</sup></li><li>▪ clustered care<sup>18</sup></li></ul></li><li>○ Encourage infants “rooming-in” with mothers.<sup>10,13,28,29</sup><ul style="list-style-type: none"><li>▪ May reduce length of stay and need for medication treatment of NOWS.<sup>29</sup></li></ul></li></ul></li></ul>

Question	Answer/Pertinent Information
<b>When are medications appropriate?</b>	<ul style="list-style-type: none"><li>• Follow facility protocols for pharmacologic interventions. Using a protocol may be more impactful than the choice of medication used for weaning.<sup>7</sup><ul style="list-style-type: none"><li>○ Protocol-based therapy reduces opioid treatment duration and length of stay.<sup>6,7</sup></li></ul></li><li>• Indications to initiate medications may include:<ul style="list-style-type: none"><li>○ 24 Rule: either three consecutive Modified Finnegan scores <math>\geq 8</math> or two scores <math>&gt;12</math>.<sup>5</sup></li><li>○ withdrawal-associated seizures (phenobarbital)<sup>17</sup></li><li>○ if using ESC, when non-pharmacologic methods are maximized and newborn is still unable to eat adequately, sleep for one hour undisturbed, and be consoled within ten minutes.<sup>5</sup></li></ul></li></ul>
<b>Which medications should be used to treat neonatal opioid withdrawal syndrome?</b>	<ul style="list-style-type: none"><li>• <b>Start with</b> opioid replacement. Methadone or morphine are first-line.<sup>12</sup><ul style="list-style-type: none"><li>○ Oral morphine is most commonly used.<sup>8</sup> It has a short half-life for ease of titration.<sup>7</sup></li><li>○ Oral methadone may provide more consistent levels with less frequent adjustments than morphine.<sup>7</sup><ul style="list-style-type: none"><li>▪ Methadone may reduce length of stay but pose a higher risk of oversedation (with a weight-based loading/taper protocol) than morphine [Evidence level B-1].<sup>12</sup></li></ul></li><li>○ There is less evidence with buprenorphine (sublingual), but it may be associated with a shorter length of stay than morphine or methadone [Evidence level B-3].<sup>9,12</sup></li><li>○ Use of methadone and buprenorphine may be limited by ethanol content (~8% to 15% [methadone solution]; ~30% [compounded buprenorphine solution]).<sup>13,15</sup></li></ul></li><li>• <b>Adjunctive medications</b> most often include clonidine or phenobarbital.<sup>16</sup><ul style="list-style-type: none"><li>○ Oral clonidine<ul style="list-style-type: none"><li>▪ Not typically used as monotherapy.<sup>8</sup> Usually added to opiate therapy (e.g., morphine).<sup>8</sup> Consider adding when total daily morphine doses is <math>&gt;1</math> mg/kg.<sup>5</sup></li><li>▪ Helps with autonomic symptoms.<sup>21</sup></li><li>▪ Clonidine may reduce the number of Nows treatment days and the total dose of opioids used to treat Nows over that period [Evidence Level B-2].<sup>19</sup></li><li>▪ Preferred over phenobarbital due to phenobarbital-associated neurotoxicity in animal studies and use being associated with adverse developmental outcomes.<sup>13</sup></li><li>▪ Monitor blood pressure and heart rate with use.<sup>2</sup></li></ul></li><li>○ Oral phenobarbital<ul style="list-style-type: none"><li>▪ Not typically used as monotherapy.<sup>8</sup> Consider adding when: total daily morphine dose is <math>&gt;1</math> mg/kg; for neurologic symptoms such as insomnia or tremors; to facilitate a difficult morphine taper in conjunction with optimized nonpharmacologic interventions; for polydrug use (especially benzodiazepines or barbiturates).<sup>5,20,28</sup></li><li>▪ Not effective for gastrointestinal symptoms of Nows.<sup>23</sup></li><li>▪ Causes central nervous system depression and impairs sucking reflex.<sup>23</sup></li><li>▪ Clonidine generally preferred over phenobarbital (see above).</li></ul></li></ul></li></ul>

Question	Answer/Pertinent Information
How should <b>morphine</b> <sup>a</sup> be dosed for neonatal opioid withdrawal syndrome?	<ul style="list-style-type: none"> <li>• <b>Initial oral dose:</b> ~0.05 mg/kg/dose every three to four hours prn or scheduled.<sup>5,30</sup> <ul style="list-style-type: none"> <li>○ Increase dose by 10% to 20% about every 12 hours until symptoms are controlled.<sup>5</sup></li> </ul> </li> <li>• <b>Max dose:</b> 0.2 mg/kg/dose every four hours.<sup>30</sup></li> <li>• Add additional therapy (e.g., clonidine) when total daily morphine doses are &gt;1 mg/kg/day.<sup>5</sup></li> <li>• Consider weaning once symptoms are controlled and stable for ~24 hours.<sup>5</sup> Reduce dose by 10% up to two or three times every 24 hours.<sup>5</sup></li> <li>• May discontinue once stable on a dose of 0.12 to 0.16 mg/kg/day (0.02 mg/kg/dose every four hours) for at least 12 hours.<sup>5</sup></li> <li>• Once morphine is discontinued, continue monitoring every three to four hours for at least 48 hours.<sup>5</sup> If Modified Finnegan score &gt;8, recheck in two hours, and give a dose of morphine if score is still &gt;8.<sup>5</sup> Morphine may need to be resumed if more than a few doses are needed.<sup>5</sup></li> <li>• May discharge home 48 hours after discontinuation, as long as all Modified Finnegan scores remain &lt;8 off therapy.<sup>7</sup></li> </ul>
How should <b>methadone</b> <sup>a</sup> be dosed for neonatal opioid withdrawal syndrome?	<ul style="list-style-type: none"> <li>• In general, oral methadone can be dosed in a couple of different ways: <ul style="list-style-type: none"> <li>○ It can be started at a low dose (e.g., 0.05 mg/kg/dose every 12 hours), then increased (e.g., by 0.05 mg/kg/dose every 12 hours) until stabilization, then tapered (e.g., by 10% to 20% per week over four to six weeks).<sup>3</sup></li> <li>○ A different method (a weight-based loading/taper protocol) starts with a higher dose (e.g., 0.25 mg [if &lt;3 kg] every six hours or 0.35 mg [if ≥3 kg] every six hours for four doses). Each day, the dose is either decreased per protocol, maintained, or an extra dose is given, based on the average modified Finnegan score over the past 24 hours.<sup>14</sup></li> </ul> </li> </ul>
How should <b>buprenorphine</b> <sup>a</sup> be dosed for neonatal opioid withdrawal syndrome?	<ul style="list-style-type: none"> <li>• <b>Initial sublingual dose:</b> 4 to 6 mcg/kg/dose every eight hours.<sup>11,15</sup> <ul style="list-style-type: none"> <li>○ Buprenorphine dose can be increased by about 25% if the sum of the previous three Modified Finnegan scores is higher than 24 or after one score ≥12.<sup>11,22</sup></li> </ul> </li> <li>• <b>Max dose:</b> 60 mcg/kg/day.<sup>11</sup></li> <li>• Consider weaning newborns off of buprenorphine by reducing the dose by about 10% per day if the total of the previous three Modified Finnegan scores is less than 18. Buprenorphine can be discontinued once the dose has been reduced to 10% of the initial dose.<sup>11,22</sup></li> <li>• Monitor newborns for at least 48 hours after discontinuation prior to discharge.<sup>11</sup></li> </ul>
How should <b>clonidine</b> <sup>a</sup> be dosed for neonatal opioid withdrawal syndrome?	<ul style="list-style-type: none"> <li>• <b>Initial oral dose:</b> 0.5 to 1 mcg/kg/dose every four to six hours.<sup>5,21,23</sup> Check blood pressure before administration.<sup>5</sup> <ul style="list-style-type: none"> <li>○ Increase by 0.5 mcg/kg/dose every six hours.<sup>5</sup></li> </ul> </li> <li>• <b>Max dose:</b> 6 mcg/kg/day.<sup>21,23</sup> Higher doses (e.g., 24 mcg/kg/day) could be used if tolerating (e.g., no hypotension, bradycardia, sedation).<sup>5,20,23</sup></li> <li>• Weaning may be attempted once the newborn is stable off opioid for 24 hours.<sup>20</sup> Taper over three to four days (e.g., reduce dose by 25% per day by increasing the dosing interval).<sup>21,23</sup></li> <li>• Monitor blood pressure for at least 48 hours after discontinuation of clonidine before discharging home.<sup>20,21</sup></li> </ul>

Question	Answer/Pertinent Information
How should <b>phenobarbital</b> <sup>a</sup> be dosed for neonatal opioid withdrawal syndrome?	<ul style="list-style-type: none"><li>• <b>Initial oral dose:</b> 16 to 20 mg/kg loading dose (as a single dose or divided as two doses of 8 to 10 mg/kg given three hours apart).<sup>5,20</sup> After 24 hours, start 3 to 4 mg/kg/dose once daily, or 1.5 to 2 mg/kg/dose every 12 hours.<sup>5</sup></li><li>• Once morphine has been weaned to 0.3 mg/kg/day, phenobarbital may be stopped.<sup>5</sup> Continue morphine wean as above.<sup>5</sup> (Some centers send neonate home on phenobarbital.<sup>20</sup>)</li></ul>

- a. Facility protocol may vary from these doses. These are general, conservative dosing examples summarized from NOWS protocols and clinical trial data.

*Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.*

### Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
<b>A</b>	Good-quality patient-oriented evidence.*	<ol style="list-style-type: none"> <li>1. High-quality randomized controlled trial (RCT)</li> <li>2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings</li> <li>3. All-or-none study</li> </ol>
<b>B</b>	Inconsistent or limited-quality patient-oriented evidence.*	<ol style="list-style-type: none"> <li>1. Lower-quality RCT</li> <li>2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings</li> <li>3. Cohort study</li> <li>4. Case control study</li> </ol>
<b>C</b>	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

**\*Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:548-56. <https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html>.]

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