

March 2021 ~ Resource #370322

## 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
<p>What are the <b>signs and symptoms</b> of neonatal opioid withdrawal syndrome?</p>	<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>
<p>How should newborns be <b>screened</b> for neonatal opioid withdrawal syndrome?</p>	<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 and/or meconium (newborn's first stool) can be tested for opiates.<sup>2,12,13</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>2,13</sup></li> <li>▪ can be found at: <a href="https://www.ashp.org/-/media/store-files/p4757-sample-chapter-5.ashx">https://www.ashp.org/-/media/store-files/p4757-sample-chapter-5.ashx</a></li> </ul> </li> <li>○ <b>Eat Sleep Console (ESC)</b> <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 few hours (e.g., every two to four hours).<sup>12</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).</li></ul></li><li>• Most institutions and studies define neonatal withdrawal as a score of <math>\geq 8</math>.<sup>1,2</sup></li><li>• The Modified Finnegan Scoring System evaluates signs and symptoms in the following areas:<ul style="list-style-type: none"><li>○ central nervous system (e.g., high-pitched crying, sleep after feeding, reflexes, tremors)</li><li>○ autonomic (e.g., sweating, nasal stuffiness, respiratory rate &gt;60 breaths/minute)</li><li>○ gastrointestinal (e.g., excessive sucking, regurgitation, loose or watery stools)</li></ul></li><li>• Facility protocols then 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="http://www.pcmch.on.ca/wp-content/uploads/2016/05/NAS-Clinical-Guidelines-Final-March-30-2012-for-website-May-2016.pdf">http://www.pcmch.on.ca/wp-content/uploads/2016/05/NAS-Clinical-Guidelines-Final-March-30-2012-for-website-May-2016.pdf</a></li><li>○ Indiana government: <a href="https://www.in.gov/laboroflove/files/NAS%20Pharmacologic%20Therapy%20Protocol.pdf">https://www.in.gov/laboroflove/files/NAS%20Pharmacologic%20Therapy%20Protocol.pdf</a></li><li>○ Illinois Prenatal Quality Collaborative: <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></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>24</sup> In addition, facilities may encourage the use of prn medications instead of using scheduled doses.<sup>25</sup> Some data suggest that using ESC, instead of traditional scoring methods, may reduce length of stay [Evidence Level B-3].<sup>24,27</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.<ul style="list-style-type: none"><li>○ Encourage <b>breastfeeding</b> for optimal nutrition unless contraindicated (e.g., mom actively abusing drugs and not in treatment program), due to potential benefits.<sup>1,3,7,10,13</sup><ul style="list-style-type: none"><li>▪ may delay NOWS onset, decrease severity, and decrease need for medication treatment of NOWS.</li><li>▪ promotes mother-infant bonding.</li><li>▪ consider even for mothers in treatment programs on stable doses (e.g., buprenorphine, methadone).<ul style="list-style-type: none"><li>• Only about 3% of maternal methadone dose reaches milk.<sup>2</sup></li></ul></li></ul></li><li>○ Utilize <b>supportive measures</b>, such as:<sup>3,10</sup><ul style="list-style-type: none"><li>▪ comforting techniques (e.g., holding skin to skin, swaying, rocking, swaddling, offering a pacifier)</li><li>▪ frequent, small volume, high-calorie feedings</li><li>▪ minimizing environmental stimuli (e.g., limit exposure to light or noise)</li></ul></li><li>○ Encourage infants “rooming-in” with mothers.<sup>3,7,10</sup><ul style="list-style-type: none"><li>▪ May reduce prevalence and severity of NOWS, as well as the likelihood for medication treatment of NOWS.<sup>3</sup></li></ul></li></ul></li></ul>

Question	Answer/Pertinent Information
When are <b>medications</b> appropriate?	<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>• Many protocols initiate medications using the following or similar cutoffs:<sup>4,5</sup><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>.</li><li>○ withdrawal-associated seizures</li><li>○ if using ESC, when non-pharmacologic methods (e.g., rooming in, swaddling, holding, minimizing light and noise) are maximized and newborns are still unable to eat at least one ounce or breastfeed well, sleep for one hour undisturbed, or be consoled within ten minutes.<sup>26</sup></li></ul></li></ul>
<b>Which medications</b> should be used to treat neonatal opioid withdrawal syndrome?	<ul style="list-style-type: none"><li>• <b>Start with</b> opioid replacement.<sup>7</sup><ul style="list-style-type: none"><li>○ Oral morphine is the most commonly used, likely because of short half-life and easy dosage adjustments.<sup>7,13</sup></li><li>○ Oral methadone or buprenorphine (sublingual) is less commonly used compared to morphine, but may be associated shorter lengths of stay.<sup>2,7,11,14,15</sup> (Note that morphine and methadone are generally preferred over buprenorphine until more data are available with buprenorphine.)<sup>17</sup><ul style="list-style-type: none"><li>▪ May provide more consistent levels with less frequent adjustments.<sup>7</sup></li><li>▪ Use may be limited by ethanol content (~8% to 15% [methadone solution]; ~30% [compounded buprenorphine solution]).<sup>7,15</sup></li></ul></li></ul></li><li>• <b>Adjunctive medications</b> most often include clonidine or phenobarbital.<sup>7,13</sup><ul style="list-style-type: none"><li>○ Oral clonidine<ul style="list-style-type: none"><li>▪ Not typically used as monotherapy. Usually added to opiate therapy (e.g., morphine).<sup>17</sup> Often added when total daily morphine doses are <math>&gt; 1</math> to 1.6 mg/kg or in patients with significant diarrhea or insomnia.<sup>5,17</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; however, may be preferred for non-opioid withdrawal.<sup>5</sup> Usually added to opiate therapy (e.g., morphine) especially when total daily morphine doses are <math>&gt; 1</math> to 1.6 mg/kg or in patients when polysubstance use is suspected or known for the mother.<sup>5,16,17</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<sup>a</sup></b> be dosed for neonatal opioid withdrawal syndrome?	<ul style="list-style-type: none"> <li>• <b>Initial oral dose:</b> 0.05 to 0.1 mg/kg every three to four hours.<sup>5,17</sup> <ul style="list-style-type: none"> <li>○ Increase doses by 10% to 20% about every 12 hours for three consistent Modified Finnegan scores &gt;8 or two consistent scores &gt;12.<sup>5</sup> Use caution with total daily doses above 1.6 mg/kg, as these doses may lead to significant sedation or hypotension.<sup>17</sup></li> </ul> </li> <li>• <b>Max dose:</b> 2.3 mg/kg in 24 hours.<sup>17</sup></li> <li>• Add additional therapy (e.g., clonidine) when total daily morphine doses are &gt;1 to 1.6 mg/kg or in patients with significant diarrhea or insomnia.<sup>5,17</sup></li> <li>• Consider weaning morphine once symptoms are stable and controlled (e.g., Modified Finnegan scores consistently &lt;8) for about 24 to 48 hours. Reduce doses by about 10% to 20% every 24 to 48 hours.<sup>5,17</sup> <ul style="list-style-type: none"> <li>○ May discontinue once stable on 0.02 mg/kg/dose every four hours or 0.12 to 0.16 mg/kg/day for 24 to 48 hours.<sup>5</sup></li> </ul> </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<sup>a</sup></b> be dosed for neonatal opioid withdrawal syndrome?	<ul style="list-style-type: none"> <li>• <b>Initial oral dose:</b> 0.05 mg/kg every 12 hours.<sup>18</sup> <ul style="list-style-type: none"> <li>○ Increase doses by ≤0.05 mg/kg/dose every 12 to 24 hours until Modified Finnegan scores stabilize.<sup>17,18</sup> Use caution with doses above 0.1 mg/kg/dose every six hours, as these doses may lead to significant sedation or hypotension.<sup>17</sup></li> </ul> </li> <li>• <b>Max dose:</b> 0.2 mg/kg/dose every six hours.<sup>17</sup></li> <li>• Consider weaning methadone once symptoms are stable and controlled (e.g., Modified Finnegan scores consistently &lt;8) for about 24 to 48 hours.<sup>17</sup> Tapering schedules vary and may be slower (e.g., lower methadone by 0.02 to 0.05 mg per dose, either once or twice weekly) compared to tapering off morphine.<sup>9</sup></li> <li>• May discharge home 72 hours after discontinuation<sup>7</sup> or some protocols may allow for tapers to be completed at home due to the slow nature of the taper in situations where caregivers can demonstrate the ability to measure appropriate doses.<sup>9</sup></li> </ul>
How should <b>buprenorphine<sup>a</sup></b> 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 given 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>

Question	Answer/Pertinent Information
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 every three to six hours<sup>1,17</sup> Higher doses (e.g., 1.5 mcg/kg/dose every four to six hours) can be used after the second week of life in newborns with severe Nows.<sup>17</sup><ul style="list-style-type: none"><li>○ Clonidine may be increased by 0.05 mcg/kg/dose every 12 to 24 hours for two consecutive Modified Finnegan scores <math>\geq 8</math> or any single Modified Finnegan score <math>\geq 12</math>. Typical clonidine doses range from 2 to 6 mcg/kg/day.<sup>17,21</sup></li></ul></li><li>• <b>Max dose:</b> 24 mcg/kg/day.<sup>20</sup></li><li>• May be added to morphine when total daily morphine doses are <math>&gt;1</math> to 1.6 mg/kg or in patients with significant diarrhea or insomnia.<sup>5,17</sup></li><li>• Wean clonidine slowly (e.g., reduce doses by 0.25 mcg/kg every six hours, reduce dose by 25% per day by increasing dosing interval [for example, change every six-hour dosing to every eight-hour dosing]) over about three days starting the taper AFTER morphine is discontinued.<sup>17</sup></li><li>• Monitor blood pressure for at least 48 hours after discontinuation of clonidine before discharging home.<sup>21</sup></li></ul>
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> 10 to 20 mg/kg loading dose. Then starting 12 hours later, give 1.5 to 2.5 mg/kg every 12 hours or 3 to 5 mg/kg every 24 hours.<sup>5,17</sup> Note: loading dose is NOT necessary in the absence of seizures.<sup>17</sup><ul style="list-style-type: none"><li>○ Phenobarbital bolus doses (e.g., 5 to 10 mg/kg) can be given for seizures occurring while on phenobarbital.</li><li>○ Adjust dose based on monitoring and clinical parameters.<sup>8</sup></li></ul></li><li>• <b>Max dose:</b> Specific maximum dosage not available.<sup>8</sup></li><li>• May discontinue (not necessary to taper phenobarbital, though some protocols may reduce dose by 20% each day<sup>5,13</sup>) after weaning has been completed for other medications (e.g., morphine).<sup>17</sup></li><li>• May discharge after discontinuation or some protocols may allow newborns to go home during phenobarbital taper.<sup>13</sup></li></ul>

a. Facility protocol may vary from these doses. These are example doses summarized from available Nows protocols and clinical trial data.

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*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. <http://www.aafp.org/afp/2004/0201/p548.pdf>.]

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