Neonatal Abstinence Syndrome

What We Know

› Use or abuse of psychoactive substances—including prescription and nonprescription drugs, alcohol, and illicit drugs—by a woman during pregnancy places her newborn at risk for neonatal abstinence syndrome (NAS; also called neonatal withdrawal syndrome)\(^ {3,4,6,9,10,11,13,16}\)
  • These substances cross the placenta and can cause dependency in the fetus; when fetal exposure to the substance(s) terminates at birth, the newborn is at risk for a spectrum of withdrawal manifestations (e.g., autonomic dysfunction, respiratory distress, gastrointestinal compromise) that can necessitate prolonged treatment, intensive monitoring, and extended hospitalization and can result in impaired maternal-infant bonding, as well as short- and long-term adverse effects on neurodevelopment\(^ {1,2,3,4,6,9}\)
  • The incidence of NAS appears to be increasing in the United States\(^ {3,4,6,9,13}\)
    – Researchers who performed a retrospective analysis of national hospital discharge data found that the annual rate of maternal opioid use increased nearly fivefold and the incidence of NAS increased nearly threefold during the period 2000–2009\(^ {13}\)
    – In the U.S., one infant is born each hour requiring treatment of NAS\(^ {3}\)
  › Opiates, including heroin and methadone, are commonly associated with NAS, which occurs in 50–95% of infants exposed to these drugs in utero\(^ {6,10,16,18}\)
  • Other substances associated with NAS include cocaine, methamphetamine, marijuana, barbiturates, diphenhydramine, chlordiazepoxide, phencyclidine, caffeine, and nicotine\(^ {3,6,18}\)
  • Withdrawal signs and manifestations can develop in neonates after in utero exposure late in the pregnancy to antidepressant medication (e.g., selective serotonin reuptake inhibitors [SSRIs])\(^ {2,3,6,7}\)
  › Manifestations of NAS include tremor, hyperirritability, jitteriness, excessive and often high-pitched crying, hypertonicity, fever, poor sucking, vomiting, diarrhea, sweating, sneezing, fever, nasal congestion, difficulty sleeping, respiratory distress, tachypnea, and seizures\(^ {1,3,6,7,9,16,18}\)
  • NAS onset and severity depend on the substance the infant is withdrawing from, the combination of substances used, and the gestational age of the infant\(^ {2,16}\)
    - The short half-lives of opiates are responsible for a rapid onset of NAS, usually within 72 hours after birth, in neonates born to mothers who abused opiates.\(^ {6}\) The dose of opiate the neonate was exposed to in utero does not seem to correlate with the severity of NAS\(^ {1,16}\)
    - Opioid maintenance therapy is the standard of care for opioid-dependent pregnant women\(^ {4}\)
      - NAS associated with in utero buprenorphine exposure is less severe than NAS associated with in utero exposure to methadone, suggesting that buprenorphine may be a superior treatment option for opioid dependence during pregnancy\(^ {2}\)
Researchers are investigating pharmacologic alternatives to opioid agonist substitution therapy for opioid dependence during pregnancy, including opioid vaccines and drugs that target the serotonergic system.(11) Investigators in Norway found evidence that medically supervised detoxification of opioid-dependent pregnant women may be an alternative to opioid maintenance therapy. Infants born to women who underwent detoxification in a residential setting during pregnancy experienced less prenatal drug exposure and had better perinatal outcomes, with no NAS. Risk of miscarriage and other complications was not increased in women who underwent detoxification.(4)

Sedative-hypnotics (e.g., benzodiazepines and barbiturates) have longer half-lives than opiates; manifestations of NAS that result from maternal abuse of sedative-hypnotics do not develop for 2–4 weeks after birth.(6)

Polysubstance abuse produces more intense manifestations of NAS than abuse of a single substance.(10,18)

Preterm infants experience a shorter, less severe course of opiate-related NAS (e.g., from maternal methadone use), and have significantly fewer central nervous system manifestations compared with full-term infants.

In a study of 129 infants who were exposed to methadone or buprenorphine in utero, factors associated with increased risk of NAS included later estimated gestational age, lower maternal weight at delivery, maternal use of SSRIs, vaginal delivery, and higher infant birth-weight.(8)

The sex of the infant may influence the severity of NAS; in a recent study of 90 infants born to women who were treated with buprenorphine during pregnancy, researchers found that male infants experienced more severe NAS than females and were more likely to require pharmacologic therapy.(12)

Genetic factors may affect the severity of NAS.(9,17)

Researchers recently reported that among infants with NAS, those with variants in the μ-opioid receptor (OPRM1) and catechol-o-methyltransferase (COMT) genes had shorter lengths of hospital stay and less need for pharmacologic therapy.(17)

Updated guidelines for patient evaluation and pharmacologic treatment of NAS were published in 2012 by the American Academy of Pediatrics (AAP); the guidelines include the following:(2)

- Each healthcare facility should develop and implement a protocol for the evaluation and management of NAS.
  - Protocol-driven weaning of infants with NAS appears to be associated with reduced duration of opioid treatment and hospital stay compared without the use of a protocol. In a study of 547 late preterm and term infants receiving inpatient pharmacologic treatment for NAS, researchers found that those who underwent protocol-driven weaning experienced significantly shorter duration of opioid treatment (17.7 vs. 32.1 days) and shorter hospital stay (22.7 vs. 32.1 days).(5)

- Urine toxicology testing should be performed on both mother and newborn.
  - Testing of meconium, umbilical cord tissue, and/or neonatal hair can be performed to identify the specific substance(s) involved; serum glucose, serum calcium, CBC, and HIV testing may also be indicated.(18)

- A standardized assessment method such as the Lipsitz Neonatal Drug-Withdrawal Scoring System (recommended by the AAP) should be administered to evaluate the extent of withdrawal manifestations in newborns(3,7,9)
  - Other standardized tools that can be administered include the Finnegan Neonatal Abstinence Scoring System, the Neonatal Withdrawal Inventory, and the Neonatal Narcotic Withdrawal Index.(3,6,9,10,16,18)

- Nonpharmacologic management for neonates with NAS involves reducing sensory stimulation, including the use of dimmed lighting, prone positioning, and swaddling(3,7,9,18)
  - Kangaroo care and use of pacifiers can help calm infants with NAS(9)
  - Breastfeeding for at least 72 hours starting at birth reduces the duration and severity of NAS and decreases the need for pharmacologic treatment; breastfeeding soothes infants and the breast milk itself contains a small amount of the abused substance(s), which relieves withdrawal signs and manifestations(2,7,14,18)

- Up to 91% of neonates with NAS require pharmacologic therapy and an extended hospital stay.(9,14)
  - Guidelines do not exist regarding the length of hospital stay considered sufficient to identify if NAS treatment is required following birth. In a study of 210 newborns 95% of those requiring treatment for NAS were identified within 5 days of birth prompting researchers to suggest that 5 days is adequate for routine post-natal observation for NAS.(15)

- Pharmacologic treatment for NAS includes the following:
  - Tincture of opium is the preferred treatment for opiate withdrawal; methadone may also be administered(3,7,11)
  - Opioid antagonists (e.g., naloxone) are contraindicated in neonates because they have the potential to cause seizures.(9)
References are rated using the following codes, listed in order of strength:

- **M**: Published meta-analysis
- **SR**: Published research
- **RCT**: Published research (randomized controlled trial)
- **R**: Published research (not randomized controlled trial)
- **C**: Case histories, case studies
- **G**: Published guidelines
- **RV**: Published review of the literature
- **RU**: Published research utilization report
- **QI**: Published quality improvement report
- **L**: Legislation
- **PGR**: Published government report
- **PFR**: Published funded report
- **PP**: Policies, procedures, protocols
- **X**: Practice exemplars, stories, opinions
- **GI**: General or background information/texts/reports
- **U**: Unpublished research, reviews, poster presentations or other such materials
- **CP**: Conference proceedings, abstracts, presentation

## References


