Newborn Critical Care Center (NCCC) Clinical Guidelines

Guidelines for Neonatal Toxicology Screening

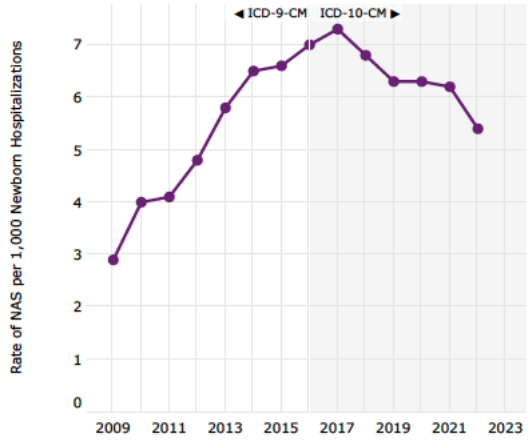
BACKGROUND

Substance use during pregnancy may result in a myriad of fetal and neonatal effects including birth defects with lifelong physical and developmental implications, prematurity, acute toxicity, and neonatal abstinence syndrome (NAS) and neonatal opioid withdrawal syndrome (NOWS).

Women are at their highest risk of developing a substance use disorder between ages 18 to 44 years old, throughout their reproductive years.[1] According to the 2024 National Survey of Drug Use and Health (NSDUH, samhsa.gov), 21.9% of pregnant women reported substance use within the last month (Table 8.22B).[1] In a universal maternal screening study, tobacco is the most common substance used during pregnancy (11.3% of pregnant women), followed by illicit drugs (5.3%), marijuana (5%), and alcohol (4.7%), with illegally made fentanyl at 0.6%. In a universal maternal screening study, 33% of maternal urine samples obtained at delivery contained a nicotine metabolite, 11.3% were positive for marijuana, 3.8% for cocaine, and 1.9% for methamphetamines, with a polysubstance use prevalence of 15%.[2] Consistent with the concept that polysubstance use is a common phenomenon during pregnancy, a 2020 study found that 10% of women self-reported alcohol use during pregnancy, and nearly half of those women reported current use of at least one other substance[3].

There is a recent increase in opiate use nationally in the general population, as well as in pregnancy, with a marked increase in synthetic opioid use since 2014.[4] Tracking ICD-9/10 data has provided similar insights into the rates of neonatal abstinence syndrome (data is available for NAS, but not NOWS specifically).[5] Nationally, NAS diagnoses peaked in 2017 at a rate of 7.3/1000 neonatal admissions, with a recent decline to 5.4/1000 neonatal admissions in 2022. North Carolina exceeded the national average with a 2017 peak of 10.5 NAS diagnoses/1000 neonatal admissions, declining to 5.9/1000 in 2023.

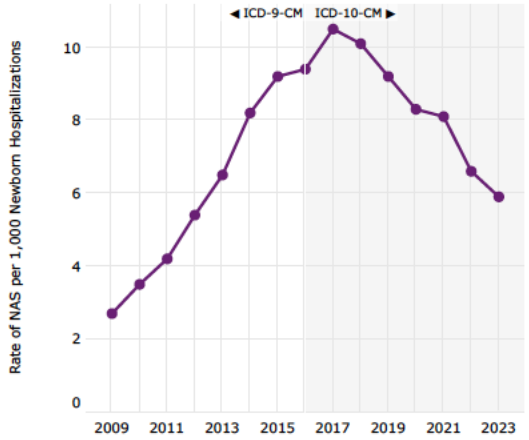
U.S. National: Rate per 1,000 Newborn Hospitalizations by All NAS, 2009 to 2022



Source: Agency for Healthcare Research and Quality (AHRQ), Healthcare Cost and Utilization Project (HCUP), National (Nationwide) Inpatient Sample (NIS) 2009 to 2022 (all available data as of 07/09/2025). Abbreviation: NAS, neonatal abstinence syndrome.

*2015 values are based on the first three quarters of data using ICD-9-CM coding.

North Carolina: Rate per 1,000 Newborn Hospitalizations by All NAS, 2009 to 2023



Source: Agency for Healthcare Research and Quality (AHRQ), Healthcare Cost and Utilization Project (HCUP), State Inpatient Databases (SID) 2009 to 2023 (all available data as of 07/09/2025). Abbreviation: NAS, neonatal abstinence syndrome.

*2015 values are based on the first three quarters of data using ICD-9-CM coding.

In 2016, the Comprehensive Addiction and Recovery Act modified child welfare legislation to expand Plan of Safe Care to include all infants affected by substance abuse withdrawals symptoms or a fetal alcohol spectrum disorder and who require services be identified for the family/caregivers of these infants. In North Carolina and at UNC, all positive urine/meconium toxicology screening results (that are not otherwise explained by prescribed maternal medications) are forwarded to the Department of Social Services (DSS) of the county where the mother resides, and DSS has full authority and jurisdiction to pursue further action.[6] Currently, ACOG recommends use of a validated verbal screening tool for substance use for all pregnant patients at the first prenatal visit, in the third trimester, and at the postpartum visit.

The decision to screen urine or meconium for the presence of opiates or other illicit drugs should be based on an assessment of risk factors for intrauterine drug exposure with the expectation that the results will inform clinical decision making for the infant. Care must be taken that the decision to test is not influenced by unconscious bias so as to not propagate health inequitites[7].

If a toxicology screen is considered, every effort should be made to discuss with families how neonatal toxicology screening will optimize care for their infant. However, written or verbal consent is not legally required to perform testing if performed for diagnostic purposes.

WHY TEST?

- The goal of toxicology testing in neonates is to evaluate gestational exposure to identify infants at risk for withdrawal and other short and long term neurologic problems.[6,8] Early intervention can help minimize acute and long-term effects of substance exposure.[9,10] The information obtained from neonatal toxicology testing can also be used to determine duration of monitoring and may inform breastfeeding guidance.
- Potential for child neglect after discharge[10]
- Offer intervention services via Plan of Safe Care which can support the safest discharge opportunity for the infant and the family[11]

HOW DO WE TEST?

- Urine and meconium are most commonly used for neonatal toxicology screening[12]

Urine Specimen

- Noninvasive - generally provides the fastest results, usually within hours, use a bag specimen
- Narrow window of detection from maternal ingestion to excretion in infant's urine
    - Results are most useful for exposures occurring in preceding 3-5 days
    - Sample needs to be obtained as soon as possible after birth
    - May detect maternal administration of medications used during labor and delivery
- *Minimum 1 mL required for initial screening*, but a larger specimen is encouraged since confirmatory testing often requires larger volumes of 5-10 mL depending on the substance
- Method of collection can influence results[13]
    - Use of cotton balls may interfere with detection of marijuana and lead to false negative rapid (immunoassay) screens.
    - The presence of some baby soap products in the specimen can generate false positives for marijuana on rapid (immunoassay) screening

- Clean catch specimen should be obtained using collection bag with adhesive, unless ELBW infant and concerns for skin integrity
- May detect maternal administration of medications used during labor and delivery

- The initial broad screening tests classes of drugs e.g. opioids, benzodiazepines, amphetamines, barbiturates, cannabinoids, cocaine, and phencyclidine

Meconium Specimen

- Noninvasive; specimen collection may be difficult in newborns who pass meconium in utero prior to delivery, and in very small or critically ill neonates
- Longer window of detection
  - Reflects exposures occurring during the third trimester. There is decreased yield for exposures that occur during the first or second trimesters due to dilution from non-linear increase in meconium during the third trimester[13].
- Minimum 1 gm (approx. 1 tsp) meconium required
  - Send-out to Mayo Medical laboratories with a 5-10 business days turnaround time

*If screen is **POSITIVE** for any individual drug in the urine or meconium specimen, confirmatory testing will be performed. This will likely not take additional time for urine, but may take up to 4 additional days for meconium.*

- A ***presumptive positive*** qualitative screening test simply indicates the presence or absence of a specific drug class in the urine; it is followed by a confirmatory test using the same specimen.
- **NOTE:** The possibility of cross reactivity with another substance could yield an initial presumptive positive, but ultimately negative result, so confirmatory testing is crucial.
- **False negatives:** can occur due to insufficient meconium sampling, contamination with urine or transitional stool, or inappropriate handling of the specimen.
- ***SCREENING SHOULD PROMPT A SOCIAL WORK CONSULT TO PROVIDE RESOURCES TO FAMILIES***

SCREEN IF THE FOLLOWING RISK FACTORS ARE PRESENT [12,14]:

Maternal History

- History of substance use documented during pregnancy
- Less than two prenatal visits
- History of child abuse, neglect, or court-ordered placement of other children outside the home
- History of bloodborne pathogen infection (ie hepatitis or human immunodeficiency virus)
- Unexplained placental abruption
- Concern for acute maternal intoxication observed around the time of delivery
- Previously unexplained fetal demise or multiple spontaneous abortions and a history of a perinatal condition such as abruption

Infant History

- Infants with evidence of drug withdrawal such as hypertonia, irritability, or tremulousness (see Table 1)

Umbilical Cord Tissue Segment Testing *(Not currently performed at UNC)*

- Advantages include ability to collect in a single encounter immediately after birth
- Window of detection believed to encompass the third trimester
- Lower yield than meconium testing is a limitation. Concentrations for many metabolites are lower in UC than in meconium[13].

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Table 1: Maternal Non-Narcotic Drugs That May Cause Neonatal Withdrawal[6]

DRUG	SIGNS	ONSET	DURATION
Alcohol**	Hyperactivity, crying, irritability, poor suck, tremors, seizures, poor sleeping pattern, hyperphagia, diaphoresis	3 – 12 hours	18 months
Barbiturates	Irritability, severe tremors, hyperacusis, excessive crying, vasomotor instability, diarrhea, restlessness, increased tone, hyperphagia, vomiting, disturbed sleep	1 – 14 days	4 – 6 months with prescription*
Caffeine	Jitteriness, vomiting, bradycardia, tachypnea	At birth	1 – 7 days
Chlordiazepoxide *(Librium)*	Irritability, tremors	Days - weeks	9 months (1.5 months with prescription)
Clomipramine *(Tricyclic antidepressant)*	Hypothermia, cyanosis, tremors	12 hours	4 days with prescription
Diazepam *(Benzodiazepine)*	Hypotonia, poor suck, hypothermia, apnea, hypertonia, hyperreflexia, tremors, vomiting, hyperactivity, tachypnea	Hours - weeks	8 months, 10 – 66 days with prescription
Ethchlorvyol *(Sedative hypnotic)*	Lethargy, jitteriness, hyperphagia, irritability, poor suck, hypotonia		10 days with prescription
Glutethimide *(Sedative hypnotic)*	Increased tone, tremors, opisthotonos, high-pitched cry, hyperactivity, irritability, colic		6 months
Hydroxyzine *(Antihistamine)*	Tremors, irritability, hyperactivity, jitteriness, shrill cry, myoclonic jerks, hypotonia, increased respiratory and heart rates, feeding problems, clonic movements		5 weeks with prescription
Meprobamate *(Anxiolytic)*	Irritability, tremors, poor sleep patterns, abdominal pain		9 months, 3 months with prescription
SSRIs	Crying, irritability, tremors, poor suck, feeding difficulty, hypertonia, tachypnea, sleep disturbance, hypoglycemia, seizures	Hours - days	1 – 4 weeks
Tetrahydrocannabinol *(THC)*	Some reports of temporary symptoms like jitteriness and irritability		30 days

* ***WITH PRESCRIPTION*** indicates the infant was treated with pharmacologic agents and the natural course of the signs may have been shortened

** ***SPECIAL NOTE ABOUT ALCOHOL:*** Alcohol is cleared quickly and will not show up in a urine or meconium screen (though assays are being developed). ***If a mother is inebriated at the time of delivery a blood alcohol level can be obtained on the mother or infant.*** Acute alcohol intoxication can cause respiratory depression, hypoglycemia or seizures in the newborn. Alcohol withdrawal can cause seizures and cardiovascular collapse.