Advances, Nuances, and Future Directions in Neonatal Toxicology Testing

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PRACTICE GAPS OR EDUCATION GAPS

Although neonatal toxicology testing is a commonly used tool to identify infants with prenatal substance exposure, literature gaps about best practices and the limitations and harms of neonatal toxicology testing exist. Medical and legal considerations likely contribute to variations in practice. Clinicians must recognize the benefits, harms, limitations, and inequities of perinatal toxicology testing to best identify and manage newborns and families with substance exposure.

OBJECTIVES *After completing this article, readers should be able to:*

1. Recognize the nuances and limitations of commonly used toxicology tests in caring for the pregnant person-newborn dyad.
2. Explain ethical, social, and legal considerations with the application of toxicology testing to this population.
3. Identify best practice guidance for perinatal toxicology testing.

ABSTRACT

Toxicology testing is a commonly used tool applied to the identification and management of infants with prenatal substance exposure. Although such testing has the potential to aid in the clinical management of newborns, clinicians who order such testing are frequently unaware of the limitations

ABBREVIATIONS

ACOG	American College of Obstetrics and Gynecology
GC/MS	gas chromatography/mass spectrometry
IPSEs	infants with prenatal substance exposure
LC-MS/MS	liquid chromatography/tandem mass spectrometry
LoD	limits of detection
LoQ	limits of quantification

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and harms of testing and the impact of the test results on the pregnant person-newborn dyad. In this review, we summarize the types and limitations of neonatal toxicology tests and identify areas for improvement, including policy change and advocacy, to drive equitable care for newborns and families with perinatal substance exposure.

Clinicians ordering toxicology testing for neonates must understand their facility's testing capabilities, the screening vs confirmatory nature of that available testing, how to proceed with confirmatory testing of a screening test, and how to accurately interpret the result of that test.

INTRODUCTION

Toxicology testing is a commonly used tool to aid in the identification and management of infants with prenatal substance exposure (IPSEs). Fetal substance exposure begins in pregnancy and has implications for the fetus, newborn, and child into adulthood.[1–4] Substance exposure may first be identified via screening assessments or toxicology testing of pregnant people during pregnancy. In some circumstances, substance exposure may not be identified until the newborn is evaluated. This review examines the nuances and limitations of toxicology testing, the current application of neonatal toxicology testing in clinical practice, and best practices to inform the future state of neonatal toxicology testing. Although this article will focus on neonatal toxicology testing, it is important to recognize the intricacies that link the pregnant person and newborn with perinatal substance exposure and to understand the implications of toxicology test results for one patient in the dyad on the management of the dyad as a whole.

BACKGROUND OF TOXICOLOGY TESTING IN PREGNANT PERSONS AND NEWBORNS

A review of the historical context of toxicology tests frames the current state of toxicology testing practices, including neonatal practices. Urine toxicology testing was first introduced in the 1960s and became more widespread by the 1970s after the military initiation of drug testing for members of the armed forces in the Vietnam War.[5] This coincided with political attention initiated under President Nixon to respond to an increase in illicit substance use among youth in the 1960s, a concurrent rise in crime rate, and an increase in heroin use among American soldiers in Vietnam.[6] Substance use in pregnant patients gained more attention in the 1980s with media coverage of crack cocaine usage in pregnancy, including the *TIME Magazine* article entitled "Medicine: Crack Comes to the Nursery."[7] Toxicology testing using urine samples was performed in newborns in the 1980s, with the use of meconium first occurring in 1989.[8,9]

Early publications in the 1980s emphasized the necessity of newborn toxicology testing for medical reasons.[8,9] Pregnant people at this time were considered less likely to be forthcoming about substance use because of the sociopolitical context and possible legal ramifications, thus prompting clinicians to search for "objective" evidence of prenatal substance exposure.[8,10] Subsequently, toxicology testing became commonplace within newborn care units.

However, over time, the limitations of newborn toxicology testing became more apparent. This included problematic false-positive results with significant legal and social implications.[11] Improved toxicology testing methods were then sought to address these problems, rather than seeking alternative means of substance use identification or limiting toxicology testing practices. Neonatal toxicology testing evolved to include additional matrices such as umbilical cord tissue[12] and sought to use more accurate or precise testing techniques, including gas chromatography-mass spectrometry (GC/MS) and liquid chromatography/tandem mass spectrometry (LC-MS/MS). These techniques are further described in this article.

Using current technology, neonatal toxicology testing can be useful when accurately interpreted alongside results of validated parental substance use screening questionnaire tools, discussion with the pregnant person, and examination findings. Importantly, toxicology testing application is also variable, fraught with limitations, and can introduce harm into the care of the pregnant person-newborn dyad with potentially significant social and legal implications of positive results.[13–18] It is crucial that neonatal clinicians simultaneously consider both the advantages and limitations of different testing strategies to optimize care for IPSEs and their families.

Employing a validated written or verbal screening tool for substance use in pregnancy is a recommended first step in the identification of perinatal substance use before any testing is performed on the newborn. In 2004, the American College of Obstetrics and Gynecology (ACOG) first recommended universal written or verbal screening to assess for substance use.[19] However, self-report of substance use has been shown to underestimate exposure in the literature.[20–22] Ideally, supportive and nonpunitive health care

responses to substance use disclosure via screening would improve the concordance of self-reported and true exposure estimates, reducing the need for additional biologic sampling. Additionally, the historical exclusion of patients with lived experience (individuals who self-identify as having experienced mental health and/or substance use conditions, and their family members) from discussions about the identification and management of substance use represents a missed opportunity for improving care, because their insights could significantly contribute to more effective and compassionate health care practices.

BENEFITS AND LIMITATIONS OF COMMON PERINATAL TOXICOLOGY TESTS

Broadly speaking, toxicology tests can be classified as either screening tests or confirmatory tests (Table 1). Most screening tests are immunoassays that use an antibody (substance detector) to bind an antigen (the substance being detected) to provide qualitative information about the presence or absence of a substance. The intended antigen, or the substance the immunoassay is designed to detect, is referred to as the target analyte. One major limitation of immunoassays is that they are susceptible to interference, a phenomenon in which the presence of a different substance affects the measurable target analyte concentration or the intended antibody-antigen interaction in some way.[23] This may result in a false-negative or false-positive test result, decreasing the accuracy of the test. Cross-reaction is a specific type of interference in which the assay's antibody binds to a substance that is not the target analyte. This is a particularly frequent problem among screening toxicology tests, affecting up to 10% to 40% of immunoassays performed in some studies.[24–26] This occurs in part because of the tendency to use a single antibody structure to test for an entire class of substances (eg, amphetamines, benzodiazepines), which comes at the cost of decreasing the specificity of that antibody. For example, a pregnant person who takes bupropion (which has a cathinone structure similar to that of amphetamines) could have a false-positive screening test result for amphetamines, unnecessarily prompting subsequent newborn testing and intervention.[27]

Different manufacturers of toxicology immunoassays use distinct antibodies to test for the same analytes, such that known interfering substances for a given immunoassay are not necessarily applicable to another immunoassay. Similarly, different manufacturers make screening immunoassays that range from very limited (test for only a few target analytes) to relatively comprehensive (test for a large number of target analytes). Additionally, the target analyte may not be

TABLE 1. Analytical Techniques, Matrices, Benefits, and Limitations for Neonatal Toxicology Testing

Analytical Techniques	Benefits	Limitations
Immunoassay	Rapid results (minutes to hours) Inexpensive Readily available	Typically only qualitative (positive/negative) results are available Interference leading to false-positive results is common A single target analyte is often used to represent a class of drugs (eg, amphetamine)
GC/MS Liquid chromatography/mass spectrometry LC-MS/MS	Highly accurate and precise Typically quantified (rather than qualitative) results	Costly (relative to immunoassays) Not readily available (requires specialized equipment and specialized laboratory personnel to operate and maintain) Longer turnaround time (days to weeks)
Matrices	**Benefits**	**Limitations**
Urine	Many decades of experience with its use as a matrix, both in newborns and the general population, to inform interpretation Relatively robust data on drug and metabolite deposition	Early urine samples can be difficult to collect in newborns Short window of detection for most drugs and metabolites (days)
Meconium	A moderate degree of experience with its use as a matrix Likely a longer window of detection for most drugs and metabolites compared with urine	Meconium passed during labor not collectable Nonhomogenous matrix (need to collect and store samples over several days before mixing and sending to laboratory) Relatively little data to inform expected drug deposition
Umbilical cord tissue	Easy and noninvasive to collect Likely a longer window of detection for most drugs and metabolites compared with urine	Relatively little experience with its use as a matrix Relatively little data to inform expected drug deposition

Abbreviations: GS/MS, gas chromatography/mass spectrometry; LC-MS/MS, liquid chromatography/tandem mass spectrometry.

the parent substance itself but a metabolite of that substance, which may or may not be found in meaningful concentrations in various biological samples or matrices being tested. An understanding of the limitations of the scope and accuracy of screening tests is paramount to accurately interpreting initial results.

In contrast to screening tests, confirmatory tests do not typically involve immunoassays but rather use different analytical techniques that are highly accurate and precise. Examples of such techniques include GC/MS, high-performance liquid chromatography, and LC-MS/MS. These tests generally yield quantitative, rather than qualitative, results and are much less susceptible to interference because of the analytical techniques themselves, which involve directly measuring physical properties (eg, mass, charge) of the analyte in question to identify and quantify it. Despite these clear advantages, confirmatory tests are not routinely used in toxicology testing because they are substantially more difficult and expensive to perform. They require specialized equipment and personnel that are not available in most hospital or clinic laboratories. As such, most confirmatory tests performed in clinical settings are sent to reference laboratories, which adds to the expense and turnaround time.

Like all analytical techniques, both screening and confirmatory tests have inherent limits of detection (LoD) and limits of quantification (LoQ) (ie, a certain concentration or amount of analyte must be present for the assay to reliably detect its presence and quantify the concentration, respectively).[28] The reporting limit is the minimum amount of analyte that must be present for the laboratory to report a positive result. Each individual laboratory determines its own reporting limit for each analyte; these reporting limits may represent a test's LoD, a LoQ, or an administrative cut-off that is determined by the laboratory director, which may be higher than the LoD/LoQ. Samples that have analyte concentrations below the reporting limit will not return a positive result, even though the analyte is in fact present. As a result, the same sample analyzed by 2 different laboratories may yield different results because the reporting limits differ, even if they use identical techniques.

Both screening and confirmatory tests can be used with a wide variety of matrices. Commonly used matrices in newborn toxicology testing include urine, meconium, and umbilical cord tissue, although in special circumstances other matrices may also be used (eg, blood, hair). Each matrix has benefits and is subject to its own limitations. Many of these benefits and limitations are outlined in the Table and can be broadly grouped as related to the ease vs difficulty of collection of the sample, and the knowns vs unknowns regarding expected drug deposition within the matrix.

Urine is a relatively easy matrix to collect and can be used for both screening and confirmatory tests. It is limited as a matrix for toxicology testing because it is formed and eliminated quickly and continuously. As a result, most substances are only detectable within urine for a few days after the most recent exposure. Even so, many pregnant people are initially toxicology tested via urine because collection is typically easy and noninvasive. Urine testing may also be used for newborns, although in some ways the limitations of urine testing in newborns are even more pronounced than for pregnant people. Urine is somewhat more difficult to collect from newborns than from pregnant people, and as soon as the umbilical cord is cut, newborns are no longer exposed to any remaining substances or metabolites that may still be circulating within the pregnant person (barring lactational exposures, which are typically negligible in the first 24–48 hours after birth).[29] As such, the window of detection for many exposures is more limited in newborn urine relative to the pregnant person, and for some substances, the sensitivity of newborn urine for toxicology testing falls more precipitously as time passes than it does in the urine of pregnant persons.[9,30,31]

Meconium begins to form within the second trimester of pregnancy, and the umbilical cord forms within the first few weeks of pregnancy. As a result, many references infer that meconium and umbilical cord toxicology testing have drug detection windows that are quite wide, encompassing at least the third trimester and often the second as well.[32–35] However, very little is known about drug deposition within meconium and umbilical cord tissue, despite its current use in newborn toxicology testing.[36]

For all methods of testing, drug distribution and deposition within the body of the pregnant person and the newborn influence test results. This a highly complex aspect of pharmacokinetics that is influenced by a wide array of variables including a drug's structure, pH, lipophilicity, degree of protein binding, and numerous person-specific variables (eg, body composition, hepatic and renal function, other drug interactions), among others.[37] Despite this complexity, a large body of literature exists outlining expected urine positivity rates and drug and metabolite concentrations within urine for both the pregnant person and newborn.[38–44] This is in part because urine drug testing has been used in medicine for many decades and has been employed outside of medicine (eg, military testing, workplace testing) for even longer. It is also by far the most common matrix submitted for testing overall, regardless of setting.[33]

In contrast to urine toxicology testing, the use of meconium and especially umbilical cord tissue is relatively new, and both of these matrices are limited to newborn testing

only—a tiny fraction of the overall volume of toxicology tests performed each year. As such, there are vanishingly few publications to inform clinicians as to whether, to what extent, and for how long they should expect a particular substance to be present within meconium or umbilical cord tissue.[36] It is worth noting that what little has been published suggests meconium and umbilical cord tissue testing is somewhat more limited than is broadly appreciated, and the results of such testing should be interpreted with caution. The complex physiologic changes during pregnancy that impact drug metabolism, pharmacokinetics, and distribution across the placenta to the fetus are challenging to quantify when meconium and umbilical cord samples are used. For example, a few studies have demonstrated numerous instances in which paired meconium and umbilical cord tissue samples from the same infant yielded discordant results, and 2 studies (Palmer et al 2017 and Alexander et al 2018) even demonstrated discordant results among twins.[15,34,35,45,46]

In terms of drug detection windows in meconium and umbilical cord tissue, one small study has attempted to investigate this using paired maternal hair samples, which can be segmented to determine (within the confines of hair testing's limitations, which is outside the scope of this review) the timing of drug exposure by trimester.[47] In this study, all meconium and umbilical cord tissue samples paired with hair samples demonstrating drug exposure within the first and/or second trimester of pregnancy were negative; meconium and umbilical cord tissue samples were only positive if maternal hair samples demonstrated drug exposure throughout all 3 trimesters of pregnancy, and even then in some cases, meconium and umbilical cord were still negative.[47] This small study suggests that isolated first and/or second-trimester use of substances is likely not reliably reflected in meconium and umbilical cord tissue. Thus, caution is recommended when interpreting toxicology test results from meconium and umbilical cord tissue.

APPLICATION OF TESTING

The clinical application of toxicology testing is nuanced. It is important to note that although toxicology testing is a medical test used to guide medical management, it is also currently used to determine social considerations such as disposition, referrals to child welfare, and legal implications. Criteria for testing, benefits, and harms of testing, the timing of testing results, and the importance of consent must be considered by the ordering clinician.

Criteria for Testing

Despite the limitations of testing detailed above, toxicology testing is commonly ordered for both pregnant people and infants during the perinatal period to evaluate for substance exposure during pregnancy. Although major medical institutions recommend screening all pregnant individuals for substance use via written or verbal tools, there is no formal guidance on who should undergo biological testing. Consequently, toxicology testing during the perinatal period varies widely across regions, health care systems, and even within individual hospitals.

Although not universally recommended, some birthing facilities conduct universal toxicology testing.[48] Others employ selective criteria, also known as "risk-based" criteria, in which testing is based on hospital-defined criteria regardless of whether the individual screens positive for substance use. Common criteria include inadequate prenatal care, history of substance use (during or outside of pregnancy), pregnancy complications (such as preterm labor, placental abruption, fetal growth restriction), and social factors (such as intimate partner violence and housing instability).[49,50] Studies assessing concordance of these toxicology testing criteria with positive results are fraught with limitations and often have conflicting findings, despite the widespread use of such criteria. Limitations include inherent bias in cohorts selected for testing, single site or region populations, and lack of adjustment for confounding variables. Although some older studies suggest that these criteria are associated with positive toxicology testing results, others indicate that peripartum toxicology testing seldom yields unexpected positive results.[51,52] Disparities exist in pregnant person selection for toxicology testing, as highlighted by various studies assessing the sociodemographic, racial, and ethnic factors. Studies have shown that perinatal toxicology testing is disproportionately performed on younger, economically disadvantaged, and pregnant people of color and their newborns, despite the fact that the prevalence of substance use during pregnancy does not differ with respect to these demographic variables.[53–58]

Benefits

It is important to note the potential benefits of toxicology testing. When appropriately screened for substance use, self-reporting of illicit and non-illicit substance use is the preferred method for identifying substance use in pregnant people, per ACOG recommendations.[19] On the other hand, there is concern that reporting reliability, particularly in pregnant persons, can be discordant with toxicology test results because of fears, stigma, and guilt surrounding substance use in pregnancy.[10,20,59] Biological testing has the ability to identify substance exposure in individuals whose verbal or written screening responses conflict with physical examination findings.

In cases when substance use is disclosed, toxicology testing can be beneficial in identifying unintended/unknown exposures, which could result in implications for the pregnant person and newborn. For example, there has been a significant increase in unintended fentanyl exposure due to the increased presence of synthetic opioids in illicit drugs.[60] Identifying such exposures could not only provide valuable information to the pregnant person but could also affect their own medical care and that of their newborn. The development of withdrawal symptoms in newborns who have been perinatally exposed can be unpredictable in timing and severity based on the substance or polysubstance exposure. Understanding the scope of exposure may be clinically helpful in newborn monitoring and determining medical safety for discharge. There may also be instances when toxicology testing is desired by a pregnant person as a means to demonstrate sobriety.

Toxicology testing in the pregnant person may also be useful as a tool that directly influences a newborn's care by determining a safe feeding plan. There are many known benefits of breastfeeding for both the newborn and pregnant person, and these must be balanced against the risks associated with breastfeeding and concurrent substance use because of the known transmission of substances into breast milk. As a result, breastfeeding while using nonprescribed substances is not recommended. The Academy of Breastfeeding Medicine supports breastfeeding when nonprescribed substance use is discontinued prior to or at delivery. When toxicology testing in the pregnant person suggests new or ongoing nonprescribed substance use, breastfeeding should be avoided until the substance is cleared.[61]

Risks/Disadvantages

Despite its potential benefits and laboratory limitations, toxicology testing also presents clinical challenges. As discussed earlier in this article, interpreting toxicology testing results can be complex, especially with immunoassays that may yield false-positive or false-negative results. Misinterpretation of results can easily occur if not considered in light of the specific type of toxicology test conducted, substances tested for, possible iatrogenic medication use, and other inherent limitations. Health care providers must carefully assess for concurrent medication administration, understand the nuances of the toxicology test that is ordered, and consult with laboratory personnel regarding analytical techniques and potential interference or cross-reactivity with medications or substances to more accurately interpret results. An example involves the use of continuous lumbar epidurals or other neuraxial analgesia during labor, which is the most common method for managing labor pain. Fentanyl is frequently included in neuraxial analgesia, which may result in positive toxicology tests for the pregnant person or the newborn if specimens are obtained after the initiation of a labor epidural.[62] If the context of the labor and birthing process is not considered, a positive toxicology test for fentanyl could lead to unnecessary interventions. For further clarification, poison control centers can be used to discuss the interpretation of specific results with a medical toxicologist. The timing of expected toxicology test results relative to the expected duration of the newborn's birth hospitalization must also be considered in developing the medical care plan. Additionally, requesting toxicology testing after verbally screening a pregnant person for substance use may impact the potential trust between the patient and the health care team.

Lastly, the cost of testing, although often overlooked, is another crucial factor to consider with newborn toxicology testing. Although all medical tests incur expenses, umbilical cord toxicology testing is particularly costly and may not assist in medical decision-making because of the long turnaround time. If a test result does not provide new information or influence the management of the pregnant person or newborn, it should prompt a reevaluation of its necessity. High-value care principles can guide practices to reduce the overutilization of neonatal toxicology testing.[63]

Consent

ACOG, the American Society of Addiction Medicine, and the Substance Abuse and Mental Health Services Administration emphasize the importance of obtaining consent before conducting toxicology testing during pregnancy, which influences the information available to the newborn provider after birth.[64,65] In newborns, informed consent for toxicology testing is not specifically addressed by any major medical organization nor is it extensively discussed in the literature. Although some attention is given to obtaining specific consent for treatments in the neonatal intensive care unit or newborn nursery, there are no specific guidelines regarding informed consent for newborn toxicology testing.[66]

Despite recommendations to obtain consent before performing toxicology testing in pregnancy, adherence to these guidelines among clinicians remains variable and challenging to verify. Hospital policies regarding toxicology testing seldom mandate explicit discussion, let alone consent, for toxicology testing by the clinician for the pregnant person.[49] Patient interviews indicate that consent is often not sought, and documentation of verbal consent varies widely.[51] Discussions with the pregnant person about toxicology testing in the newborn are even less common, with one study

suggesting that less than 3% of hospital toxicology testing protocols required consent for newborn testing.[67]

Considerations for Testing

Toxicology test results have the potential to significantly impact care during the peripartum period, directly or indirectly impacting the newborn. These tests can positively or negatively influence medical care, social situations, and legal outcomes for families. Important considerations include who is selected for testing, how patient selection for testing aligns with verbal or written screening results, the impact of testing on the relationship between the pregnant person and provider relationship, the necessity of the test for informed decision-making, and the process of obtaining consent for the test. If new information is identified from the test results, it should be communicated to the pregnant person/family of the infant and the dyad's multidisciplinary care team and used to guide additional support, resource allocation, medical care decisions, and safe discharge planning. Mandatory referrals to Child Protective Services and effects on the infant's disposition in the setting of perinatal substance exposure vary across states based on abuse and neglect definitions and reporting laws.[68]

SYNTHESIS AND BEST PRACTICES

Policy Development and Implementation

With well-demonstrated challenges and disparities in perinatal toxicology testing, the development of clear and concise hospital or clinic policies for such testing is essential.[53] The language used in policies needs to be clear, concise, and easy to understand for all staff. Criteria for both pregnant people and newborn toxicology testing must be well delineated and evidence based. Consent processes and documentation requirements should be clearly outlined. The benefits and limitations of toxicology testing need to be defined, including details on laboratory methods and their clinical and social effects on the pregnant person-newborn dyad. Guidance on resource connection and support for families impacted by substance use should be clear, regardless of the results of potential toxicology testing. When developing care plans for dyads with substance exposure, it is important to emphasize multidisciplinary decision-making. This includes the expectation for communication with behavioral health, prenatal care, and addiction medicine providers, determining the need for toxicology testing, and determining transitions of care before and after the birth hospitalization. Figure 1 demonstrates a proposed clinical algorithm for the care of the substance-exposed dyad upon presentation to the birth hospitalization.

Policy implementation is an important initial step of hospital or unit-level work; additionally, post implementation, the mere presence of a policy does not guarantee appropriate use of or adherence to the policy recommendations.[69] However, the presence of a policy is associated with improved consent rates in perinatal toxicology testing.[70] Quality improvement and/or dissemination and implementation science methods are essential to understanding barriers and facilitators to policy adherence. Following policy development, ongoing data review is recommended to allow teams to benchmark progress and to enable successful and sustainable implementation of equitable toxicology testing policies within the local context.

Successful implementation of perinatal toxicology testing policies and evidence-based best practices depends on multiple factors. These include the dissemination of such policies, involvement of key stakeholders in policy development and implementation, and varying state regulations that influence the management of the newborn.

Legal Influences on Health Care System Policies for Toxicology Testing

With frequent changes to legislation, pediatric providers are faced with the challenge of staying current and developing or revising hospital policies to reflect the current recommendations. Geopolitical variation in both laws and reporting requirements of perinatal substance use exists. Many states have definitions of child abuse and neglect that include positive toxicology test results, despite the clear limitations of the testing discussed earlier.[18] Understanding current state laws is essential for pediatric providers caring for newborns and their families. These should be explored and included in the implementation or revision of hospital or clinic policies. Pediatric clinicians are also important advocates to inform and improve state-specific legislative definitions incorporating neonatal toxicology test results.

State-specific best practice resources, such as *Indications for Toxicology Testing in Colorado Birthing Facilities*, published in 2023 by Supporting Perinatal Substance Use Prevention, Recovery, and Treatment Colorado, provide guidelines relevant to the applicable state laws for Colorado health care facilities.[71] It is important to know, however, that best practice guidelines alone do not necessarily equate to legislative requirements. Adopting state-level best practice guidelines into individual hospital policy requires engagement with all invested clinical and nonclinical groups. This includes physicians, advanced practice providers, nurses, lactation consultants, social workers, risk management, patients with lived experience, legal teams, and adherence teams to develop hospital-level policies that are evidence based and

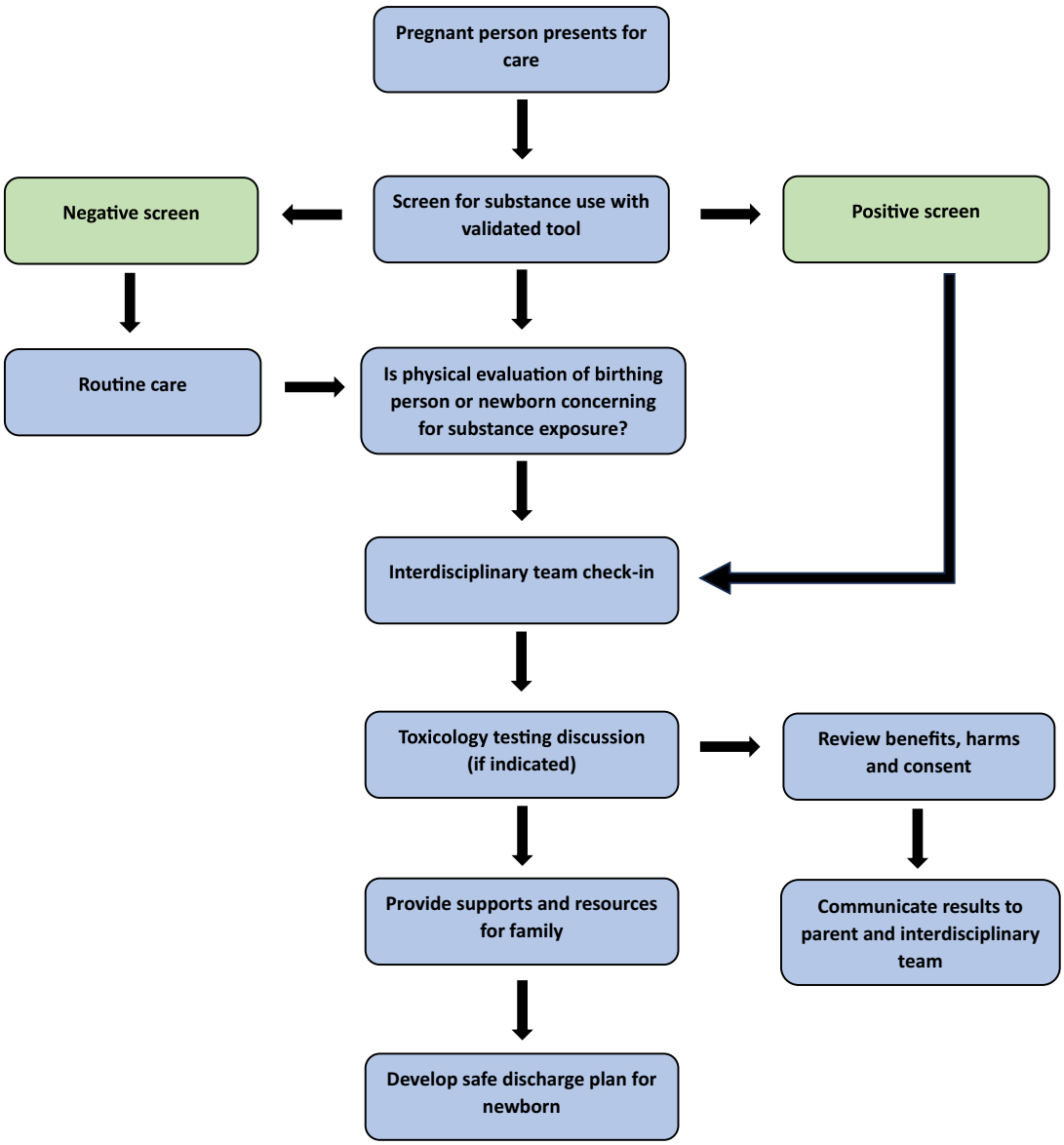

FIGURE 1. Updated clinical algorithm to identify pregnant patients and newborns with substance exposure.

deliver equitable care to our newborns and families within legal frameworks. Clear guidance on the required consent processes for newborn toxicology tests is essential within health care policies.

Reducing Stigma and Bias

Staff engagement to reduce perinatal stigma and bias is paramount to cultivate an inclusive culture free of judgment when interacting with all patients, including those with substance use, and in communicating plans for perinatal toxicology tests. Stigma and bias training addresses and mitigates negative bias for patients and improves comfort in treating patients with opioid use disorder.[72] Lack of appropriate training for health care providers and the stigma associated with opioid use disorder during pregnancy are cited as barriers that health care providers face when caring for these patients.[73] Conversations among providers, staff, and pregnant people/parents about toxicology testing must occur in a trauma-informed manner. Furthermore, the impact of stigmatizing language in medicine must be considered, which can lead to higher negative perceptions of patients and less appropriate management of patient's medical conditions (including substance use).[74]

Specific to substance use, the "Words Matter" program from the National Institute on Drug Abuse provides continuing educational credit for health care professionals who

interface with families affected by substance use and is focused on person-first language to reduce stigma and negative bias.[75] Education about thoughtfully crafted visual and written language on the importance of nonstigmatizing language has been shown to impact health care professional's perceptions of patients with opioid use disorder.[76] Applications of this tool for toxicology testing include the use of terms such as "positive or negative" results, instead of "clean or dirty" results, or identifying a parent as a person with a substance use disorder instead of an "addict." Provider and patient educational materials should leverage appropriate person-first language terminology.

Aside from formal training, in-unit or clinic case reviews of perinatal substance use cases and toxicology testing usage can aid in the review of policy adherence. Encouraging staff discussions about opportunities to reduce bias in testing can be beneficial. These informal venues also provide opportunities for staff to learn from each other and engage in productive dialogue about toxicology testing practices.

Family Education

Education of families throughout the perinatal period regarding substance exposure helps families anticipate the potential postnatal needs of their infants, including the potential use of toxicology testing. Ideally, this education would begin during the prenatal period. However, barriers to prenatal education, including the inability to seek prenatal care, fragmented care, and limited time during prenatal visits, influence the ability to optimize prenatal education. Implementation of office-based education for pregnant individuals receiving medication for opioid use disorder therapy has demonstrated success.[77] Antenatal consultation with pediatric providers caring for newborns during the birth hospitalization may offset the challenges for pregnant patients with substance use in anticipating the birth hospitalization. This may include why a toxicology test may be indicated, how this test would be performed, the process of consent for the test, and the ways in which results are timed and can influence the medical care of a newborn. Although integration of specific educational programs is ideal, the importance of universal education cannot be understated given the prevalence of substance use in the general population.

Policies and systems to encourage and support family presence at the bedside are also key. Increased parental presence for infants being treated for neonatal opioid withdrawal syndrome is associated with shorter lengths of stay, fewer days of postnatal opioid therapy, and decreased withdrawal scores.[78,79] Pregnant people should be empowered to participate in team decisions applicable to the care of their newborns, and decisions around newborn toxicology testing should support, rather than hinder, the pregnant person/family's engagement with the newborn medical team.

Lived Experience

Integration of people with lived experience with substance use disorders into aspects of policy development, including toxicology testing indications, trainee and staff education, and peer support is a powerful way to educate, reduce stigma, and optimize neonatal care. Peer support programs have documented success, including fostering trust and safety, supporting participants in various aspects of parenthood, and navigating the health care system, especially when peer support workers are of the same race or ethnicity as the participants.[80,81] Participants note that peer support has a positive impact on their recovery.[82] Despite the presence of peer support systems, further work is needed to expand access to peer support services across systems.

CONCLUSION

Despite the current challenges in neonatal toxicology testing practices, many opportunities exist for improved patient care and equity. Future state neonatal toxicology testing practices should be less variable across institutions with standardized alignment of evidence-based criteria after leveraging validated screening tools for the pregnant person. To achieve this, more multisite studies are needed regarding the association of criteria and toxicology testing results across large populations. This would ideally lead to the creation of governing body best practice statements to inform neonatal providers about standard neonatal toxicology testing practices. Stigma and bias training should be implemented for all health care teams, and policy creation for toxicology testing should include person-first language. State policies should better align with supportive patient care practices, reducing the presence of toxicology testing results in the definition of child abuse and neglect and removing criminal penalties for pregnant people who report or are identified via testing to have substance use. Overcoming barriers to parenting and treatment access for pregnant people with substance use, with or without the presence of toxicology test results, is crucial to achieving better outcomes. Pediatric providers play a crucial role in the improvement of care for IPSEs and their families, especially with regard to driving policy development and change. Together alongside patients with lived experience and health care teams, variations in toxicology testing application can be reduced to improve health and equitable outcomes for our patients.

American Board of Pediatrics Neonatal-Perinatal Content Specification

- Know the laboratory features of neonatal abstinence syndromes.

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NEO QUIZ

1. An immunoassay is performed on a pregnant person and is concerning for substance use. Screening toxicology tests use a single antibody structure to test for an entire class of substances, which makes them susceptible to interference and can lead to false-positive and false-negative results. This cross-reaction can occur in up to what percent of screening toxicology tests?

   A. 10%.
   B. 20%.
   C. 30%.
   D. 40%.
   E. 50%.

2. A term infant presents with symptoms concerning neonatal opioid withdrawal syndrome. You are concerned about maternal substance use earlier in pregnancy and decide to perform a meconium toxicology screen. What is the earliest gestational age substances can be detected in meconium?

   A. 8 weeks.
   B. 12 weeks.
   C. 15 weeks.
   D. 18 weeks.
   E. 21 weeks.

3. Several studies have highlighted significant disparities in the selection of pregnant persons for toxicology screening with regard to sociodemographic, racial, and ethnic factors. Which of the following factors is most predictive of a positive toxicology screen?

   A. Lower socioeconomic status.
   B. Multiparous patients.
   C. Pregnant people of color.
   D. Younger patients.
   E. None of the above.

4. Although much attention is given to obtaining consent for treatments in the neonatal intensive care unit or newborn nursery, there are no specific guidelines regarding informed consent for newborn toxicology screening. According to recent studies, less than what percent of hospital toxicology protocols require consent for newborn testing?

   A. 3%.
   B. 5%.
   C. 8%.
   D. 10%.
   E. 15%.

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5. A term infant is born to a pregnant person who endorses opioid and other substance use throughout their pregnancy. In addition to routine care, the team performs toxicology screening on both the pregnant person and the newborn. When selecting a matrix to test, which of the following offers the longest window of detection?

   A. Blood.
   B. Paired maternal and neonatal hair sample.
   C. Meconium.
   D. Umbilical cord tissue.
   E. Urine.