



Universal Maternal Drug Testing in a High-Prevalence Region of Prescription Opiate Abuse

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Objective To evaluate the efficacy of a universal maternal drug testing protocol for all mothers in a community hospital setting that experienced a 3-fold increase in neonatal abstinence syndrome (NAS) over the previous 5 years.

Study design We conducted a retrospective cohort study between May 2012 and November 2013 after the implementation of universal maternal urine drug testing. All subjects with positive urine tests were reviewed to identify a history or suspicion of drug use, insufficient prenatal care, placental abruption, sexually transmitted disease, or admission from a justice center, which would have prompted urine testing using our previous risk-based screening guidelines. We also reviewed the records of infants born to mothers with a positive toxicology for opioids to determine whether admission to the special care nursery was required.

Results Out of the 2956 maternal specimens, 159 (5.4%) positive results were recorded. Of these, 96 were positive for opioids, representing 3.2% of all maternity admissions. Nineteen of the 96 (20%) opioid-positive urine tests were recorded in mothers without screening risk factors. Seven of these 19 infants (37%) required admission to the special care nursery for worsening signs of NAS, and 1 of these 7 required pharmacologic treatment.

Conclusion Universal maternal drug testing improves the identification of infants at risk for the development of NAS. Traditional screening methods underestimate in utero opioid exposure. (*J Pediatr* 2015;166:582-6).

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Widespread abuse of new, powerful prescription narcotics now accounts for a major source of opioid addiction. In the US, there was an almost 3-fold increase in the incidence of neonatal abstinence syndrome (NAS) between 2000 and 2009.¹ In Ohio, a 6-fold increase in hospitalization for NAS was recorded between 2004 and 2011.² The incidence of in utero drug exposure has increased 6-fold over the past 5 years in the Cincinnati region (Figure). Approximately 60% of infants exposed to methadone develop NAS, presenting with signs of narcotic withdrawal after delivery.³ The number of infants who develop NAS after prescription drug exposure has not been widely examined, but prevalence appears to be lower than that of NAS after methadone exposure.⁴ The manifestations of NAS include extreme irritability, feeding intolerance and diarrhea, abnormalities of tone, and seizures.⁵ Newborns with NAS require extended hospitalization and present social and economic burdens for families, healthcare providers, social service institutions, and government agencies.^{1,2,6}

Prompt diagnosis of NAS allows for timely initiation of treatments, including nonpharmacologic interventions such as swaddling and, in more severe cases, administration of narcotics, which are weaned over a period of days to mitigate signs of withdrawal, optimize feeding, and reduce the possibility of seizure activity.⁷ The consequences of a missed diagnosis and lack of treatment are significant. Affected newborns may fail to thrive, develop seizures, and experience respiratory compromise. Their extreme irritability also may prove challenging for caregivers, increasing the susceptibility to abuse and neglect.⁸

Signs of NAS may not appear until 72 hours after birth and can vary in intensity,⁹ not consistently related to the extent of maternal opioid exposure.³ A maternal history of narcotic use during pregnancy can alert providers to the risk of NAS in a newborn, but accurate information is inconsistently obtained at the time of delivery. Risk-based screening criteria are often applied to trigger maternal testing for opioid exposure¹⁰; however, this strategy might not be sufficiently robust to identify all newborns at risk for NAS, especially before discharge from the newborn nursery,¹¹ given the underreporting of maternal drug use.¹²

Considering the importance of prompt, accurate NAS diagnosis, we studied the efficacy of a universal testing protocol for all mothers delivering at a community hospital that has experienced a 3-fold increase in the prevalence of NAS over the past 5 years. We hypothesized that universal testing would identify

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NAS	Neonatal abstinence syndrome
SCN	Special care nursery
UDS9	Siemens 1650 enzyme immunoassay

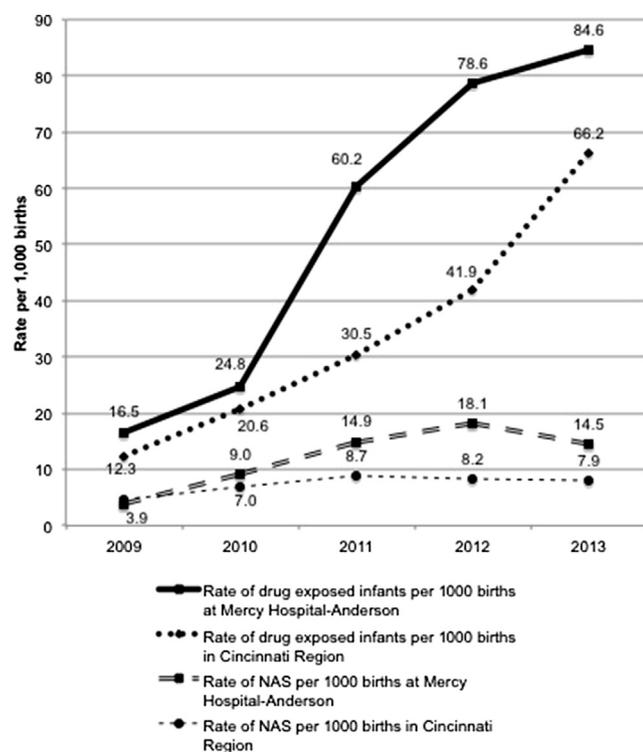


Figure. Rates of NAS and drug-exposed infants per 1000 births obtained from *International Classification of Diseases, Ninth Revision* codes 760.70, 760.71, 760.72, 760.73, 760.75, 760.77, and 779.5 at Mercy Anderson Hospital and the Cincinnati region (unpublished local data, Perinatal Institute, Cincinnati Children's Hospital Medical Center, November 2013).

opioid-exposed infants born to mothers who did not meet the criteria for urine drug testing under current risk-based assessment protocols.

Methods

We conducted a retrospective cohort study from May 2012 through November 2013 at Mercy Anderson Hospital, a community hospital in southwestern Ohio that serves the eastern Cincinnati metropolitan area. During the study period, the hospital cared for 2995 mothers for delivery of 2979 infants (with 38 intrauterine fetal deaths and 22 multiple births), of whom 95% were Caucasian, 52% were married, and 53% had private insurance. Hospital mother-infant services, including a level II nursery and high-risk maternity services, are provided through the Family Birth Center. Our query identified newborns born at Mercy Anderson Hospital with an *International Classification of Diseases, Ninth Revision* code of 760.70, 760.71, 760.72, 760.73, 760.75, 760.77, or 779.5. We used code 779.5 if the infant required pharmacologic treatment for NAS. Birth rates were calculated from data provided by the Hamilton County Public Health Department.

All mothers who delivered at the Family Birth Center during the study period were eligible for enrollment. The Mercy Anderson Hospital Institutional Review Board reviewed and approved the screening protocols. All data were collected through our review of the electronic health record. The hospital's Obstetrics Patient Safety Committee and Department of Risk Management were consulted regarding maternal consent for urine drug testing and determined that the general consent for care and treatment at admission was appropriate support for the institution of universal drug testing. Hospital-based risk management determined that the previously established screening policy promoted "profiling"; thus, universal maternal urine testing was deemed a preferable alternative.

Patient care staff explained the nature and rationale for urine drug testing to each patient admitted for labor or scheduled cesarean delivery. The discussion included information on how the test results would be used. Mothers had the opportunity to opt out of testing.

Current practice at Mercy Anderson Hospital and most newborn nurseries in the US limits nursery length of stay to <48 hours for an uncomplicated vaginal delivery and <72 hours for an uncomplicated cesarian delivery. Signs of NAS might not become evident until 48 hours after delivery, however. Our recent work demonstrated a mean onset of signs at 46.2 hours¹³; thus, we observed all infants exposed to opioids for a minimum of 72 hours in the hospital nursery, or a minimum of 96 hours total if methadone or buprenorphine exposure was identified. This is consistent with the current American Academy of Pediatrics guidelines for opioid exposure.¹⁴

Family Birth Center registered nurses documented Finnegan scores¹⁵ for infants with opioid-positive maternal tests within 24 hours of delivery. Those with a score of >8 on 3 occasions over a 24-hour period or a score of >12 on 2 occasions over a 24-hour period were admitted to the level II nursery for observation and treatment. Initial treatment included a nonpharmacologic bundle composed of swaddling, parental education, use of lactose-free formula when necessary, and decreased stimulation. For an infant with persistent high Finnegan scores, a methadone taper was initiated in the level II nursery.

Hospital-based social service providers conducted a discharge safety assessment for all women or infants with a positive toxicology test, as well as those who opted out. During this safety assessment, resources for addiction treatment programs were provided if appropriate. The social service safety assessment was not modified during the study period.

Standard neonatal care was maintained throughout the study period. This included neonatal urine and meconium drug testing if the mother had a positive drug test at the time of delivery that could not be explained by medications administered during labor and delivery. Standard practice also included submission of infant meconium for drug testing if maternal risk factors were present (Table I).

Urine testing was performed at the Mercy Anderson Hospital laboratory using a Siemens 1650 enzyme immunoassay

Table I. Maternal risk-based screen used at Mercy Anderson Hospital before universal testing

Documented, suspected, or acknowledged maternal history of drug use
 Insufficient prenatal care, defined as starting care after 12 weeks gestation
 Placental abruption
 Admission from a justice center
 Positive for HIV
 Positive for hepatitis B surface antigen
 Positive for hepatitis C virus
 Maternal history of gonorrhea or syphilis

(UDS9) (Siemens, Maryland Heights, Missouri), which detects 9 substances: amphetamines, barbiturates, benzodiazepine, cannabinoids, methadone, opiates, phencyclidine, propoxyphene, and cocaine metabolites. Meconium samples were sent to ARUP Laboratories (Salt Lake City, Utah). A second sample of meconium was tested for buprenorphine by US Drug Testing Laboratories (Des Plaines, Illinois) if exposure to this opiate was suspected on the basis of maternal history or interview.

We reviewed all maternal records with a positive urine drug test to identify a history or suspicion of drug use, insufficient prenatal care, placental abruption, sexually transmitted disease (ie, HIV, hepatitis B or C, gonorrhea, chlamydia, or syphilis), or admission from a justice center, which would have prompted urine testing using our previous screening guidelines. We reviewed the records of infants born to mothers who had a positive toxicology test. We evaluated for admission to the special care nursery (SCN) and for NAS treatment. Results of meconium tests were made available to hospital-based social service providers to facilitate risk assessment and discharge planning. Primary care providers were notified of these results, and the relevant county Child Protective Services agency was updated when necessary.

Statistical Analyses

Basic frequencies with percentages were calculated to describe the rate of opioid-exposure among mothers, as well as maternal risk factors for drug exposure. Sensitivity and specificity of the maternal risk factor screen for identifying maternal drug use (based on the urine drug test) were calculated with 95% CIs for proportions. Positive and negative predictive values of the maternal risk factor–based assessment were reported as well.

Results

During the study period (May 2012 through November 2013), there were 2995 maternal admissions. Hospital staff obtained 2956 urine drug tests; 38 tests were not done owing to precipitous delivery, emergent cesarean delivery, or inadvertent omission. One uninsured mother refused to provide a urine specimen for financial reasons. Among the 2956 specimens were 159 positive results, corresponding to 5.4% of the mothers. Of these 159 positive tests, 96 (60%) were positive for opioids, representing 3.2% of all maternity admis-

sions. Nineteen of the 96 opioid-positive urine tests (20%) occurred in mothers without screening risk factors. Seven of those infants (37%) required admission to the SCN, and 1 infant required pharmacologic treatment for worsening signs of NAS.

Seventy-seven infants were born to mothers with positive risk factors on the traditional risk screening (Table I) and had a positive urine drug test for opioids. Of those 77 infants, 44 (57%) required admission to the SCN for increasing Finnegan scores, and 20 (26%) required pharmacologic treatment for NAS.

In our study, 14 of the 2797 infants (0.5%) born to mothers with a negative urine drug test on admission required pharmacologic treatment for NAS. These included 7 mothers on buprenorphine for medication-assisted treatment, which is not detected on the UDS9. One mother delivered at home and did not undergo a urine test, and in another mother the test inadvertently was not obtained, but she had a history of opioid use during the pregnancy. The other 5 mothers had a positive drug test sometime during the pregnancy, but were negative on admission.

Eighty-five urine samples tested positive for substances other than opioids (ie, amphetamines, cocaine, marijuana, and benzodiazepines). Of those 85 mothers, 17 (24%) had negative risk-based screens. Multiple exposures were noted in 22 (14%) of the maternal UDS9 specimens. Thirty-six mothers had a positive drug test but negative risk-based screen, representing 1.2% of all maternal admissions (Table II).

In addition, during the study period, all infants with mothers with risk factors identified on admission or a positive toxicology result had a meconium specimen sent for MEC9 testing (same drug profile tested as UDS9), or MEC13 testing if buprenorphine was suspected. MEC13 tests for the same drugs as the MEC9 and UDS9, as well as oxycodone, meperidine, tramadol, and buprenorphine.

Of the 2995 admissions, 700 infants (23%) were born to mothers with risk factors for substance abuse. Of these 700 infants, 231 (30%) had positive toxicology results, corresponding to 7.7% of maternal admissions.

We calculated sensitivity, specificity, and positive and negative predictive values for maternal risk factors to identify a positive urine drug test for opioids and for any drugs (Table II). The traditional risk-based screening strategy yielded positive predictive values of 11% for detecting mothers who were positive for opioids and 17.6% for mothers who were positive for any drug. The sensitivity and specificity of this traditional screening strategy was

Table II. Maternal risk factors and association for a positive urine drug test

Variables	Positive for an opioid	Positive for any drug
Sensitivity, % (95% CI)	80.2 (72.2-88.2)	77.4 (70.9-83.9)
Specificity, % (95% CI)	78.2 (76.7-79.7)	79.4 (77.9-80.9)
Positive predictive value, % (95% CI)	11 (8.7-13.3)	17.6 (14.8-20.4)
Negative predictive value, % (95% CI)	99.2 (98.8-99.5)	98.4 (97.9-98.9)

80.2% and 78.2%, respectively, for detecting mothers positive for opioids, and 77.9% and 79.4% for detecting mothers positive for any drug.

Discussion

With the implementation of universal maternal drug testing, we identified 19 opioid-exposed infants who would have been missed with our previous screening approach. Owing to our standard of care of observing opioid-exposed infants for 72–96 hours, these 19 infants were prevented from premature discharge and possibly poor outcomes.⁸ We initiated Finnegan scoring earlier for infants with a positive maternal opioid drug test, and initiated the nonpharmacologic treatment bundle in affected infants. Seven of these 19 infants (37%) developed signs of NAS and required admission to the SCN for observation, and 1 infant required pharmacologic treatment. Thirty-five of the 2956 infants born during the 19-month study period required pharmacologic treatment for NAS. This rate is higher than the Cincinnati regional rate of 8.4 per 1000 births. Twenty of the 96 opioid-exposed infants whose mothers had a positive maternal opioid drug test on admission required pharmacologic treatment for NAS. This NAS rate among opioid-exposed infants is lower than that reported previously,^{1,2,14} and does not include mothers treated with buprenorphine; however, this rate may be more accurate, given that previous studies did not determine NAS risk in the context of universal testing. All positive results were communicated to the infants' primary care physicians to facilitate their follow-up care.

Universal drug testing meets the criteria for an appropriate screening tool established by Wilson and Jungner, and as updated by the World Health Organization in 2008.^{16,17} The objective is to identify infants with in utero opiate exposure. This testing addresses an important public health problem involving a large, vulnerable population for which treatment options exist. Early identification allows for a thorough safety assessment that includes education, and enables provision of additional clinical services. Urine testing is noninvasive and is easily collected routinely during pregnancy and labor. This testing should include informed consent¹⁰ with full confidentiality consistent with Health Insurance Portability and Accountability Act guidelines.¹⁸ The latent phase of NAS may delay the onset of signs until after hospital discharge. Early identification of infants by universal maternal drug testing can provide economic benefit¹⁹ by promoting earlier initiation of nonpharmacologic therapies, and can optimize care across the continuum from birth to the primary care setting.

We chose universal maternal testing over infant testing because results are available promptly, typically by the time the infant is delivered. Infants may only void once during the first 24 hours, delaying testing, and require special collection methods for obtaining the specimen. By testing mothers on admission to the hospital, we can also more reliably exclude iatrogenic exposure. Buprenorphine is now used by

some providers for medication-assisted treatment²⁰; thus, we recommend a urine drug-testing panel that includes buprenorphine. During our study period, 7 of the 35 infants (20%) who required pharmacologic treatment for NAS were exposed to buprenorphine. These mothers had a negative admission urine test, because the UDS9 cannot detect this substance.

Standard clinical obstetric management includes testing all maternal admissions for high-prevalence sexually transmitted diseases. Current rates for mothers delivering in Ohio for hepatitis B and syphilis are 2 and 1.5 per 1000, respectively (unpublished data, Ohio Department of Health), lower than the local NAS rate of 7.6 per 1000 births (Figure). It is also relevant to note that hepatitis C rates in Ohio now exceed those for hepatitis B.

In our single-center study, a traditional risk-based maternal screening strategy had a positive predictive value of only 11% for opioids and only 17.6% for all drugs. We also showed that traditional risk-based strategies have a low sensitivity and specificity for detecting maternal drug use (Table II). Our data also demonstrate that utilization of meconium testing with our risk-based approach generated a higher rate of detection than universal urine testing (7.7% vs 5.4%). Meconium testing will identify more exposed infants than urine testing, because it can detect remote maternal exposure up to 20 weeks before a term delivery²¹; however, the current 3- to 5-day turnaround from sample collection to receipt of results makes meconium testing impractical for identifying at-risk infants for NAS before discharge from the newborn nursery. In addition, this remote exposure information might not be relevant to nursery management.

Universal urine testing for opioids raises important ethical and social considerations. Mothers may find such testing intrusive, and may further fear investigation by local child protective services agencies, which have variable responses to positive test results,²² including potential criminal prosecution or loss of custody of the newborn. Testing for such conditions as sexually transmitted diseases, tuberculosis, and leprosy has raised similar concerns among specific populations during various historical periods.²³ A universal testing approach does not require that providers screen patients, an approach that could be considered discriminatory if perceived as targeting individuals with specific socioeconomic, geographic, or racial origins. Furthermore, concerns for universal testing must balance the imperative to optimize neonatal outcomes. The potential for infants to experience symptomatic withdrawal outside of the hospital can have severe consequences, such as seizures, which occur in 2%–11% of infants.²⁴

The proliferation of narcotic use and abuse warrants careful evaluation of a universal testing strategy. During our 19-month study period, 1.2% of births were positive for substances in mothers with no detectable risks. We believe that universal testing provides the opportunity to identify mothers and infants who would not be identified through risk-based screening. We also support the American College

of Obstetrics recommendation that patients be aware and consent for drug testing.¹⁰

The present study was limited to a single center. Expansion to multiple sites will further elucidate the strengths and limitations of universal urine testing for opioids. For example, our approach might not be effective in jurisdictions focused on criminal prosecution of opioid-positive mothers rather than on social support and treatment. We realize that universal testing will not influence the opioid epidemic, but this approach will help increase detection and define the magnitude of the problem. As with any screening test, there are limitations, such as the potential for false-positive and false-negative results. All results must be interpreted in the context of a comprehensive patient history and evaluation. Our study did not address neonatal outcomes beyond diagnosis, and we did not measure patient understanding, but all patients were given the opportunity to question and decline the testing. Future studies will further define the value of peripartum universal urine testing for women, their infants, and families. ■

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