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Universal Screening Programs for Gestational Exposures

Screening: Newborn, Gestational, and Perinatal

Since the discovery of phenylketonuria in the 1960s, newborn screenings have been a staple of perinatal care. The American Academy of Pediatrics and the American College of Medical Genetics recommend a core screening panel of 29 treatable congenital medical conditions.[1] In April 2013, the Secretary of Health and Human Services' Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children updated their recommendations to recommend screening for a total of 31 medical conditions.[2] Ultimately, neonatal screening is determined by state law.

See related article, p 582

Prenatal screening is an important part of obstetrical care, and is implemented with more variability than newborn screening. Recommendations for routine testing of all pregnancies includes both objective tests (eg, cultures for group B streptococcus, oral glucose challenge test for gestational diabetes, and antibody detection for HIV) and subjective self-report screening tools for high-risk behaviors, such as alcohol, tobacco, and drug use. The American College of Obstetricians and Gynecologists recommends routine interview-based screening for opioid and narcotic drug use during prenatal care.[3] Our comprehensive search did not yield any research literature indicating how often, and in what settings, prenatal opioid screenings are actually done. Maternal toxicology testing at delivery is generally not routine and used only in situations of high suspicion (ie, obvious perinatal intoxication).

In this issue of *The Journal*, Wexelblatt et al[4] report the use of a perinatal maternal urine test to achieve both a newborn and maternal screening, a "dual screening." These researchers have provided an opportunity to intervene on behalf of the newborn, and provide a safety net to identify women in need of addiction intervention, by the use of a single test. Similarly, universal newborn meconium screening has been suggested to provide a cost beneficial opportunity for early intervention in infants with fetal alcohol spectrum disorders, while also offering a chance to discuss alcohol cessation with identified mothers.[5,6]

An at-birth "dual-screening" approach may play an important role in treating or preventing harm attributable to occupational or environmental exposures, such as tobacco smoke, heavy metals, or pesticides to which a woman may not know she has been exposed.[7] Researchers have successfully used umbilical cord blood, meconium, placenta, and maternal blood to test for heavy metals,[8,9] environmental tobacco smoke,[7] and pesticides.[10] Perinatal biomarker testing could provide a logistically simpler avenue to remove mothers and infants from sources of exposure to prevent further damage, start early monitoring of the infant for signs of developmental delay, and prevent future affected pregnancies.

Maternal Self-Report and the Need for Biomarkers

Fear of legal repercussions prevents women from disclosing complete information about alcohol and drug use during pregnancy.[11] Historically, medical professionals have obtained court orders at times when fetal health is at odds with maternal choices. Medical staff have ordered mandatory detention for gestational diabetes treatment, intrauterine

LBW	Low birth weight infants
NAS	Narcotic abstinence syndrome
NBW	Normal birth weight infants
VLBW	Very low birth weight infants

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blood transfusions, and cesarean deliveries.[12] Women have been charged with child endangerment for prenatal alcohol exposure and, in at least one case, homicide after a stillbirth because of prenatal cocaine exposure.[13]

Maternal self-report of substance abuse remains a concern. In a recent study, as few as one-third of drug test-positive pregnant adolescents self-reported their drug use.[14] Wexelblatt et al similarly found that 20% of test-positive mothers would have been missed under the traditional screening protocol, though that protocol did not rely solely on self-report.[4] Nevertheless, the unique moral situation of maternal risk behaviors (especially smoking, alcohol use, and drug abuse) makes universal biomarker testing increasingly useful in measuring under-reported exposures.

Screening: Targeted vs Universal

Targeted screening for drug and alcohol use has been implemented with limited success. In one well-recognized initiative in the early 1990s, the Medical University of South Carolina adopted a program requiring prenatal maternal drug counseling and threatening legal action against those who failed to comply. Women were selected for screening based on a number of factors, including, but not limited to, absence of prenatal care, unexplained intrauterine growth retardation, and previous self-report of drug use.[15] Between 1989 and 1994, 42 women were arrested under a range of charges that depended on the status of the pregnancy or birth. The program was eventually discontinued after a number of concerns were raised.

The primary argument in favor of targeted gestational screening is cost control. Universal intervention and follow-up is expensive. Targeted screening aims to devote resources where they are statistically most likely to be needed. In contrast, universal platforms, although more expensive, prevent profiling of disparate populations. The targeted structure of the South Carolina program affected a disproportionate number of poor African-American women. Indeed, demographic evidence suggests that drug abuse during pregnancy spans socioeconomic status and racial groups, though low-income women of color are the most likely to be reported to social workers and child protective services for drug use.[16,17]

To Screen or Not to Screen: Considering the Pros and Cons

Screening is considered ethically appropriate for conditions for which there are available treatments,[1] and perinatal opioid screening allows for readily available early intervention for narcotic abstinence syndrome (NAS) in the infant. Wexelblatt et al[4] suggest that prompt diagnosis of NAS expedites interventions such as swaddling and pharmacotherapy, and prevents complications of withdrawal, such as failure to thrive, seizures, respiratory compromise, and extreme irritability. Financial cost:benefit would be useful in this setting. Adequate research literature is needed to identify long-term sequelae of NAS[18] and the financial cost savings of early intervention.

False positive biomarker tests are problematic. Beyond the cost of implementing the test, false positive follow-up costs clog the schedules of social workers, pediatricians, and other specialists with unnecessary referrals, generating "opportunity cost" (ie, lost time). The emotional burden of being incorrectly identified as a drug user or a person in a toxic environment opens up mothers to loss of employment, for example, if medical records are turned over for a workplace physical or if the workplace is identified as the toxic environment. More systemically, false positives may introduce mistrust in the patient–doctor relationship. Hospitals may be vulnerable to lawsuits claiming malpractice or emotional damage. Likewise, false negative tests results also represent a missed opportunity to treat.

Increasing the sensitivity and specificity of biomarkers is an important direction for future research. One strategy to reduce false positives is creative, cost-effective second-tier screens. In addition to refining laboratory techniques, second-tier screens such as cranial ultrasound, in-depth patient interview, or behavioral assessment might help provide context for indeterminate results. The combination of biomarker and self-report has been shown to improve ascertainment of exposure status. In one study, maternal self-report provided an estimated prevalence of exposure to cocaine of 13.9% in very low birth weight infants (VLBW), 16.4% in low birth weight infants (LBW), and 5.3% normal birth weight infants (NBW). Results from the meconium analysis yielded prevalence rates of 9.2% (VLBW), 16.7% (LBW), and 5.6% (NBW). Using both the self-report data and the meconium results, the prevalence rates were 18.6% for VLBW infants, 21.1% for LBW infants, and 7.8% for NBW infants.[19] Biomarker testing, when incorporated with history taking and routine care, can help complete an accurate assessment of health status.

Close consideration of ethics of universal screening policies is recommended. As we risk alienating women who fear repercussions, mothers must be assured that screenings are not to be used punitively. In practice, this involves training a multi-disciplinary team to implement screening protocols in a non-judgmental, supportive environment, where follow-up is closely monitored. With careful implementation, research on universal gestational screening has profound implications for the management of neonatal abstinence syndrome in newborns, opioid abuse in childbearing women, and potentially for all known or unknown exposures to the mother and fetus. ■

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Are We Doing Right by Dying Children?

In this issue of *The Journal*, Ragsdale et al present the first available large scale overview of clinical practice in providing opioids and sedation at end-of-life for children who die in the hospital.[1] Previously published data on this important topic is sparse, mostly based on experiences at single institutions with small sample sizes. In contrast, Ragsdale et al utilized large administrative data sources to analyze information from 37 459 children dying at 430 hospitals across the US. Retrospective analyses of such large population-level data sets have many limitations but serve the important purpose of generating new hypotheses and honing research questions for future studies.

See related article, p 587

Dying children have a high symptom burden in the last week of life regardless of their underlying disease process,[2] and inadequately treated symptoms are highly distressing to the child, parents, and caregivers. The most prevalent symptoms at end-of-life are pain and dyspnea, and thus opioids and sedatives are among the most important pharmacologic interventions provided. It is of concern, therefore, that 26% of patients in the authors' analysis were not exposed to any opioid or sedative in the days prior to their death. The authors appropriately indicate that their lack of clinical data precludes any conclusions about the adequacy or inadequacy of treatment. They hypothesize that some portion of these children died suddenly of unexpected causes, precluding assessment of the need for pain and symptom management. A separate population who would be very unlikely to receive opioids or sedatives prior to death is the cohort of children with brain death. Burns et al recently published a prospective case series of the epidemiology of deaths in the pediatric intensive care unit (PICU) at five US teaching hospitals, 16% of whom were declared brain dead.[3] As these patients had lost all brain function, they were also unable to perceive or experience pain or any other uncomfortable

PICU	Pediatric intensive care unit

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