

Neonatal Abstinence Syndrome: A Challenge for Medical Providers, Mothers, and Society

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Maternal use of opioids and other substances, the primary cause of neonatal abstinence syndrome (NAS), is a leading cause of medical and developmental problems in the newborn. Substance

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use by pregnant women is also accompanied by medical, legal, and economic consequences for the mother. Substance abuse during pregnancy and consequent NAS in infants is a costly and significant clinical and social problem reaching epidemic proportions in the United States.¹ In this issue of the *Journal of Pediatric Pharmacology and Therapeutics*, Siu and Robinson² provide a timely review of NAS and the current treatments used by most neonatal intensive care units. Although we must continue to study and refine the therapy for NAS, the challenges for the medical provider, mother, and society merit further discussion.

Desai and colleagues³ recently published a report of prescription opioid use that evaluated prescribing trends in a large sample of Medicaid-enrolled pregnant women. Data from 46 states found that 21.6% of women filled at least one prescription for an opioid during pregnancy, which represents a 17.2% increase between 2000 and 2007. They described significant regional distribution of opioid prescriptions across states, ranging from 9.5% to 41.6%. The states with the highest rate of opioid prescriptions were Utah (41.6%), Idaho (35.6%), New Hampshire (34.4%), Wyoming (34.1%), and Tennessee (33.6%). During a similar time period (2000-2009), Patrick and colleagues¹ described a 3-fold increase in the incidence of NAS and the associated clinical and financial burden.

Why has this increase occurred in this population once protected so strongly? Although the use of illicit opioids is still present, most of the increase seen is in the use of prescribed opioids and diverted prescription medications. During 2013, there were 855 cases of NAS in Tennessee, of which 547 (64%) were from the eastern part of the state.⁴ As of May 31, 2014, there have been 386 cases reported, with 222 from East Tennessee.⁵ Of the total cases of NAS, 51.8% are from a supervised medication-assisted treatment program (i.e., methadone or buprenorphine), 42% are from the use of prescribed opioids *without* a prescription, and only 23.8% are from the use of illicit drugs. Some overlap is noted because some pregnant women supplement methadone or buprenorphine obtained through a medication-assisted treatment program with illegally obtained substances.

The pharmacotherapy of NAS has continued to be refined over the years. Although many neonatal intensive care units used paregoric and tincture of opium, these practices are discouraged because of other ingredients in paregoric and the risk of medication errors associated with tincture of opium.^{6,7} Although morphine and methadone remain the standard treatment for NAS, there is increased interest in and research being conducted with buprenorphine.⁸ Studies are now focusing on the choice of drug and different methods of administration in order to provide effective relief of symptoms for the infant while striving to shorten the length of stay (LOS) in the hospital. Pharmacists must continue to be part of this research and refinement of treatment protocols while evaluating the role of adjunctive

therapies, such as clonidine and phenobarbital. We must also be cognizant of research being pursued with alternative drugs, like chloral hydrate and chlorpromazine.^{9,10}

NAS is an identifiable and treatable condition. However, many mothers do not self-disclose drug use during pregnancy because of the significant stigma associated with the disease of addiction.¹¹ Stigma presents a significant barrier to treatment during the time of pregnancy because women who feel guilt and shame about their addiction tend to have difficulty seeking and accessing appropriate treatment.¹¹ When women with addiction do reach out to health care professionals, they often encounter misinformation, denial, inaction, and even judgmental and punitive attitudes toward their substance use.¹²

In states with high levels of opioid abuse, societal anxiety over NAS is leading to legislation that could result in legal or civil penalties for women who use drugs or participate in drug treatment programs during pregnancy. Currently, 17 states treat drug exposure at delivery as a form of civil child abuse. Most recently, Tennessee enacted a law that allows women to be criminally charged with an assaultive offense for the illegal use of a controlled substance while pregnant if her child is born dependent upon or harmed by the controlled substance, or with criminal homicide if her child dies as a result of her illegal use of a substance taken while pregnant. Proponents of the law see it as a way to force more women into substance abuse treatment through the drug court system, whereas opponents fear increased stigmatization and criminalization of patients with the chronic, relapsing disease of addiction. Tennessee also has a "Safe Harbor" law enacted in 2013 for addicted pregnant women that encourages treatment and protects parental rights. Health care providers are challenged on how to answer questions from patients and appropriately direct addicted pregnant women for care because of the conflict noted in these legislative initiatives. To further complicate matters, appropriate treatment resources for addiction during pregnancy are often lacking.

NAS has traditionally focused on symptoms of withdrawal attributed to opioid use by the mother. As Siu and Robinson² note, substances such as nicotine, alcohol, and other prescription medications, such as benzodiazepines and antidepressants, often cause or exacerbate NAS. It is

important to remember that most women with addiction suffer from a psychiatric disorder, such as a mood or anxiety disorder. Many are exposed to trauma early in life from sexual, physical, or emotional abuse. These conditions often require management with psychotropic agents. Medical providers play an important role in determining the action of each medication prescribed to the pregnant woman in terms of what is to be expected in terms of neonatal withdrawal.

Future directions in NAS research must address the need for clinical trials of new medications to establish optimal protocols for maternal opioid dependence. Early identification and aggressive treatment of NAS may help to decrease severity and LOS. As noted by Siu and Robinson² in their review, mothers with addiction should be encouraged to breast-feed. Breast-feeding may reduce the treatment rate of NAS and shorten LOS. Indications of fetal-neonatal dependence and risk of NAS are emerging from studies of placental transfer of opioids and other medications during gestation; the relationship of maternal opioid dose changes during pregnancy; infant pharmacogenomics; and the evaluation of meconium metabolites to determine exposure to other substances during gestation.¹² In addition, validation of a simplified scoring tool for NAS and exploring options for home management of NAS are needed.² These additional data will help lead to better postnatal care of infants with NAS while decreasing LOS in the hospital and overall financial costs to society.

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Abbreviations LOS, length of stay; NAS, neonatal abstinence syndrome

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