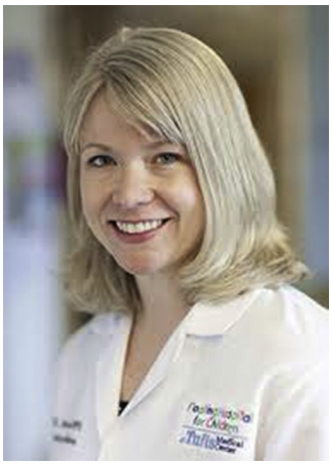
Editorial

Finding Hope: Clinical Strategies to Combat the Devastating Impact of the Opioid Epidemic on our Youth



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Addiction to opioids has become a global public health threat that does not discriminate based on sex, socioeconomic status, race, ethnicity, or age. In recent years, there has been an exponential increase in opioid overdoses and drug-related deaths. According to the National Institute on Drug Abuse, in 2017 > 70,200 Americans died of drug overdoses, including >17,000 deaths that involved prescription drugs.[1] These sobering statistics equate to a 2-fold increase in drug-related deaths in the United States in the past decade alone.[1] Tragically, children have not been spared from this epidemic. Gaither et al[2] recently reported that between 1999 and 2016 the pediatric mortality rate from prescription and illicit opioid poisonings increased by 268.2%. These deaths were not limited to the adolescent population, but rather spanned the pediatric age spectrum from 0 to 18 years.[2] Effects of opioids on the health of our children may start as early as in utero and continue through adolescence with devastating and often unmitigated effects of addiction. Compounding these effects are the multigenerational and transgenerational consequences of drug exposure. Parental drug exposure produces behavioral, biochemical, and neuroanatomic changes in future generations through a combination of genetic, epigenetic, and environmental influences that results in a vicious cycle of chronic drug abuse.[3] In this Specialty Update, we consider the impact of opioids throughout the pediatric age spectrum—from fetuses to teenagers—and present new therapeutic and treatment strategies aimed at reducing the burden of drug addiction and improving the health outcomes of our youth.

In 2016, 1 in 5 women of reproductive age filled at least 1 prescription for an opioid, and an estimated 15.3% of women reported the misuse of prescription drugs or illicit drug use.[4] As a result, an estimated 32,000 babies are born in the United States each year with neonatal abstinence syndrome (NAS), now commonly referred to as neonatal opioid withdrawal syndrome. These numbers equate to an infant being born every 15 min in the United States addicted to opioids, a greater than 5-fold increase since 2004, and result in medical costs of US$563 million per year.[4] The long-term effects of these narcotics on the developing fetal brain remain largely unknown.[5] Most adults exposed to illicit drugs in utero may be physically healthy, but data suggest that vulnerability to health and neurocognitive issues are pervasive and long lasting.[6]

Perhaps the optimal strategy to reduce drug exposure in infants is to limit drug use in pregnant women. It is well known that abrupt cessation of narcotics during pregnancy poses significant health threats for both mother and fetus.[7] Thus, strategies to engage mothers in treatment programs during pregnancy, along with the development of new treatment agents, are a priority. The pure opioid antagonist, naltrexone, is currently used by 11% of young adults with opioid use disorders.[8] To date, the safety profile and efficacy of this drug in pregnant women are unknown. In a single-center, retrospective analysis that compared pregnancy outcomes in women treated with buprenorphine versus naltrexone, Wachman et al[8] are the first to report that, although 92% of the infants born to women treated with buprenorphine experienced NAS, no infant born to mothers treated with naltrexone required treatment for withdrawal symptoms. Although this pilot study found no immediate perinatal complications for mothers or their infants, it highlights the need for prospective, randomized case–control clinical trials to further

understand the potential positive impact that new treatment strategies in pregnant mothers may have on offspring. Optimizing treatment strategies during pregnancy, combined with management after delivery of exposed newborns, are the first steps in alleviating the burden of opioid addiction in children.

Reflecting on one institution's strategies to improve care provided to infants addicted to opioids, Minear and Wachman[9] highlight Boston Medical Center's (Boston, Mass) new 6-tiered clinical approach to treating NAS. Boston Medical Center tackled the impact of the opioid epidemic on newborns in their city through nonpharmacologic approaches, the integration of round-the-clock cuddler volunteers, improved prenatal parental education along with increased parental contact after delivery, and by limiting treatment of infants with narcotics to periods when they cannot eat, sleep, and be consoled while prioritizing treatment with methadone over morphine. This collaborative, multidisciplinary quality improvement initiative resulted in reduced pharmacotherapy treatment for NAS from 85.7% to 42.7% with a dramatic reduction in adjunct therapy (ie, clonidine or phenobarbital) from 34% to 2%. Further, the hospital saw a reduction in length of stay from 18.4 to 10.4 days in infants exposed to narcotics in utero.[9]

In an accompanying report, Squillaro et al[10] address new pain management in neonates. Although it is essential to optimize pain control in this population, it is equally important to minimize oversedation and to limit opioid exposure. With the use of various pharmacologic strategies, including the use of nonopioid medications, local and regional anesthesia, and nonpharmacologic alternatives, their group found that caregivers can "optimize periprocedural comfort and minimize the negative sequelae of uncontrolled pain in the neonate."[10] These clinical care approaches are vital to improving the health outcomes of newborns undergoing surgical and/or painful procedures. As McLaughlin et al[11] report in one of the largest analyses to date that explored perioperative opioid use for infants undergoing pyloromyotomy, there is huge site-to-site variation in opioid pain management. Exploring data from >25,000 infants who underwent pyloromyotomy, the investigators report that receiving opioids on the day of surgery resulted in decreased odds of prolonged hospital stay, whereas receiving opioids on both the day of surgery and postoperatively increased the odds of a prolonged hospitalization.[11] This report highlights the need to consider standardization of opioid pain therapy in infants and young children and to optimize the timing of drug delivery.

Although a focus of this issue centers on perinatal opioid exposure and treatment, the effects of opioids on adolescents are equally as devastating. The Centers for Disease Control and Prevention reports that the death rate due to drug overdose among adolescents aged 15−19 years more than doubled from 1999 to 2007, declined by 26% from 2007 to 2014, only to increase again by 2015.[12] Most of these deaths are unintentional. Describing her own personal interactions with treating adolescents and young adults with opioid dependence, Dr. Laura Grubb[13] shines a light on the real challenges limiting access to medication-assisted treatment programs and active recovery in teenagers with opioid use disorders. Personal and socioeconomic barriers, including homelessness, limited access to medication-assisted treatment care programs, transportation, insurance barriers, stigma, and scarce resources, are affecting the ability to get addicted teens healthy. Although the solutions to these problems are complex, Dr. Grubb lays forth a compelling step-by-step guideline to improve treatment strategies.

As Erin Winstanley[14] writes in this issue of the *Journal*, "an epidemic of opioid-related overdose deaths have continued to increase in the United States for the past two decades, yet its impact on children is rarely mentioned in national discussions or policy initiatives." Children who grow up in households with opioid abuse are at increased risk of mental health problems, drug addiction, accidental poisonings, foster care placement, and parental death due to overdose.[14] This Specialty Update aims to bring to the forefront the strong need to address this epidemic in our youth, describe successful intervention programs to limit opioid exposure in our newborns, and discuss the social determinants that affect drug treatment and recovery in our adolescents. Marginalizing our children in the opioid epidemic only ensures continued abuse and multigenerational addiction. We must strive to limit opioid exposure, beginning at conception, and develop nonpharmacologic approaches to reduce or eliminate opioid treatment in infants altogether. We must not only empower our teens to "just say no" to drugs of abuse, but we must also provide

access to treatment, reduce the stigma associated with drug addiction, and address the personal and socioeconomic barriers to care. Only then can we provide hope for the next generation.

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