

VIEWPOINT

Perinatal Marijuana Use and the Developing Child

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Increasing public attention has recently been paid to the opioid epidemic and attendant effects on prenatally exposed infants and children.¹ Current literature has emerged proposing marijuana as a safe alternative to opioids in addressing pain² and cannabis legalization as a way to decrease opioid fatalities.³ As a result, perceptions of cannabis safety have increased, and the prevalence of marijuana use among pregnant women has expanded; past-month cannabis use among pregnant US women increased from 2.4% to 3.9% between 2002 and 2014.⁴ Further, cannabis potency has been substantially increasing over the past 4 decades in the United States, and will likely continue to do so as extraction procedures of active components improve.

Although cannabis does have known medical utility for some conditions, its associated acute and long-term psychoactive effects on brain function are also known. Expanding use of cannabis among pregnant and lactating women (as likely will occur with legalization) may lead to increased risk from fetal and child exposures if the teratogenic potential of cannabis remains underappreciated.

Delta-9-tetrahydrocannabinol (THC), the major psychoactive component of marijuana (1 of more than 500 components, 104 of which are cannabinoids), crosses the placental barrier readily. Accumulating evidence in animals and humans indicates that prenatal

related regions of the brain (eg, the nucleus accumbens, amygdala, and cortical areas), potentially altering their functioning in postnatal life and introducing epigenetic alterations with consequences for transgenerational offspring. Because endocannabinoids dynamically regulate fetal development, the timing and duration of prenatal exposure (eg, first or second vs third trimester) may have differential effects and long-term consequences. Studies are needed to characterize common patterns of cannabis use during stages of pregnancy and their subsequent effects on fetal neural development.

Prenatal THC exposure has been documented to adversely affect infant neurobehavior and child development up through the teen years,⁵ and postnatal exposures may compound prenatally acquired deficits. Neurobehavioral effects associated with prenatal THC exposure range from dysregulated arousal and motor difficulties at birth to disturbed sleep, memory impairment, aggression, and other developmental and behavioral concerns in childhood.⁵

As cannabis potency and maternal use continue to increase, it will be critical to systematically evaluate the long-term outcomes of THC-exposed individuals, inform breastfeeding guidelines, and identify interventions to manage resultant developmental, psychiatric, and behavioral effects at different developmental stages among THC-exposed individuals.

The influence of perinatal THC exposure on the developing fetus and infant can be amplified among mothers with cannabis use disorder (CUD). The *DSM-5* characterizes CUD as significant impairment due to the inability to control cannabis use despite negative consequences, spending inordinate amounts of time using or procuring can-

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exposure may be related to harm for the developing fetus and child.⁵ THC exposure can adversely affect the developing fetal endocannabinoid system. Endocannabinoid receptors form very early in fetal life (ie, at 14 weeks' gestation) and have critical functions in fetal and postnatal brain development, neuronal connectivity, and glial cell differentiation. Endocannabinoids are important neuromodulators of multiple central neurotransmitter systems that are essential for fetal brain development, and optimal outcomes rely on normal physiologic activity at cannabinoid receptors. The exogenous supply of cannabinoids resulting from THC exposure can adversely affect fetal growth as well as structural and functional neurodevelopment.⁶

Prenatal THC exposure can modify not only the endocannabinoid system, but also can affect the maturation of dopamine, opioid, glutamate, and GABAergic neurotransmitter systems in key reward- and stress-

nabis, tolerance (such that increasing amounts of drug are required to achieve intoxication), and withdrawal symptoms during cessation of use. All of these symptoms can adversely affect a mother's ability to care for a child. Short-term effects of CUD, such as impairments in attention, judgment, and coordination, can affect child development and safety. Longer-term effects of maternal THC use, such as depression, high-risk behaviors, impaired executive functioning, and an increased risk of psychiatric comorbidity, could further adversely affect the well-being and development of children. Efforts to reduce and discourage cannabis use during pregnancy and breastfeeding are further complicated by cannabis withdrawal symptoms (including irritability, anxiety, insomnia, appetite loss, and depressed mood), which can be major deterrents to abstinence and relapse prevention.

The extent to which cannabis-using mothers also engage in additional substance use (eg, opioids,

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nicotine, alcohol) remains unknown. It is imperative to characterize the prevalence of prenatal CUD and CUD/polysubstance use among pregnant and lactating women to better predict fetal/child outcomes and inform intervention efforts for both the mother and child.

Despite these risks, it appears that clinicians are not addressing cannabis use during pregnancy or lactation; in one study of 74 lactation professionals, 85% encouraged breastfeeding among marijuana-using mothers.⁷ Most national breastfeeding guidelines (eg, the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists) have remained steadfast in recommending against cannabis use during lactation. However, the Academy of Breastfeeding Medicine has changed guidelines (2009 and 2015) to allow the potential use of cannabis during lactation, citing "data...not strong enough to recommend not breastfeeding with any marijuana use" despite urging caution due to "possible long-term neurobehavioral effects."⁸

The medical community should advise pregnant women to avoid perinatal THC exposure and intervene for women needing treatment, for children at risk for neurobiological and developmental problems, or for dyads at risk for negative outcomes associated with an untreated substance use disorder. Advice from medical professionals should be consistent: pregnant and lactating women should be advised to avoid cannabis use, and women (and men) caring for developing children also should be advised to maintain abstinence. Treatment programs for women with CUD should be available and accessible, and gender and culturally specific, particularly during pregnancy and postpartum periods. Converging, systematic research is necessary at both the preclinical and clinical levels to address insufficient evidence regarding maternal cannabis use⁹ and to fully understand the short- and long-term effects of perinatal THC exposure, the effects of maternal cannabis use on fetal outcomes, and the consequences of polysubstance use in treatment and intervention efforts.

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