Editor's key points

- In utero exposure to cannabis has been associated with long-term neurodevelopmental outcomes that persist into young adulthood. Pregnant women should be counseled regarding these risks and encouraged to abstain from use.
- Maternal risks of cannabis use are related to the mode of ingestion and its addictive potential. Harm reduction options should be offered to those not able to quit completely.
- The relationship between cannabis and nausea in pregnancy is complex and remains poorly defined. While women using it in pregnancy often find it effective, chronic use might be associated with cannabinoid hyperemesis syndrome, a condition characterized by episodes of acute abdominal pain, nausea, and vomiting. There are other safe and effective treatments for nausea and vomiting that should be used first line.
- Tetrahydrocannabinol is excreted in human breast milk. Human data have suggested possible impaired infant motor development at 1 year in children exposed to cannabis while breastfeeding; however, these data are limited.

Cannabis use during pregnancy and postpartum

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Abstract

Objective To help obstetric care providers, including family physicians, nurse practitioners, midwives, and obstetricians, educate patients on the risks of cannabis use in pregnancy and postpartum and its relationship to nausea and vomiting in pregnancy.

Sources of information The Ovid MEDLINE database was searched using the MeSH terms *pregnancy, cannabis, lactation,* and *cannabinoid hyperemesis* in various combinations. The relevant articles were reviewed and further sources were found within the references of these articles.

Main message In utero exposure to cannabis has been associated with long-term neurodevelopmental outcomes that persist into young adulthood. Cannabis should not be used to treat nausea and vomiting in pregnancy and its chronic use might lead to the development of cannabinoid hyperemesis syndrome.

Conclusion There is no known safe level of cannabis use during pregnancy or lactation. Pregnant women should be counseled regarding the risks of in utero exposure and encouraged to abstain from use in pregnancy and while breastfeeding.

As cannabis has been legalized in Canada, and increasingly is being legalized worldwide, our lack of information regarding its safety in the pregnant and lactating population has become apparent.

Cannabis is the most commonly used illicit drug during pregnancy.[1] Self-reported rates of use in pregnancy are 2% to 5%; however, these likely represent an underestimate. In one study exploring the outcomes of prenatal cannabis and alcohol exposure on academic achievement, Goldschmidt et al[2] reported on the frequency of concurrent cannabis and alcohol use during pregnancy. In their study, 14% of women reported heavy use of cannabis (ie, smoking 1 or more joints per day) during the first trimester of pregnancy, compared with 5.3% and 5.0% during the second and third trimesters of pregnancy, respectively. Risk factors for continued use include single or unmarried status, lower income, less education, or a partner who also uses cannabis.[1,3] Women using cannabis in pregnancy are more likely to use alcohol, tobacco, and illicit drugs, which might have additive or synergistic effects.[1,4] At the same time, studies have demonstrated that cannabinoids readily cross the placenta[5] and appear in human breast milk,[6] resulting in fetal and neonatal exposure.

Case description

Julie is a 23-year-old nulliparous woman who is currently at 18 weeks' gestation. Her pregnancy has been uncomplicated to date. She presents to your office with an urgent concern of diffuse abdominal pain and intractable nausea and vomiting. Findings of investigations, including bloodwork and imaging, are unremarkable. On history she admits to increasing cannabis use during the past week to mediate worsening symptoms of "morning sickness." Nausea and vomiting were not an issue in her first trimester. You wonder whether her cannabis use is contributing to the overall clinical picture.

Sources of information

The Ovid MEDLINE database was searched using the MeSH words *pregnancy, cannabis, lactation,* and *cannabinoid hyperemesis* in various combinations. The relevant articles were reviewed and further sources were found within the references of these articles. This is not a complete systematic review of the literature; instead, this is meant to be a clinical review of relevant articles to date.

Main message

Within the literature there is an overall lack of good-quality research on cannabis use in pregnancy and postpartum. For obvious reasons, there are no randomized controlled trials on cannabis use in pregnancy, and many studies do not exclude or control for polysubstance use. A reliance on self-reported measures might underestimate the prevalence of drug use in pregnancy, and the rising tetrahydrocannabinol (THC) potency in cannabis products during the past decade might act as a confounder. Finally, pregnant women who use cannabis are more likely to be underweight, have less education, and have a lower household income, and are less likely to take folic acid, compared with nonusers.[7,8]

Worthy of note, there are 3 important prospective longitudinal cohort studies that are ongoing and have provided some insight into both short-term and long-term effects of in utero exposure to cannabis products (**Table 1**[1,2,9-11]): the Ottawa Prenatal Prospective Study (OPPS),[9] the Maternal Health Practices and Child Development (MHPCD) study,[2,10] and Generation R (GenR).[1,11] These studies all recruited women who were pregnant and have followed their children into early childhood (GenR), adolescence (MHPCD), and early adulthood (OPPS). They all controlled for sex, ethnicity, home environment, maternal socioeconomic status, prenatal alcohol and tobacco exposure, and current maternal substance use. A summary of their findings can be found in **Table 2**.[1,2,9-11]

Neonatal outcomes. Proposed neonatal outcomes of in utero cannabis exposure include lower birth weight and long-term neurologic sequelae.[12]

Birth weight: A large number of studies on cannabis use in pregnancy focus on fetal growth. Results are mixed, with some studies showing lower birth weights and others showing no effect. Of the large prospective studies, GenR alone showed a statistically significant decrease in birth weight associated with cannabis use while controlling for tobacco smoking. This result was dose dependent, with those continuing to use cannabis throughout pregnancy showing a mean reduction in birth weight of 277 g compared with 156 g in those who only used it in early pregnancy.[11,13] A recent meta-analysis by Gunn et al showed a pooled mean difference for birth weight of 100 g, which is similar to previous estimates.[14] There is debate as to whether this represents a clinically meaningful difference, but it certainly identifies a fetal effect. Others have proposed that with increasing THC potency over time, we might see a greater magnitude of difference between users and nonusers.[11]

Neurodevelopment: Probably the greatest contribution that the OPPS, MHPCD, and GenR studies have provided is information on the effects of cannabis on neurodevelopment and mental health. In utero exposure to marijuana has been linked to a "withdrawal"-like syndrome in newborns, demonstrated by an increase in startles and tremors and reduced habituation to light.[15] In the GenR population, increased aggressive behaviour and attention deficits were seen as early as at 18 months.[15,16] By preschool age, difficulties with verbal and visual reasoning, hyperactivity, attention deficits, and impulsivity became apparent in both the OPPS and the MHPCD populations and persisted throughout the school years.[15,17] At age 10, depressive and anxious symptoms became apparent and were found to predict earlier cannabis use and poorer adolescent and early adult achievement.[2,10,18-22]

While these findings suggest that marijuana is not without potential harm, these studies are limited in terms of their ability to control for several environmental and socioeconomic factors. Furthermore, some findings were not reliably reproduced between the cohort studies, suggesting a complex relationship between the effects of marijuana on neurodevelopment. For example, in the OPPS and MHPCD studies, the preschool population was found to have lower scores on memory and verbal reasoning testing, a finding not reproduced by the GenR study.[15,17] Further information and clarity on the effects of cannabis on the developing brain will require future study, but at this time, it does not appear that cannabis use in pregnancy portends a specific phenotype that can be reliably reproduced.

Maternal risks. Maternal risks of marijuana use are related to the mode of ingestion and its addictive potential. Approximately 8% of people who try marijuana will develop cannabis dependence.[13] Cannabis use disorder, like other substance use disorders, is characterized by impaired control, social difficulties, risky use, tolerance, and withdrawal as defined by the *Diagnostic and Statistical Manual of Mental Disorders,* 5th edition. Treatment programs are limited and no single method has been proven superior. That being said, any treatment appears to be better than none, and where outpatient treatment programs are available, they should be used.[23] No pharmacotherapy has been shown to be effective at mitigating withdrawal symptoms other than THC replacement.[13] Harm reduction options include using vaporizers or edibles instead of smoking (reducing the maternal carcinogenic risk, but not risk to the fetus), avoiding smoking indoors and around children, and using prescribed tapering doses of a synthetic cannabinoid.[13]

Table 1. Comparison of characteristics of 3 important prospective longitudinal studies

CHARACTERISTIC	OPPS[9]	MHPCD[2,10]	GENERATION R[1,11]
Year study began	1978	1982	2001
Population	Caucasian, primarily middle class	Largely African American (57%) and single (71%), with low SES	Multiethnic cohort; slightly higher SES compared with nonresponders or incomplete responders
Recruitment	Self-referral for study participation based on posters in prenatal clinics and information from prenatal providers	Actively recruited from an inner-city prenatal clinic in the 4th or 5th mo of pregnancy	Enrolled based on residence in the study area with a due date during recruitment. Recruited from early pregnancy until birth
Cannabis-exposed population and total sample size, n/N	78/698	307/763	220/7531
Polysubstance use	Yes: tobacco (21%) and alcohol (76%)	Yes: alcohol (65%), tobacco (53%), cocaine (3.6%), and other illicit drugs (8.6%)	Yes: alcohol (31%), tobacco (39%), and other substances (4.5%)
Method of data collection to determine cannabis use	Repeated interviews largely within each woman's home by the same trained, female interviewer for each interview	Standardized interviews	Self-reported questionnaires
Categorization of cannabis exposure	Nonuser, light user (≤ 1 joints/wk), moderate user (2-5 joints/wk), or heavy user (> 5 joints/wk)	Based on ADJ: light (0-0.4 ADJ), moderate (0.5-1 ADJ), or heavy (> 1 ADJ) use	Nonuse, occasional (monthly), moderate (weekly), or heavy (daily) use
Cannabis use measured	Each trimester	First, second, and third trimester, and 8 mo, 18 mo, and 36 mo postpartum	Prepregnancy, early pregnancy, and late pregnancy
Retention rate	At 22 y only 49 (63%) of the group exposed to cannabis remained	Of the total sample, 636 (83%) followed up at 10 y, 580 (76%) at 14 y, and 608 (80%) at 22 y	Follow-up rates for the total sample at 6 y exceed 80% for most measures
Limitations	• Small sample with small number of heavy (n = 25) and moderate (n = 37) users • Low-risk sample • Self-reported use, although used the same interviewer for all interviews in an effort to build rapport	• Large, high-risk sample with potential for multiple confounding variables • Substantial polysubstance use with alcohol, tobacco, cocaine, and other illicit substances • Self-reported use of cannabis	• Likely highest-potency THC products owing to increasing potency over time and increased potency of Dutch cannabis products • Self-reported use of cannabis • Use of self-report questionnaires skewed the sample to a higher SES and more educated sample compared with nonresponders or incomplete responders

ADJ—average daily joints, MHPCD—Maternal Health Practices and Child Development, OPPS—Ottawa Prenatal Prospective Study, SES—socioeconomic status, THC—tetrahydrocannabinol.

Nausea and vomiting in pregnancy. The antiemetic properties of cannabis products are widely known to the public and even depicted in Hollywood films and popular media. There is a prevalent belief that cannabis is "natural" and an "herb" that can be safely used for nausea in pregnancy.[24] Unsurprisingly, pregnant women with access to cannabis products have been reported to use it for the treatment of nausea and vomiting in pregnancy.[25,26] In a survey of women using medical cannabis products, 77% reported nausea and vomiting in pregnancy, and 68% reported using cannabis specifically for this purpose. Most pregnant women using cannabis for nausea and vomiting (92%) found it "effective" or "extremely effective."[26] Paradoxically, marijuana use before pregnancy has been associated with increased reports of nausea in pregnancy.[25] Adding to the confusion, cannabinoid hyperemesis syndrome (CHS), a syndrome of episodic abdominal pain, nausea, and vomiting in chronic cannabis users, is being increasingly identified clinically. Thus, the relationship of cannabinoid

Table 2. Summary of findings of 3 important longitudinal prospective studies

CATEGORY	OPPS[9]	MHPCD[2,10]	GENERATION R[1,11]
Gestational age and birth weight	• Delivery at earlier gestational age in exposure group • No differences in birth weight	• Shorter gestation for exposure after first trimester only • Increased birth weight after third trimester exposure	• Fetal growth reduced from second trimester onward • Lower birth weight in exposed group
Neonatal	• Increased startle response	• No differences in neonatal behaviour	• Not examined
Infant	• 6 mo to 3 y: no neurobehavioural defects	• Not examined	• 18 mo: increased aggression and inattention problems in exposed girls only
Preschool	• 4 y: poorer performance on verbal and memory subscales • No effect on global intelligence	• 3 y: lower short-term memory and verbal reasoning scores	• 3 y: no significant deficits in cannabis-exposed group
School age	• 6 y: poorer sustained attention. No effect on impulse control • Higher parental ratings of inattention and misconduct • 6 to 9 y: impaired visual perception, visual memory, and language comprehension • Increased distractibility	• 6 y: more impulsivity, hyperactivity, and delinquency • 9 y: impaired abstract and visual reasoning • Impaired executive functioning • Poorer reading, spelling, and academic achievement • Depressive and anxious symptoms	• 6 to 8 y: altered brain morphology in the frontal cortex
Teens and young adults	• 14 to 16 y: deficits in visual-cognitive functioning • 17 to 22 y: deficits in executive functioning, response inhibition, and visual-spatial working memory • Increased smoking and early substance use	• 14 to 16 y: deficits in academic achievement (especially reading), information processing speed, and visual motor coordination • Increased rates of delinquency • 17 to 22 y: increased rates of smoking and early initiation of substance use	• Not yet examined

MHPCD—Maternal Health Practices and Child Development, OPPS—Ottawa Prenatal Prospective Study.

products and nausea in pregnancy appears to be complex and, as of yet, poorly defined.

Cannabinoid hyperemesis syndrome is largely described in case series and small retrospective studies in the emergency medicine literature (**Box 1**).[27-29] Episodes of diffuse abdominal pain, nausea, and vomiting are typically acute in onset and last 24 to 48 hours. They are often preceded by a prodromal phase of escalating nausea, which leads to increased use of cannabis products.[27] The symptoms of CHS are often alleviated by hot showers.[28] Cannabinoid hyperemesis syndrome is thought to be largely underdiagnosed and overinvestigated, and it responds poorly to traditional antiemetics.[29-31] Proposed effective treatments include topical capsaicin cream (applied to the abdomen every 4 hours), haloperidol, and benzodiazepines, although long-term resolution requires the cessation of cannabis products.[27,30,31] Consideration of a diagnosis of CHS might be warranted in patients with nausea and vomiting in pregnancy that is atypical and difficult to treat.

Box 1. Characteristics of cannabinoid hyperemesis syndrome

The following are characteristics of cannabinoid hyperemesis syndrome:
- Chronic marijuana use
- Acute-onset nausea, vomiting, and abdominal pain
- Symptoms alleviated by hot showers
- Episodes typically last 24 to 48 h

Data from Richards,[27] Simonetto et al,[28] and Hernandez et al.[29]

As a treatment option, cannabis products have a greater side effect profile than alternate options, with insufficient data for safety. Given the potential for neurodevelopmental effects, cannabis is not recommended

for the treatment of nausea and vomiting in pregnancy, and pregnant women should be encouraged to abstain from use.[23,26,32]

Postpartum. Tetrahydrocannabinol is a fat-soluble molecule excreted in human breast milk in moderate amounts. In chronic heavy users, the milk-to-plasma ratio can be as high as 8:1 and metabolites of cannabis are found in infant feces and urine, suggesting that it might be absorbed and metabolized by the infant.[33] Animal studies suggest that exposure to cannabis while breastfeeding has implications on neurodevelopment similar to in utero exposure.[9] Human studies are few and generally small. In 1990, a prospective cohort study by Astley and Little found that exposure to THC through breast milk in the first month of life was associated with a mean (SD) increase of 14 (5) points on the Bayley Scale of Infant Development at 1 year of age.[34] The adverse effect was persistent after controlling for maternal smoking, alcohol drinking, and cocaine use during pregnancy and lactation. The results, however, were confounded by maternal marijuana use in the first trimester, and it was unclear which exposure was to blame for the effect seen. Given the small sample sizes of studies to date and the lack of more recent studies, there is a paucity of data from which to make a conclusion about the risks of cannabis use in lactating mothers. While the Academy of Breastfeeding Medicine urges careful consideration of the risks and benefits of breastfeeding in the setting of moderate, long-term marijuana use, they also acknowledge that the data remain "not strong enough" to recommend against breastfeeding with any marijuana use.[35]

Further considerations include the risks of second-hand cannabis exposure and impaired caregivers. Second-hand cannabis exposure is an independent risk factor for sudden infant death syndrome.[36] Considering that breastfeeding is protective for sudden infant death syndrome, this warrants a careful weighing of the risks and benefits of breastfeeding while using cannabis. At the very least, lactating mothers should be counseled to smoke outside of the home and change their clothing before caring for their infant.

Finally, although no studies have been done on the subject, a mother's ability to care for her child while she is impaired might be compromised owing to cannabis's effect on mood and judgment.[10] What implications this might have with regard to the involvement of child protective services will likely depend on an assessment of elements such as support systems, other substance abuse, and the extent of their cannabis use. Cannabis use itself is not an indication for involvement of child protective services, and punitive discussions can lead to further harms such as discontinuation of prenatal care.

Instead, an assessment for dependency, education regarding the risks of marijuana use, an assessment of willingness to quit, and a discussion of harm reduction options as described above are the mainstays of interventions available at this time. While community resources for marijuana substance use disorder are currently scarce across the country, with the legalization of marijuana, we might see this change in the coming years. Recently, the Society of Obstetricians and Gynaecologists of Canada has created excellent online educational tools including interactive websites, videos, and posters on marijuana use in pregnancy and lactation. These are valuable resources to which we can point our patients to further explore these topics and concerns.[37]

Case resolution

Julie is admitted to the hospital for 48 hours of intravenous fluids and antiemetic medications. Her symptoms do not respond to most interventions during her admission other than hot showers, where she spends most of her time. After 48 hours her symptoms resolve spontaneously and she requests discharge home.

Before discharge she is counseled regarding the safety of cannabis and its contribution to her clinical picture, and is given the following information:

Cannabis is a complex plant with more than 400 chemicals that pass from the mother to the baby in pregnancy and in breast milk postpartum.

Cannabis use in pregnancy has been associated with a "withdrawal" syndrome in the newborn and can make your baby more irritable.

Exposure in the uterus might have long-term effects on your child's brain development and mental health.

Chronic cannabis use can lead to cannabinoid hyperemesis syndrome, which causes episodes of diffuse abdominal pain, nausea, and vomiting often relieved by hot showers. These symptoms last 24 to 48 hours. The only way to stop them from recurring is to stop using cannabis products.

There are alternate options for management of nausea and vomiting in pregnancy that have been proven to be safe and effective, with fewer side effects. If you are having trouble with nausea and vomiting in pregnancy, please contact your pregnancy care provider.

Conclusion

Exposure to cannabis in utero has been associated with neurodevelopmental outcomes that persist into young adulthood. Maternal risks of cannabis use are related to the mode of ingestion (eg, smoking, edibles) and its addictive potential. Pregnant women should be counseled regarding these risks and encouraged to abstain from use. Harm reduction options should be offered to those not able to quit completely. Tetrahydrocannabinol is excreted in human breast milk and might be associated with impaired motor development in breastfeeding infants, but data are limited.

The relationship between cannabis and nausea in pregnancy is complex and remains poorly defined. While women using it in pregnancy often find it effective, chronic use might be associated with CHS. There are other safe and effective treatments for nausea and vomiting in pregnancy.

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Contributors
Both authors contributed to the literature review, its interpretation, and preparing the manuscript for submission.

Competing interests
None declared

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