

Cannabis the Pregnant Woman and Her Child

Weeding Out the Myths

SC Jaques, A Kingsbury, P Henschke, C Chomchai, S Clews, J Falconer, ME Abdel-Latif, JM Feller, JL Oei
J Perinatol. 2014;34(6):417-424.

Abstract and Introduction

Abstract

To review and summarise the literature reporting on cannabis use within western communities with specific reference to patterns of use, the pharmacology of its major psychoactive compounds, including placental and fetal transfer, and the impact of maternal cannabis use on pregnancy, the newborn infant and the developing child. Review of published articles, governmental guidelines and data and book chapters. Although cannabis is one of the most widely used illegal drugs, there is limited data about the prevalence of cannabis use in pregnant women, and it is likely that reported rates of exposure are significantly underestimated. With much of the available literature focusing on the impact of other illicit drugs such as opioids and stimulants, the effects of cannabis use in pregnancy on the developing fetus remain uncertain. Current evidence indicates that cannabis use both during pregnancy and lactation, may adversely affect neurodevelopment, especially during periods of critical brain growth both in the developing fetal brain and during adolescent maturation, with impacts on neuropsychiatric, behavioural and executive functioning. These reported effects may influence future adult productivity and lifetime outcomes. Despite the widespread use of cannabis by young women, there is limited information available about the impact perinatal cannabis use on the developing fetus and child, particularly the effects of cannabis use while breast feeding. Women who are using cannabis while pregnant and breast feeding should be advised of what is known about the potential adverse effects on fetal growth and development and encouraged to either stop using or decrease their use. Long-term follow-up of exposed children is crucial as neurocognitive and behavioural problems may benefit from early intervention aimed to reduce future problems such as delinquency, depression and substance use.

Introduction

About 3.9% (or 180.6 million) of the world's population between 15 and 64 years of age use cannabis, making it one of the most widely used illegal psychoactive drugs in the world.^[1] In some countries, cannabis has been used by up to 40% of adults at some point during their lives.^[2] Cannabis is accepted as a relatively harmless recreational agent in many parts of the world^[3] despite gathering evidence of its detrimental impact on both the adult^[4] and the developing^[5] central nervous system. Severe cannabis use, for example, decreases the metabolism of the prefrontal and temporal cortex,^[6,3] and chronic exposure doubles the risk of psychosis and memory and cognitive dysfunction, most likely from neurotransmitter dysregulation.^[7] This risk of neurological impairment is especially pronounced if cannabis is consumed during periods of critical brain development, such as adolescence.^[8]

Cannabis, however, is one of the most commonly used illicit drugs in pregnancy and lactation.^[1,2] Approximately 2.5% of women admit to continued cannabis use even during pregnancy.^[9] This is of great concern because its lipophilic nature^[10] allows it to readily cross many types of cell barriers, including the blood/brain and transplacental membranes. Cannabis metabolites are consequently easily detectable in many types of human tissues,^[11] including the placenta, amniotic fluid and the fetus.^[12] The effects of cannabis on the developing fetus may, however, be subtle and not be detectable for many months to years after birth, as the aetiology of some of the 'softer' neurological signs such as aggressive behaviours^[5] or other neuropsychological problems^[13] are difficult to be attributed unequivocally to cannabis exposure due to frequently concurrent negative environmental influences such as parental drug use, poverty^[14] and psychiatric co-morbidity.^[15]

Evidence regarding the effects of perinatal cannabis exposure, that is, during pregnancy and lactation, is plentiful but, unfortunately, ambiguous. In this review, we offer an overview of this problem, including discussion about the potential effects of this practice on the unborn, newborn and older child and adolescent.

We also discuss some of the pertinent issues associated with perinatal management, including the utility of drug screening and the practical aspects of breast-feeding in the known cannabis user. Our overall aim is to provide the health practitioner with some guidance for advising women who use cannabis in pregnancy, including best available information on the potential effects of cannabis use on their unborn baby and future childhood development.

What Is Cannabis?

Cannabis is a genus of flowering plant with three main varieties: sativa, indica and ruderalis. It has been used for thousands of years for its fibre (hemp) and for its medicinal and psychoactive effects that are mediated through a unique family of at least 85 different compounds called cannabinoids, the most abundant of which are cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC). THC is the only cannabinoid with psychoactive properties, and plants are categorised according to the amount of THC or ratio of THC/CBD they contain. Hemp-producing cannabis strains are specifically bred, as per the United Nations Convention, to produce low THC levels.^[16]

Cannabinoids are most abundant in the floral calyxes of the plant. The forms and strengths of THC obtained are dependent on the part of the plant that is used as well as the process used to extract and manufacture the plant product. Hash oil is the strongest, followed by hashish (resin) and marijuana (dried leaves/flowers). Cannabis may be inhaled by smoking with tobacco or through a water pipe or ingested in foods and drinks.^[17] Most countries in the world have criminalised the growing and recreational use of cannabis, but controlled programmes in some countries such as the United States, Holland and Canada allow regulated use of medicinal cannabis, including the synthetic compounds dronabinol and nabilone, for the management of conditions, such as cancer-related nausea^[18] and neuropathic pain.^[19]

Pharmacodynamics of Cannabis

Endocannabinoids are naturally occurring arachidonic acid metabolites^[20] that are essential for the regulation of movement, memory, appetite, regulation of body temperature, pain and immunity.^[21] Endogenous endocannabinoids and plant-derived phytocannabinoids exert their effects by activating the cannabinoid receptors of the endocannabinoid system. To date, five cannabinoid receptors have been identified, including the cloned CB1 and CB2 receptors.^[22] The CB1 receptor is predominantly located in the central nervous system while the CB2 receptor is largely confined to immune cells and the retina.^[23,24]

Psychoactive drugs, such as cannabis, are generally lipophilic and of small molecular size, enabling them to readily cross the blood–brain or other cellular (for example, placental) barriers. In animal studies, fetal blood and tissue THC concentrations are around 10% lower than maternal blood levels,^[25] but in the rat model repeated dosing of the dam, particularly at higher doses, resulted in significantly higher plasma concentrations in the fetus as compared with single acute dosing. This suggests that heavy and chronic cannabis use may result in concentration of active cannabinoids in the developing fetus.^[26] No similar human studies exist, but when plasma concentrations were measured in human cord blood samples, THC levels were found to be 3 to 6 times lower than in simultaneously collected maternal blood, with a similar concentration gradient being noted for the metabolite 9-carboxy-THC.^[27]

Endogenous cannabinoids and cannabinoid receptors are expressed early in the developing fetal brain. CB1 receptors are identifiable in white matter and cell proliferative regions and are involved in critical neurodevelopmental events, such as neuronal proliferation, migration and synaptogenesis. Endocannabinoids are also pivotal in regulating neural progenitor cell commitment and survival.^[28] Cannabis exposure during pregnancy therefore has the potential to induce supra-physiological stimulation of the endogenous cannabinoid system, which may then disrupt the ontogeny of endogenous endocannabinoid signalling and interfere with synaptogenesis and the development of neuronal interconnections. In addition to the possible effects of cannabis use on endocannabinoid-mediated neuronal maturation, it appears that cannabis exposure in pregnancy may also disrupt developing neurotransmitter systems. Dopaminergic neurones are expressed very early in the developing brain and exert trophic effects on neuronal

cells.^[29] Cannabis exposure during pregnancy disrupts tyrosine hydroxylase activity, the rate-limiting enzyme in dopamine synthesis, which has the potential to impact on the maturation of dopaminergic target cells.^[28] Disturbances in dopamine function have consequently been associated with an increased risk of neuropsychiatric disorders, such as drug addiction,^[30] schizophrenia^[31] and depression.^[32] Prenatal THC has also been noted to alter endogenous enkephalin precursor and the expression of opioid and serotonin receptors in animal models.^[28] Whether these changes are implicated in the future risk of addictive behaviours and depression in the human is as yet uncertain.

Is There a Genetic Susceptibility to the Effects of Cannabis?

The effect of phytocannabinoids on mature neuronal cells is complex. Both neurotoxic and neuroprotective effects have been described depending on the cannabinoid, the cell type and the stage of cell differentiation.^[22] There is evidence that individual susceptibility to cannabis, at least in the adolescent onset user, may be substantially influenced by heredity. Adolescent catechol-O-methyltransferase (COMT) knock-out mice, as compared with wild type, are more vulnerable to cannabinoid-induced modification of expression of schizophrenia-related behaviours.^[33] In humans, neuroimaging studies demonstrate that chronic consumption of cannabis beginning before the age of 16 years is associated with alterations in the volume of the caudate nucleus and amygdala in users with specific COMT gene polymorphisms that produce increased copies of the val allele.^[34] The presence of the COMT gene polymorphism val158met and the SLC6A4 gene 5-HTTLPR polymorphism in young adult cannabis users, on the other hand, has a moderating effect of decreased performance on executive functioning.^[35] Whether genetic susceptibility influences the long-term neuropsychiatric and cognitive outcomes of gestational cannabis-exposed children has not been explored but could lead to individual direction of early intervention and supportive services to ameliorate possible undesirable outcomes.

The Prevalence of Cannabis Use in Pregnant Women

Cannabis is the most frequently used substance in any drug-taking population. In the gravid population, it accounts for >75%,^[35] and generally self-reporting from developed Western countries such as Australia^[36] and the United Kingdom^[37] place the prevalence of cannabis use at up to 5% of all pregnant women. However, the certainty of these estimates is limited due to the variability of self-reporting rates.^[37] Although many illicit drug users stop or decrease drug use during pregnancy, cannabis users often continue to use throughout pregnancy and while breast feeding.^[38] Persisting cannabis use throughout pregnancy may, in part, be due to widespread societal acceptance of cannabis as a relatively harmless recreational agent compared with other 'hard' drugs of dependency such as heroin,^[3, 36] and certainly more study into why this occurs is warranted. It must be noted that cannabis use in pregnancy is frequently accompanied by other forms of drug use or abuse. Many women continue to smoke tobacco and/or consume alcohol. Using record linkage data collected over a 5-year period, Burns *et al.*^[39] demonstrated that 12% of cannabis users were concurrently identified as using opioids, 10% as using stimulants and 4% were identified as having an alcohol-related diagnosis during pregnancy. Almost 50% reported that they smoked >10 cigarettes per day. Identifying cannabis use in a pregnant woman therefore should prompt investigation into exposure to other substances.

Detecting Cannabis Use in Pregnancy

Optimal identification of drug exposure has a crucial impact on pregnancy and long-term health outcomes for both the mother and her child.^[40] Early detection of drug use allows for timely implementation of harm-reduction strategies designed to moderate drug use as well as to minimise the impact of drug-using lifestyles (for example, unstable home situations, poor nutrition, poverty) on the family. Supportive care may favour changes that alter drug-using behaviours,^[41] although it must also be acknowledged that complete cessation or abstinence of drug use is not possible for many women. Nevertheless, early detection facilitates ongoing support and may produce potentially valuable lifestyle changes that go beyond the perinatal period.

Other health issues may be addressed with timely detection of drug use. Ongoing drug use and abuse is frequently associated with psychiatric co-morbidities, and the impact of this on the mother and her family can be further complicated by socioeconomic problems, such as domestic violence and ongoing drug use by co-addicted partners.^[42] Reducing drug use may also not be possible without appropriate identification and management of underlying psychiatric co-morbidities, such as anxiety disorders or depression. Evidence suggests that these psychiatric co-morbidities themselves may be a significant trigger for drug use^[33] and that the co-existence of mental health problems may independently impact on pregnancy outcomes. Maternal depressive illness, for example, is strongly correlated with an increased risk of preterm delivery,^[43–46] and of course, the earlier in pregnancy drug-dependent women have access to psychosocial supports, the higher the likelihood is of them to establish appropriate living conditions for their family and of addressing financial and any associated legal problems.

In addition to specific supports targeting drug use, detection of drug use in pregnancy also permits implementation of strategies that provide drug-using mothers with specific mothercraft and intensive postnatal support, such as intensive home-visiting programmes. Such programmes have been demonstrated to decrease the risk of childhood morbidity and mortality in high-risk disadvantaged adolescent parents.^[47] Similarly, targeted education in other aspects of routine parenting, such as safe sleeping practices, may be beneficial as the incidence of night-time Sudden Infant Death Syndrome is significantly higher (for as yet uncertain reasons), in cannabis-exposed infants.^[48]

Screening for drug and alcohol use should be considered a normal part of the standard antenatal interview process. Screening tools used in this setting are generally questionnaires that are designed to be administered face-to-face by the provider to the patient. They are not intended to specifically diagnose a substance abuse problem but rather to determine if a patient may be at risk for alcohol or drug problems and would therefore benefit from a more comprehensive evaluation. Ideally, a screening tool should be administered multiple times during each pregnancy, because patients may be more willing to disclose substance abuse problems once they develop rapport with a provider. Screening tests can also provide an opportunity to educate the patient about alcohol and drug abuse and the benefits of addressing these problems while pregnant. Asking every patient relevant but sensitive questions in a health context lessens the stigma associated with the topic. However, administering these screens in the antenatal period can be problematic. Seib *et al.*^[49] demonstrated that while only 15% of the patients being screened were uncomfortable with the process, staff compliance was an issue, with 25% of women not being screened adequately or not being screened at all. All maternity hospitals should therefore encourage staff training to ensure that health providers are comfortable and familiar with screening processes used for their particular local area.

In contrast to the proven effectiveness of specific screening tests for identifying alcohol consumption in pregnancy,^[50] the evidence for the efficacy of formal screening tests for drug use in the antenatal period is not as clear. Few screening tools have been directly evaluated for their efficacy in detecting drug, or more specifically cannabis, use in pregnancy. Phillips *et al.*^[102] found that direct questioning by midwives using a structured screening tool facilitated drug use disclosure during early antenatal consults but that the use of some forms of questionnaires, for example, the Drug Abuse Screening Test (DAST-10), had only a sensitivity of 0.47 when self-reporting was validated against positive toxicology screens.^[51] Again, we suggest that all staff involved in maternity care be trained to administer (and act on) drug screening tools confidently and without prejudice.

Toxicology screening for drug metabolites is generally carried out with the expectation of increasing the likelihood of detecting undisclosed drug use in pregnancy. Either maternal urine and hair samples or newborn urine, hair and meconium samples can be collected and analysed for the presence of drug metabolites, but only maternal toxicology screening has any value if the intention is to implement harm-minimisation strategies early in pregnancy. Newborn toxicology screening primarily focuses on identifying families at risk of ongoing drug use, to address child protection concerns that may be associated with parental drug use and to provide appropriate treatment for suspected cases of withdrawal or intoxication.^[41]

Depending on the locale, toxicology screens may increase the chance of drug detection by up to fivefold,^[52] but the general applicability of such screening programmes has often been limited by their selective application to perceived high-risk groups, such as infants of certain racial groups.^[51,53] The value of screening maternal urine for drug metabolites is limited by the narrow time frame in which many drugs are excreted after use. Drug testing for cannabis is particularly problematic as there is generally a wide variability in individual excretion profiles.^[53] Cannabis metabolites may also be undetectable in the naive user after 48 h. However, they can be potentially detectable in the urine for several weeks in chronic users, making it difficult to determine whether or not a positive urine sample represents past or recent ongoing use.

Maternal hair samples can also be used to detect substance use in pregnancy. However, hair toxicology has not been proven to be of great value in the detection of undisclosed cannabis use in pregnancy. Ostrea *et al.*^[54] compared the sensitivity and specificity of maternal interview, maternal hair analysis and newborn meconium analysis in detecting perinatal exposure to opioids, cocaine and cannabis. Although hair and meconium analysis showed a high sensitivity in detecting opioid and cocaine exposure as compared with interview, hair and meconium analysis demonstrated a sensitivity of only 21% and 23%, respectively, as compared with a sensitivity of 58% for detection by maternal interview. The use of maternal hair samples is further complicated, because results may be affected by passive exposure to environmental cannabis smoke.^[55] It is possible to distinguish between environmental contamination and true exposure by assaying for the derivative, Δ 9-tetrahydrocannabinolic acid-A (THCA-A), as low concentrations of THCA-A compared with other metabolites suggests environmental contamination,^[56] but this increases the complexity and expense of maternal hair analysis and will therefore not be considered suitable in most facilities for routine screening purposes.

Neonatal urine testing by immunoassay provides rapid results but is limited by the short time frame in which an infant will excrete recently used drug metabolites post delivery, resulting in a high rate of false negatives. In contrast, meconium that is collected within the first 2 days of life can be used to detect maternal cannabis use from the second trimester onwards. Neonatal hair samples can also be examined for evidence of exposure during the last trimester of pregnancy, as this is when fetal hair grows. Both meconium and neonatal hair sampling have been shown to be helpful in confirming suspicion of maternal cannabis use, at least in the second and third trimesters of pregnancy. A direct comparison between sensitivity of meconium and neonatal hair testing has found meconium to be more sensitive but is limited by the need to collect a sample within a few days of birth. Hair samples may be useful in confirming prenatal exposure to cannabis for up to 3 months after delivery but facilities for hair analysis remain limited for many care practitioners.

Although both maternal and newborn toxicology screening can increase the likelihood of detecting drug use in pregnancy, most authors do not recommend their routine use because of the expense and the burden on laboratory time constraints. Rather, they suggest toxicology testing be selectively used where there is a suspicion of maternal drug use that can not be confirmed by maternal interview.^[41,57]

The Impact on the Fetus and Newborn Infant

It is difficult to determine the direct effects of maternal cannabis use on the developing fetus because of the often high prevalence of other concurrent drug use, including tobacco,^[48, 58] and other adverse parenting and lifestyle issues, including poor nutrition, poverty and stress. The endogenous cannabinoid system has a crucial role in maintaining and regulating early pregnancy. Human placental studies have determined that the CB1 receptor is present in all the placental membrane layers^[59] and that stimulation of these receptors will impair fetal growth by inhibiting cytotrophoblastic proliferation.^[60] In a large population-based prospective cohort study, maternal cannabis use during pregnancy was found to be associated with growth restriction in mid-pregnancy and late pregnancy, with effects on low birth weight being most pronounced if maternal cannabis use continued throughout pregnancy.^[61] These growth effects remained significant even after adjustment for potential confounding variables, such as exposure to tobacco and self-reporting of cannabis use (raising the possibility of selection bias). To date, there is no known association between cannabis

exposure and spontaneous abortions of either chromosomally normal or abnormal fetuses,^[62] and any such links are probably more likely to be related to concomitant stressful life events than to cannabis use *per se*.^[63]

Although some animal studies indicate that cannabis may be teratogenic in very high doses, there is no firm link between gestational cannabis use and congenital malformations in humans.^[64] Reports of associations between cannabis use in pregnancy and gastroschisis remain unsubstantiated.^[65] A study of almost 420 000 Australian live births over a 5-year period by Burns *et al.*^[39] found that *in utero* cannabis exposure increased the risk of neonatal intensive care unit admissions, predominantly for prematurity, but there was no relation to any increased risks of perinatal death.

Significant newborn withdrawal or intoxication syndromes requiring pharmacological treatment have not been described with exclusive gestational cannabis exposure, but subtle neurobehavioural disturbances such as exaggerated and prolonged startle reflexes and increased hand–mouth behaviour have been described.^[66] High-pitched cries^[67] and sleep cycle disturbances with EEG (electroencephalography) changes have been noted,^[68] suggesting that prenatal cannabis affects newborn neurophysiological function. Pharmacological treatment for neonatal cannabis withdrawal has not been described, although this may be secondary to a lack of definitive evaluation techniques. Indeed, cannabis withdrawal has been described as a 'mild narcotic withdrawal',^[69] and further study into additional treatments, evaluation and long-term outcomes is required.

Long-term Growth and Neurodevelopment

Of greater concern, however, is the increasing evidence that *in utero* cannabis exposure may impair long-term growth and neurodevelopment, particularly in terms of cognition and behaviour. Evidence from population-based human studies and *in vitro* animal data indicates that interference with the endocannabinoid system disrupts normal neurobiological development,^[70] particularly of neurotransmitter maturation^[5] and neuronal survival.^[22]

A longitudinal cohort study of growth parameters in children exposed to cannabis and cigarettes during pregnancy found that cannabis-exposed children have smaller head circumferences at birth, which increase in disparity in adolescence.^[71] It must be noted that head growth, especially during the first month of life, is significantly associated with future intelligence quotient.^[72]

Most studies, nevertheless, do not support measureable differences in neurodevelopmental outcomes in infants aged <2 years after cannabis exposure, but by early childhood and school age, cannabis-exposed children acquire visual–perceptual tasks and language skills more slowly and show increased levels of aggression and poor attention skills, particularly in girls.^[73] The levels of cognitive and intellectual deficits are also related to the timing and degree of *in utero* exposure. Heavy use (defined as >1 joint per day) during the first trimester was associated with lower verbal reasoning scores in 648 children at 6 years of age when compared with their non-exposed peers, while second trimester use was associated with deficits of composite, short-term memory and quantitative scores.^[74]

Problems with tasks requiring visual memory, analysis and integration appear to persist beyond late childhood^[75] into adolescence.^[76] The long-term effects of *in utero* cannabis exposure on visuospatial working memory were explored by Smith *et al.*^[78] using functional magnetic resonance imaging. They demonstrated that in 19 to 21-year olds, high levels of maternal prenatal cannabis use was associated with significantly more neural activity in the left inferior and middle frontal gyri, parahippocampal gyrus, middle occipital gyrus and cerebellum and right inferior and middle frontal gyri.^[77] The specific learning problems identified in these children appear to significantly interfere with school achievement scores^[78] from as early as 6 years of age.

The aetiology of these problems is uncertain. *In utero* cannabis exposure alters neurotransmitter homeostasis, including ventral striatal dopamine D2 gene regulation^[79] and expression,^[80] and these changes have been linked to a risk of future neuropsychiatric problems, including disorders of impulse control associated with addiction behaviours.^[79] Further, a significantly increased risk of childhood depressive

symptoms and attention problems was identified at age 10 years in a large prospective cohort study documenting the use of cannabis in low-income pregnant women.^[81] The same group of investigators also demonstrated that the risk of delinquency at 14 years was significantly increased in a prospective longitudinal study of cannabis-exposed children.^[82] Other factors, however, are undeniably important in the expression of adverse behaviours during the teenage years. For example, the risk of adverse behaviours, including early initiation of drug abuse, is more likely in an intrauterine drug-exposed child if they are male or simultaneously exposed to other problems such as violence.^[83] There is no firm association with prenatal cannabis and future psychiatric problems such as psychosis,^[84] but depressive symptoms are increased.^[82] Assisting the family unit with moderating adverse environmental influences from as early as possible after birth may have the potential to decrease future problems in young people affected by prenatal cannabis exposure.

The effects of cannabis on future physical growth are still to be determined. CB1 receptors mediate energy incorporation into adipose tissue and reduce energy expenditure. The Ponderal Indices of adolescents exposed to prenatal cannabis are higher than non-exposed children,^[85] but further work needs to be done to determine their risk of developing clinically important sequelae such as appetite problems, dyslipidemia and diabetes, which are all common manifestations in chronic adult cannabis users.^[86]

Medical Cannabis

In recent years, there has been a re-emergence in the use of medicinal cannabis to treat a variety of conditions, including amelioration of neurogenic pain and management of chemotherapy- and pregnancy-associated hyperemesis.^[87] Increasing numbers of states in the United States, for example, have legalised medical marijuana for certain specific indications.^[88] However, it is not known whether the long-term effects of prenatal exposure to medicinal cannabis used in a controlled manner differ from the effects of cannabis used as a recreational drug during pregnancy, and urgent study is required. At this point in time, any advice about medicinal cannabis use during pregnancy must take into consideration both the potential benefits of the substance with regards to maternal well being and potential impact of this type of cannabis exposure on the developing fetus.

Lactation

Cannabis and its metabolites readily pass in to breast milk in variable concentrations that depend considerably on the amount of drug ingested by the mother. When cannabis is regularly consumed by breast-feeding mothers, human milk THC concentrations may be up to eightfold higher than simultaneously measured maternal plasma concentrations.^[89] Certainly, even bovine consumption of cannabis results in detectable metabolites in at least 30% of children even up to the age of 3 years.^[90] There are substantial concerns that continued maternal cannabis use during the first month of life may impede neurodevelopment at 1 year of age,^[91] but the effects of postnatal exposure is difficult to delineate from prenatal use as most mothers will not begin using cannabis as a *de novo* habit after birth.

Delta 9-THC inhibits gonadotropin, prolactin, growth hormone and thyroid-stimulating hormone release and stimulates the release of corticotropin, thereby inhibiting the quantity and reducing the quality of breast milk.^[92] The Academy of Breastfeeding Medicine, in line with most professional bodies, recommends against breastfeeding whenever illicit drug use has occurred in the 30-day period before birth. This is especially pertinent if substance abuse is ongoing post delivery or if the mother is not engaged in substance abuse treatment programmes.^[93–95] Unfortunately, specific recommendations with respect to breast feeding while using cannabis are hampered by the lack of substantial and definitive studies. In particular, occasional users should be counselled on a case-by-case basis and made aware of the risks of maternal intoxication while caring for an infant and the potential neurodevelopmental sequelae on their child, should cannabis usage become a regular activity.

Recommendations for the Management of Women Using Cannabis in Pregnancy

There are no known 'safe' threshold limits for cannabis use in pregnancy, and currently, there are also no specific pharmacological treatments for cannabis dependency. Evidence overwhelmingly indicates that cannabis use during pregnancy and possibly in the postnatal period remains a significantly under-recognised problem that has the potential to cause long-term harm. However, there are a variety of approaches that can facilitate identification of cannabis use in women presenting for pregnancy care that may allow implementation of harm-minimisation procedures to reduce long-term risks for both the mother and her child.

Carefully directed and sensitive histories should be routinely taken to elucidate cannabis and other substance use in pregnancy. In some high-risk cases, toxicological screening may be appropriate where heightened suspicions are not in keeping with maternal history offered. Due to increasing concerns about long-term neurodevelopmental, behavioural and possibly even metabolic consequences of perinatal cannabis exposure, women should be objectively informed of the possible impact of cannabis use during pregnancy and lactation and be strongly advised to stop using cannabis wherever possible. If complete abstinence is not possible, women should be advised to reduce regular cannabis use during pregnancy, as current evidence indicates that daily use of cannabis is most strongly associated with future adverse neurobehavioural outcomes. A harm-reduction approach focusing on minimising risks to the woman and her baby rather than complete cessation may be most effective in this scenario. Engaging women into an antenatal service that provides drug relapse prevention support or referring women to drug and alcohol services should be considered, particularly where an antenatal service cannot offer specific drug and alcohol counselling services itself. Cognitive behavioural therapy centred around drug relapse and prevention support and tobacco cessation education is recommended. Midwives and doctors should ask women about their level of cannabis use and their willingness to change their drug-use behaviours at each antenatal contact. General health education, including the adverse effects from continued cannabis and tobacco exposure and safe sleeping guidelines should be reinforced. Depending on family circumstances, the benefits of breast feeding, even with continued cannabis use, may outweigh the negative side-effects, especially in infrequent cannabis users. Each institution should work towards a policy of ensuring best practices for their particular population of cannabis users.

During the postnatal period, mothers should be advised not to smoke either tobacco or cannabis around their infants and children. They should be educated about the risks of passive smoke exposure as well as the potential effect of cannabis use on a mother's decision-making ability. Mother-crafting support may be required to ensure best infant care, including safe sleeping practices. Of particular note, counselling cannabis-using fathers is also crucial as continued paternal cannabis triples the risk of Sudden Infant Death Syndrome^[96] ().

Table 1. Summary of recommendations.

Issue	Recommendations
Detection of maternal use	Antenatal drug and alcohol questions best to screen large populations Maternal and infant toxicology most likely unhelpful unless maternal history is ambiguous ⁵⁶ Early detection may help implement harm-minimisation strategies
Fetal effects	No definitive link to increased spontaneous abortions ⁹⁷ or congenital abnormalities ^{64, 65} Intrauterine growth restriction, including head size of fetus, common ⁶¹
Neonatal effects	Severe withdrawal uncommon but mild symptoms similar to an opioid-type withdrawal is recognised ⁶⁹

	<p>Need for pharmacological treatment from cannabis only exposure uncommon</p> <p>Transient high pitched cry⁶⁷ and sleep disturbances⁶⁸ noted</p> <p>Increased risk of sudden infant death syndrome⁹⁶</p>
Effects on childhood and later life	<p>Small head circumference may persist into teenage life</p> <p>Risk of long-term problems correlated with severity of prenatal exposure,⁷⁴ particularly on visual memory and executive function^{74, 75} that may persist to late childhood⁷⁵ and adolescence⁷⁶</p> <p>Aggression and attention problems noted in toddlers (especially girls)⁷³</p>
Lactation	<p>Cannabis and metabolites cross the milk barrier, and levels in milk may be higher than maternal plasma⁸⁹</p> <p>Effects of continued use during lactation may impair early (<1 year) neurodevelopment⁹⁰</p>
General	<p>Screen all pregnant women for drug use with a well-validated questionnaire</p> <p>Cease or decrease use as early as possible—chronic/heavy use (>1 joint per day) increases risk of long-term adverse outcomes for the child</p> <p>Lactation recommendations must be taken on a case by case basis. Mother must be aware of dangers of breast feeding while intoxicated, of passage of cannabis and metabolites into milk and of possible adverse influence of continued cannabis exposure via breast milk on childhood neurodevelopmental outcomes</p> <p>There is insufficient current evidence to provide definitive recommendations for the use of medicinal cannabis</p>

Conclusion

It is not uncommon for the health-care professional caring for pregnant women to encounter the problem of maternal cannabis use during the antenatal period. Although cannabis is viewed by many as a harmless recreational drug when compared with other illicit drugs, there is mounting evidence to suggest that prenatal cannabis exposure can have a negative effect on fetal growth and that exposure to cannabis during periods of critical brain development, particularly during the fetal and adolescent periods, has the propensity to significantly adversely impact on neurodevelopmental and behavioural outcomes. Ultimately, long-term changes in neurobehaviour, particularly those involving executive functioning, may adversely affect adult educational and vocational outcomes. As health-care professionals, we have a responsibility to seek to actively identify women who use cannabis in the antenatal period and inform them of the possible risks of their cannabis use in a non-threatening and non-judgemental manner. Currently, pregnant and breast-feeding cannabis users should be advised to cease use where possible or substantially decrease their drug use. At this point in time, there remains ongoing uncertainty about both short- and long-term implications of

cannabis use during pregnancy and lactation, especially if use is intermittent. Further adequately powered studies are required to resolve this pressing dilemma.

Key Notes

1. Regular cannabis use in pregnancy is a widespread but an under-recognised problem.
2. Fetal growth is possibly affected by gestational cannabis exposure, but the dose-response relationship has not been well defined.
3. There is evidence that regular cannabis use in pregnancy significantly increases the risk of future neurodevelopmental and behavioural problems, with particular effect on executive functioning.
4. Pregnant and breast feeding cannabis users should be identified early and advised to either decrease or where possible cease cannabis use entirely.

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