

Not to be reproduced without permission. Copyright 2017 Laurel Wilson.

## Up In Smoke: Marijuana and Breastfeeding Handout

By Laurel Wilson, BS, IBCLC, CLE, CLD, CCCE

While Cannabis (marijuana) has been used for more than 5000 years as a medicinal and ceremonial herb, its use as a recreational and daily medicine has spiked over the past decade. Legalization and anti-punitive laws for both medicinal and recreational use of Cannabis around the world has increased its use, in the mainstream population and also during pregnancy and lactation. In the United States there are 29 states that have either some form of legalized marijuana use or decriminalization laws. Eight states have legalized both recreational use and medicinal use. Even though many states have passed laws decriminalizing the use of marijuana, it is still considered to be a Schedule 1 illegal substance by the federal government, meaning that it has been classified as offering no potential medical benefits and having a high risk of abuse.

Women who use Cannabis during the perinatal period believe the herb to be natural and less toxic to their bodies and their babies than pharmaceutical medications and alcohol. With little in the way of quality human research, medical and lactation professionals are left wondering how to guide and counsel their clients. Today Cannabis is the most commonly used illicit substance during pregnancy in Western societies. It is the world's third most popular recreational drug, after alcohol and tobacco. Cannabis is by far the most widely consumed and available illicit drug in France, as well as in Europe (Costes, 2009). In France, there are 17 million lifetime users. There are estimated to be 1.4 million regular users of the drug and 700,000 daily users according to the French Observatory of Drugs and Addictions (OFDT).

What about use during pregnancy and breastfeeding? Moore et al. (2010) found that in British communities, Cannabis was the ONLY illicit drug that pregnant women continued to use to term. A 2010 study on Cannabis use during pregnancy in France found that out of 13,545 self-reporting women, 1.2% freely admitted to using the drug (Saurel-Cubizolles, 2010). Fifteen percent of those women reported using marijuana at least 10 times a month. Women with severe nausea during pregnancy, compared with other pregnant women, were significantly more likely to use marijuana (3.7% vs. 2.3%, respectively) (Robertson, 2014). The top reasons women report using cannabis during pregnancy are depression, anxiety, stress, pain, nausea and vomiting. Approximately 3.85% of the pregnant population in the US use Cannabis (Brown, 2016).

Cannabis is a flowering plant with three species – indica, sativa, and ruderalis. Indica and sativa species are the plants that are associated with human consumption. Cannabis sativa is a tall and thin plant, with light green leaves and high concentrations of tetrahydrocannabinol (THC). It tends to be known for a brain high. Cannabis indica (C. Indica) is a short and dense version of the plant with dark green leaves. C. Indica tends to be higher in Cannabidiol (CBD), and thus is known for a body high instead of for its psychotropic effects. This is the version that tends to be home grown because it does not grow very tall. Most marijuana on the market

Not to be reproduced without permission. Copyright 2017 Laurel Wilson.

today is a genetically engineered version of the two herbs that have been hybridized for specific qualities.

These modified versions of marijuana are not the same chemically as what one would find naturally growing in the wild, nor are they similar to what people were using only 25-30 years ago. Today the marijuana that is sold on the street and over the counter is genetically engineered to produce the either high levels of THC for its psychotropic and medicinal effects (ex: reducing nausea) or high levels of CBD for its medical qualities, such as reducing seizures. In the 1970's the level of THC was approximately 1%. Since that time, the THC levels have steadily been climbing, and today one finds THC levels an average of 12-15% potency in the dried herb and 20-60% in hashish and marijuana resins such as hash oil or budder preparations. At the Cannabis Cup 2016, which is a worldwide cannabis festival held every year, there were Cannabis strains that registered THC as high as 30% and 20% plus CBD.

Cannabis can be consumed in a myriad of ways. As a dried herb it can be smoked as cigarette, placed in a water bong, vaporized in a vaping system, or smoked in a pipe. Hashish is the extracted resin from the marijuana plant, and can be smoked or added to edibles. Marijuana oil is the oil from the Cannabis buds that has been extracted with a solvent. This oil is used to enhance cigarettes or using in edibles. This form of marijuana has a much higher concentration of THC, from 20%-60%. Edibles have a higher bioavailability of THC, from 6-20%, and thus can be longer acting and more intense for the user. Many cannabis users have switched from smoking or vaping Cannabis to edibles to reduce the lung cancer risk.

A newer form of use is called dabbing. Dabbing is inhaling Cannabis resin in the form of hash or honey oil, wax or "budder", and shatter – a hard, amber colored solid. Resin is made by heating Cannabis soaked in a solvent, like ethanol, isopropyl alcohol, or butane, which results in a resin. Dabbing involves placing the resin on a metal device and inhaling. This can be done with dabbing pens, domes or nails, and other specialized devices. The resulting high is said to provide an intensified high. Some Cannabis users prefer to dab to avoid the risks associated with smoking (carcinogen exposure, those with asthma, etc.), though there is no evidence of increased safety.

Those who use Cannabis for pain relief medicine may also use it as transdermal patch or topical crème. There are three forms of pharmaceutical Cannabis in the United States. The first is Dronabinaol (Marinol), which is synthetic THC. It is used in US for nausea associated with chemotherapy and HIV. Nabilone (Cesamet) is another synthetic version of Cannabis. It is synthesized THC and it is used for reduction of nausea due to chemotherapy. The third medication is Sativex. This is synthetic THC and CBD, used primarily throughout Canada and Europe and recently legalized in France, for the treatment of neuralgia associated with Multiple Sclerosis. Many who use synthetic or pharmaceutical THC or CBD complain about the side effects. In fact, in a 2011 survey, only 1.8% of 953 patients preferred synthetic THC pharmaceuticals over natural forms of Cannabis (Hazekamp, 2013). The entourage effect that comes from using the Cannabis plant in natural form, allows the plants

cannabinoids and terpenes to work together providing better efficacy and reduced side effects.

While there are hundreds of chemicals in Cannabis, the most studied and well known are the cannabinoids, of which there are upwards of 60. THC and CBD are the most well known. In the raw plant material, THC and CBD are found in acid form, that of THCA and CBDA. The acid forms must be heated to transform to the active ingredients into THC and CBD. This is why you can't just eat raw Cannabis plant, or hemp, and get high. The plant material, specifically the buds of the plant, must first be heated. This is why you have to bake or cook edibles, or use the extracted hashish or marijuana oil, which has already been heat processed. The half-life of THC is one to 2.3 days, but the non-active metabolites can stay in the body's system for 4-6 weeks. CBD is the cannabinoid that offers potential for many medical treatments, such as arthritis, diabetes, alcoholism, MS, chronic pain, schizophrenia, PTSD, antibiotic-resistant infections, and epilepsy. It is a non-psychoactive cannabinoid and there are strains of Cannabis available that are very low THC and high CBD.

Even though THC and CBD are the main concerns regarding safety for Cannabis use during pregnancy and breastfeeding, another worry involves the pesticides that are used on Cannabis. Due to the fact that the Cannabis is a Schedule 1 substance, the FDA cannot regulate safety requirements for pesticide use, as it is an illegal crop in US. Most states approve of the use of 75-200 pesticides for crops. However, many of the grow houses use pesticides that are not only illegal but not approved for indoor use to combat the mites and other pests that damage indoor Cannabis crops. The four most common illegal pesticides found in Cannabis raids are:

- **Myclobutanil:** This fungicide is considered "slightly hazardous" by the World Health Organization. It is labeled as a "Bad Actor" by the Pesticide Action Network. The product label warns of nervous system problems and toxic fumes.
- **Imidacloprid:** This insecticide is found in Merit and Mallet pesticide brands. It is deemed "moderately hazardous" by the WHO. The National Pesticide Information Center reports that it is moderately toxic if ingested or inhaled.
- **Abamectin and Avermectin:** These insecticides are found in Avid and Lucid pesticide brands. The Pesticide Action Network lists avermectin as a "Bad Actor". The products themselves are labeled as "harmful if inhaled."
- **Etoxazole:** This insecticide is found in TetraSan 5 WDG pesticide brand, which is a product that generally is not used for food crops only ornamental and landscape plants. Its safety for ingestion is highly questionable.

A 2013 Journal of Toxicology Report found that up to 70% of the pesticides used on Cannabis can pass through the body during inhalation (Sullivan, 2013). Smoking marijuana can mean ingesting 10 times that which one would through oral ingestion of pesticides. The practice of dabbing can intensify the risk of pesticide exposure, as

well (Raber, 2015). Mothers who use Cannabis should be educated on pesticide risk, and the importance of organically produced products.

When someone inhales marijuana, the smoke goes in to the lungs and immediately passes through the membranes and enters the bloodstream. From here it dilates the blood vessels, which can make the user feel warm and also cause the bursting of the small blood vessels in the eyes, giving the typical red eye appearance of marijuana smoking. Marijuana reaches the brain within seconds. With ingestion, this process can take much longer, from 30-60 minutes. When marijuana enters the brain it affects the following regions and cause the following outcomes:

- Hippocampus/Hypothalamus> Regulates hunger> Leads to “munchies”, improves appetite, reduces nausea
- Hippocampus> Affects short-term memory> Leads to lack of memory
- Cerebellum> Coordination> Lack of coordination
- Amygdala> Regulates fear> Feeling paranoid
- Limbic System> Releases dopamine> Feelings of pleasure

Once in the brain, the cannabinoids hijack the brain's natural endocannabinoid receptors, CB1 and CB2. The endocannabinoid system is an incredibly important system in the body. It provides homeostasis for most organ systems in the body. The human body naturally produces endogenous cannabinoids, Anandamide (AEA) and 2-arachidonoyl glycerol (2-AG). These ligands attach to the body's endocannabinoid receptors, CB1 and CB2. There are CB1 receptors in the human nervous system, connective tissue, glands, gonads, and organs. The CB2 receptors are found in the immune system and associated structures. Marijuana has such a powerful effect on the human body because the molecular shape of THC and CBD closely approximates the body's own endogenous cannabinoids. THC and CBD can take over the systems that employ the cannabinoid receptors.

The endocannabinoid system is multifunctional. It works with human memory and learning, can impact anxiety and depression, affects appetite and addiction behavior, and provides neuro-protection. Marijuana can alter these systems by preventing or forcing out the endogenous cannabinoids, AEA and 2-AG, from binding to the receptors. There is potential risk to the function of these systems long-term from chronic Cannabis exposure, particularly when the systems are being formed in utero and the first years of life. Kenney et al. (1999) found that the placenta has CB1 and CB2 receptors. They suggested that marijuana use in pregnancy could potentially affect placental clearance of serotonin, which could have an impact on mood, sexual desire and function, appetite, sleep, memory and learning, temperature regulation, and some social behavior. Animal studies several decades ago showed that when THC was directly administered to rhesus monkeys, the THC readily passed the placenta to the fetus. The THC in the fetus did not seem to convert to the first THC metabolite, 11-nor-9-carboxy-THC (Bailey, 1987). While this study is old and not performed on human subjects, it leaves questions about the endocannabinoid role of the placenta, and how marijuana can impact the fetus.

The fetal endocannabinoid system exists in the preimplantation stage of the embryo. There are CB1 receptors detected at week 14 in the cerebral cortex, hippocampus, caudate nucleus, putamen and cerebellar cortex. In gestational week 20 there is intense receptor expression in amygdala and hippocampus. In early fetal and newborn life the endocannabinoid system modulates neuronal generation, differentiation, migration and neural circuit wiring during development. It is intricately involved in the development of the human brain. How marijuana interacts with this system in human fetal life, we don't have clear answers. However, in animal studies there is pretty clear indication that marijuana exposure in the fetal and newborn period can disrupt synaptogenesis, interrupt endocannabinoid signaling, and alter serotonin, opioid, and dopamine receptors so crucial to mood stability. The most significant development to CBR1 neural cell growth occurs in the zero to five-year period, and endogenous AEA may cause the necessary neural differentiation for proper brain development. Researchers speculate that there is the potential for future issues with pain perception, cognition, emotional regulation, and addictive behaviors for those babies exposed to chronic marijuana (Wu, 2011).

There have been only three longitudinal studies looking at the impact of prenatal and postpartum exposure of marijuana to the fetus/newborn. These are the Ottawa Prenatal Prospective Study (OPPS), the Maternal Health Practices and Child Development Study (MHPCD), and the Generation R Study (Gen R). The OPPS study started in 1978 in Canada and was assessing prenatal exposure of tobacco and marijuana in a low-risk, mainly Caucasian and middle-class cohort (Fried, 1987). The MHPCD began in 1982. It looked at prenatal alcohol and marijuana exposure in a cohort of low socioeconomic Caucasian and African-American women living in Pittsburg, Pennsylvania (Richardson, 2002). The Gen R Study was started in 2001 in the Netherlands and studied a multi-ethnic population focusing on cannabis use in both mothers and fathers (Marrun, 2009). With regard to birth weight, the studies all had differing results. OPPS showed no difference and Gen R showed reduced birth weight, while MHPCD actually showed increased birth weight after third trimester exposure. The OPPS study showed gestational age reduction with marijuana exposure. Both the MHCPD and Gen R showed growth restriction. MHPCD showed reduced birth length exposure after exposure in the first trimester and Gen R showed reduced fetal growth from 2<sup>nd</sup> trimester exposure.

In terms of infant behavior, only the OPPS study showed increased startles and tremors. It also found that exposure led to a reduced habituation to light and at 48 months the babies had lower memory and verbal skills. MHPCD also showed lower memory and verbal skills at 36 months. The OPPS and MHPCD both found more impulsivity and hyperactivity once the exposed babies became children (the Gen R has not studied this yet). Furthermore, the OPPS study also found that Cannabis exposed children had impaired visuo-perception function. MHPCD found increased inattention in exposed children. As far as adult behavior, only the OPPS study has published results on this aspect of prenatal marijuana exposure. They found as adults the exposed babies had response inhibition and an altered neural functioning

during visuo-spatial working memory processing. Although inconsistent, these clinical studies indicate that prenatal exposure to heavy marijuana use may have: little to no effect in early infancy, some specific cognitive or behavioral outcomes in childhood, and altered executive function in adolescence. The largest effects were seen with heavy users and in the Gen R study, results were dose dependent. While these studies all showed some potential impact from Cannabis use, they were not able to effectively control for factors of low income, poor nutrition, and smoking tobacco, as well as many other confounders. Most researchers today consider these studies to be of poor quality when considering the long-term impact of Cannabis use during pregnancy and breastfeeding.

What about marijuana and exposure through breastmilk? Due to the lipophilic nature of THC, it is tremendously fat-soluble and potentially can access breastmilk readily. Due to the fact that the levels of THC have been increasing in marijuana consumables, this is particularly concerning. How much THC does get in to breastmilk? There have been just two publications that addressed this, totaling only 4 mothers. The Perez-Reyes study found that a mother who smoked marijuana only once day had a breastmilk concentration of 105 mcg/L (Perez-Reyes, 1982). The other mother in the study smoked 7-8 times daily and had a concentration of 340 mcg/L. In the Marchei study, they looked at two users who smoked an unknown amount of marijuana and both had breastmilk concentrations of 86 mcg/L (Marchei, 2011). There is simply not enough information from these published studies to know for certain how much marijuana exposure leads to THC concentration in breastmilk.

Currently, Dr. Thomas Hale and Dr. Teresa Baker are starting a study at Texas Tech University to look at the transfer of THC into breastmilk. They are trying to determine the peak transfer times of THC. Hopefully this study will give health care providers better information to share with mothers who use cannabis and breastfeed. The team assumes that the active metabolites of THC when a mother smokes Cannabis will only be accessible for about 20-30 minutes in breastmilk, as previous studies looking at active metabolites in the bloodstream have only been shown for approximately 20 minutes after inhalation (Grotenhermen, 2003). After that, THC metabolites turn into non-active metabolites. Studies that have looked at how long THC stays active in the body after ingestion show a much longer period of time than smoking. It appears that ingestion allows THC to stay active for more than 10 hours in the human body. This could mean a much longer period of time that active THC could be transferred via breastmilk. If the Hale and Baker study show that only non active metabolites are in the breastmilk after 20 minutes of smoking Cannabis or 10 hours of ingesting Cannabis, perhaps health care workers can modify their counseling to encourage limited or restricted breastfeeding immediately after smoking (for at least 30 minutes) and for half a day after ingestion. Much more research needs to be done before one can come to these conclusions.

There are concerns that both prenatal exposure, as well as exposure through breastmilk, can have potential impact on the child. The zero through 3 period is a critical period of development for both the brain and the endocannabinoid system. Remember, too, that there are endogenous cannabinoids found in breastmilk that are important to the development of the newborn, something to consider when counseling mothers. There is some evidence found by Frideric that the CB2 receptor in humans does have a role in both a baby's ability to suckle and also in milk ingestion (Frideric 2008; Frideric, 2003). Delta 9 THC has been found to inhibit gonadotrophin, prolactin, growth hormone, and thyroid stimulating hormone release and stimulates the release of corticotrophin, which can potentially impact the quantity of breastmilk (Jaques, 2014). However, the duration of breastfeeding does not seem to be impacted.

Overall the potential risk for babies includes the following:

- Increase risk SIDS
- Positive urine screens
- Metabolites not found in human milk are found in infant feces (Perez-Reyes)
- Potential double exposure
- May cause epigenetic damage
- Potential for exposure to other drugs. Marijuana not always "clean".

Even though there are potential risks to the growing baby, what is not known is whether the negative consequences of not receiving breastmilk is more detrimental than that risk of slight THC exposure through breastmilk. In the United States, most healthcare organizations and researchers have come out with statements that support continuation of breastfeeding even if a mother uses cannabis. Lactmed states "...it appears preferable to encourage mothers who use marijuana to continue breastfeeding while minimizing infant exposure to marijuana smoke and reducing marijuana use." In *Cannabis, the pregnant woman and her child; weeding out the myths*, the researchers concluded that, "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." The updated Academy of Breastfeeding Medicine Protocol #21 advises healthcare professionals to counsel those who admit marijuana use and strongly advise those with a positive screen to avoid or reduce use, advise on long-term neurobehavioral risks, and avoid direct exposure of smoke to infant (ABM, 2015).

The key to successful counseling when working with mothers who may be using Cannabis during breastfeeding (or pregnancy) is to have open-ended conversations. Health care workers already have wonderful models for talking to parents about using substances of concerns in a manner that is advisory and not punitive. For example, we know that alcohol and cigarette are not ideal for the breastfeeding woman, and yet healthcare providers do not tell a woman that she has to stop

breastfeeding. The US Surgeon General's Call to Action to Support Breastfeeding asks health care providers to make the following considerations when counseling family on drug use:

- Benefit of drug for mother
- Impact of not taking med for mother and infant (Example: untreated maternal depression has negative impact on both mother and infant)
- Impact of drug on milk supply
- Quantity of drug infant receives
- Impact of drug exposure on infant
- **Risk of NOT breastfeeding**

It is always advised to use the three step counseling model – Ask, Affirm, and Counsel. The first step is asking open-ended questions. Ask about marijuana use with non-judgmental approach. Ask about the frequency and amount of use. Ask why she is using Cannabis, as there may be better alternative for pain or medical management during breastfeeding. Ask about who is caring for child when use occurs. Ask if mother is open to alternative forms of medication. The next step is to affirm her feelings. Assure the mother that she is not alone in her feelings. Let the mother know that her reasons for using are understood, but there are other options. Validate the mother's feelings without validating her choice of substance use. Finally offer appropriate counseling. Educate on potential risks of use, including the potential of having social service take the baby away if it has a positive urine screen. Talk to mother about alternatives during breastfeeding. Offer services/counseling/cognitive behavior therapy. Suggest specific screening for developmental milestone. Depending on chronic or occasional use, one can advise appropriately. It is always advised that health care workers look to their organization's policy on marijuana counseling.

Many who counsel families only see two options for those who use Cannabis and breastfeed: breastfeed and stop using Cannabis or quit breastfeeding. Dr. Larry Nice offers a continuum of options for general medications during breastfeeding that parents can discuss with their health care provider. While this continuum is designed for consideration of pharmaceuticals, it works well when counseling about marijuana use. The considerations (I have modified for this topic) include the following:

- Use Cannabis and continue to breastfeed
- Withhold Cannabis
- Try alternative nondrug therapy
- Delay therapy until after weaning
- Choose alternate drug that passes poorly into breast milk
- Choose more breastfeeding compatible dosage forms (unknown at this time)
- Choose an alternative route of administration (smoking may be better option than ingestion due to potential shorter THC availability, though need further studies to confirm this)

Not to be reproduced without permission. Copyright 2017 Laurel Wilson.

- Avoid nursing at times of peak drug concentrations in milk (based on little and poor data looking at blood serum, this may be 20 plus minutes for smoking and 10 plus hours for ingestion)
- Use Cannabis immediately after breastfeeding and/or before infant's longest sleep
- Temporarily withhold breastfeeding
- Discontinue breastfeeding (wean)

While marijuana is legal for recreational use and medicinal use, there is a grey area regarding fetal and newborn exposure. Positive THC tests in either the mother or baby have led to social services getting calls regarding infant drug exposure and risk to child safety. Even though there is little concrete evidence of absolute risk to child, some parents have had their lives turned upside down and some have even had their children placed into the foster care system. For families who may be dealing with these issues the following resources can be shared:

- Family Law and Cannabis Alliance [fcalliance.org](http://fcalliance.org)
- National Advocates for Pregnant Women [advocatesforpregnantwomen.org](http://advocatesforpregnantwomen.org)
- Elephant Circle [elephantcircle.net](http://elephantcircle.net)

Remember, that use does not equal abuse. We also need to keep in mind that the lack of quality data also does not necessarily mean that marijuana is safe. Parents have a right to the current information available, and deserve the right to act autonomously once they have made their decisions regarding Cannabis without punitive actions on behalf of healthcare workers considering the fact that most major organizations support breastfeeding even with use of Cannabis. Until there is more concrete data that offers clear indication of safety or risk, it is imperative to not undermine the breastfeeding relationship between a mother and child.

### **Questions or Requests for Speaking Engagements:**

[info@motherjourney.com](mailto:info@motherjourney.com)

[www.motherjourney.com](http://www.motherjourney.com)

720-291-9115

### **References:**

Abbey, James. Infant Risk Center website: BF and Marijuana Thread. Accessed Feb 4, 2015. <https://www.infantrisk.com/forum/showthread.php?1797-BF-and-marijuana>

Academy of Breastfeeding Medicine Protocol Committee. (2015). ABM Clinical protocol #21: Guidelines for breastfeeding and Substance Use or Substance Use Disorder. *Breastfeeding Medicine*, 10(3). DOI: 10.1089/bfm.2015.9992

American Academy of Pediatrics (2004). Legalization of marijuana: Potential impact

[info@motherjourney.com](mailto:info@motherjourney.com)

[www.motherjourney.com](http://www.motherjourney.com)

- on youth. *Pediatrics*, 113, 1825. Retrieved from <http://pediatrics.aappublications.org/content/113/6/1825.full.pdf+html>
- Astley SJ, Little RE. Maternal marijuana use during lactation and infant development at one year. *Neurotoxicol Teratol* 1990;12(2):161–8.
- Bailey, JR et al. Fetal disposition of  $\Delta$ 9-tetrahydrocannabinol (THC) during late pregnancy in the rhesus monkey. *Toxicology and Applied Pharmacy*. Volume 90, Issue 2, 15 September: 15-321. 1987.
- Benke et al. Prenatal Substance Abuse: Short- and Long-term Effects on the Exposed Fetus. AAP Technical Report, 2013. doi:10.1542/peds.2012-3931
- Committee on Obstetric Practice. **[Committee opinion no. 722: marijuana use during pregnancy and lactation](#)**. *Obstet Gynecol*. 2017;130:e205-e209.
- Cossu G, Ledent C, Fattore L, Imperato A, Bohme GA, Parmentier M et al. Cannabinoid CB1 receptor knockout mice fail to self-administer morphine but not other drugs of abuse. *Behav Brain Res* 2001; 118: 61–65.
- $\Delta$ 9-Tetrahydrocannabinol (THC), 11-Hydroxy-THC, and 11-Nor-9-carboxy-THC Plasma Pharmacokinetics during and after Continuous High-Dose Oral THC". *Clin. Chem*. **55**: 2180–9. December 2009. doi:10.1373/clinchem.2008.122119. PMC 3196989. PMID 19833841.
- Dreher, Melanie et al. Prenatal Marijuana Exposure and Neonatal Outcomes in Jamaica: An Ethnographic Study. *Pediatrics*. 1994; vol 93, No 2, pp. 254-260.
- EMCDDA. European Drug Report 2015: Trends and Developments. JUNE, 2015. <http://www.emcdda.europa.eu/publications/edr/trends-developments/2015>
- Fernandez-Ruiz, J et al. Cannabinoids and gene expression during brain development. *Neurotoxicity Research*. 2004; vol. 6, no. 5, pp. 389–401, 2004.
- Fried PA, Makin JE. Neonatal behavioural correlates of prenatal exposure to marijuana, cigarettes and alcohol in a low risk population. *Neurotoxicol Teratol*. 1987;9(1):1–7.
- Fride, E, T. Bregman, and T. C. Kirkham. Endocannabinoids and food intake: newborn suckling and appetite regulation in adulthood. *Experimental Biology and Medicine*. 2005; vol. 230, no. 4, pp. 225–234.
- Fride, E, A. Foxx, E. Rosenberg, et al. Milk intake and survival in newborn cannabinoid CB1 receptor knockout mice: evidence for a “CB3” receptor. *European Journal of Pharmacology*. 2003; vol. 461, no. 1, pp. 27–34.
- Fride, E. Multiple roles for the endocannabinoid system during the earliest stages of life: pre- and postnatal development. *Journal of Neuroendocrinology*. 2008; vol. 20, supplement 1, pp. 75– 81, 2008.
- Galve-Roperh I, et al. The endocannabinoid system and the regulation of neural development: potential implications in psychiatric disorders. *Eur. Arch*. 2009; *Psychiatry Clin. Neurosci*. 259(7), 371–382.
- Garry, A., Rigourd, V., Amirouche, A., Fauroux, V., Aubry, S., & Serreau, R. (2009). Cannabis and breastfeeding. *Journal of Toxicology*. Doi: 10.1155/2009/596149
- Gerrits MA, Lesscher HB, van Ree JM. Drug dependence and the endogenous opioid system. *Eur Neuropsychopharmacol* 2003; 13: 424–434.

- Ghozland S, Matthes HW, Simonin F, Filliol D, Kieffer BL, Maldonado R. Motivational effects of cannabinoids are mediated by mu-opioid and kappa-opioid receptors. *J Neurosci* 2002; 22: 1146–1154.
- Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. *Clin Pharmacokinet* 2003;42(4):327-60.
- Gunn JKL, Rosales CB, Center KE, et al. Prenatal exposure to cannabis and maternal and child health outcomes: a systematic review and meta-analysis. *BMJ Open*. 2016;6(4):e009986.
- Harkany T, Keimpema E, Barabas K, Mulder J. Endocannabinoid functions controlling neuronal specification during brain development. *Mol. Cell Endocrinol*. 286(1–2 Suppl. 1), S84–S90 (2008).
- Hale, TW. Infant Risk Center Website: marijuana and breastfeeding thread. Accessed Feb 4, 2015. <https://www.infantrisk.com/forum/showthread.php?192-marijuana-and-breastfeeding&highlight=Marijuana>
- Hale, T.. Medications and mothers' milk (2014). Amarillo, Texas: Hale Publishing.
- Hale, T., & Hartman, P. (2006). Textbook of Human Lactation. Amarillo, Texas: Hale Publishing.
- Hazekamp, Arno, et al. "The medicinal use of cannabis and cannabinoids—an international cross-sectional survey on administration forms." *Journal of psychoactive drugs* 45.3 (2013): 199-210.
- High Times Website. The Strongest Strains on Earth 2016. Accessed 2/2017. <http://hightimes.com/strains/the-strongest-strains-on-earth-2016/>
- Huestis, MA; Henningfield, JE; Cone, EJ (1992). "Blood cannabinoids. II. Models for the prediction of time of marijuana exposure from plasma concentrations of delta 9-tetrahydrocannabinol (THC) and 11-nor-9-carboxy-delta 9-tetrahydrocannabinol (THCCOOH)". *Journal of analytical toxicology* **16** (5): 283–90. doi:10.1093/jat/16.5.283. PMID 1338216.
- Huestis MA. Human cannabinoid pharmacokinetics. *Chem Biodivers*. 2007 Aug;4(8):1770-804. Review. PubMed PMID: 17712819
- Hill M, Reed K. Pregnancy, breast-feeding, and marijuana: A review article. *Obstet Gynecol Surv*. 2013;68:710-8. PMID: 25101905
- Huestis, M et al. Blood Cannabinoids. I. Absorption of THC and Formation of 11-OH-THC and THCCOOH During and After Smoking Marijuana. *Journal of Analytical Toxicology*. 1992; Vol. 16: 276-282. <http://www.canorml.org/healthfacts/drugtestguide/drugtestdetection.html>
- Jacques, SC et al. Cannabis, the pregnant woman and her child; weeding out the myths. *Journal of Perinatology*. 2014; 34, 417-424. doi:10.1038/jp.2013.180
- Jakabek, David, et al. "An MRI study of white matter tract integrity in regular cannabis users: effects of cannabis use and age." *Psychopharmacology* 233.19-20 (2016): 3627-3637.
- Johnson JR, Jennison TA, Peat MA, Foltz RL (1984). "Stability of delta 9-tetrahydrocannabinol (THC), 11-hydroxy-THC, and 11-nor-9-carboxy-THC in blood and plasma". *Journal of analytical toxicology* **8** (5): 202–4. doi:10.1093/jat/8.5.202. PMID 6094914.
- Jutras-Aswad D, DiNieri J, Harkany T, et al. Neurobiological consequences of

- maternal cannabis on human fetal development and its neuropsychiatric outcome. *Eur Arch Psychiatry Clin Neurosci* 2009;259:395–412
- Kenney, Sean et al. Cannabinoid receptors and their role in regulation of the serotonin transporter in human placenta. *American Journal of Obstetrics and Gynecology*. 1999;Vol 181(2), 491-497.
- Klonoff-Cohen H, Lam-Kruglick P. Maternal and paternal recreational drug use and sudden infant death syndrome. *Arch Pediatr Adolesc Med*. 2001;155:765-70. PMID: 11434841
- Kogan NM, Mechoulam R. Cannabinoids in health and disease. *Dialogues Clin Neurosci*. 2007;9(4):413-30. Review. PubMed PMID: 18286801
- Kurtz, J., Markoff, J., McNall, B., & Shimohara, S. (2011). 16 legal marijuana states and DC. Retrieved from [www.Procon.org](http://www.Procon.org)
- Lopez-Quintero C, Pérez de los Cobos J, Hasin DS, et al. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). *Drug Alcohol Depend* 2011;115:120-30.
- Marrun, H. et al. Intrauterine Cannabis Exposure Affects Fetal Growth Trajectories: The Generation R Study. *J. Am. Acad. Child Adolesc. Psychiatry*. 2009; 48:12.
- Marchei E, Escuder D, Pallas CR et al. Simultaneous analysis of frequently used licit and illicit psychoactive drugs in breast milk by liquid chromatography tandem mass spectrometry. *J Pharm Biomed Anal*. 2011. PMID: 21330091
- Moore DG, Turner JD, Parrott AC et al. During pregnancy, recreational drug-using women stop taking ecstasy (3,4-methylenedioxy-N-methylamphetamine) and reduce alcohol consumption, but continue to smoke tobacco and cannabis: initial findings from the Development and Infancy Study. *J. Psychopharmacol*. 2010; 24(9), 1403–1410.
- National Academies of Sciences, Engineering, and Medicine. 2017. The health effects of cannabis and cannabinoids: The current state of evidence and recommendations for research. Washington, DC: The National Academies Press. doi: 10.17226/24625.
- National Institute on Drug Abuse. NIDA Website DrugFacts: Marijuana. Accessed Feb 6, 2015. <http://www.drugabuse.gov/publications/drugfacts/marijuana>
- Nesto, Ricahard and Ken Mackie. Endocannabinoid system and its implications for obesity and cardiometabolic risk. *European Heart Journal Supplements*. 2008; 10 (Supplement B), B34–B41 doi:10.1093/eurheartj/sum052
- Perez-Reyes M, Wall ME. Presence of delta9-tetrahydrocannabinol in human milk [letter]. *N Engl J Med* 1982;307(13):819–20.
- Raber, Jeffrey C., Sytze Elzinga, and Charles Kaplan. "Understanding dabs: contamination concerns of cannabis concentrates and cannabinoid transfer during the act of dabbing." *The Journal of toxicological sciences* 40.6 (2015): 797-803.
- Ranganathan M, Braley G, Pittman B, et al. The effects of cannabinoids on serum cortisol and prolactin in humans. *Psychopharmacology (Berl)*. 2009;203(4):737-744.
- Richardson GA, Ryan C, Willford J, Day NL, Goldschmidt L. Prenatal alcohol and

- marijuana exposure: effects on neuropsychological outcomes at 10 years. *Neurotoxicol Teratol.* 2002;24(3):309–320.
- Rigucci, s. et al. Effect of high-potency cannabis on corpus callosum microstructure. *Psychological Medicine.* Cambridge University Press. 2015.  
doi:10.1017/S0033291715002342
- RobersonEK, PatrickWK, HurwitzEL. Marijuana use and maternal experiences of severe nausea during pregnancy in Hawai'i. *Hawaii J Med Public Health.* 2014;73(9):283-287.
- Rowe, Hilary et al. Maternal Mediation, Drug Use, and Breastfeeding. *Pediatr Clin N Am.* 2013; 60, 275–294 <http://dx.doi.org/10.1016/j.pcl.2012.10.009>
- Russo, E. Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. *British Journal of Pharmacology.* 2011; Volume 163, Issue 7, pages 1344–1364. DOI: 10.1111/j.1476-5381.2011.01238.x
- Schuel H, Burkman LJ, Lippes J et al. N-acylethanolamines in human reproductive fluids. *Chem Phys Lipids.* 2002;121:211-27. PMID: 12505702
- Substance Abuse and Mental Health Services Administration (SAMHSA), Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings, NSDUH Series H-48, HHS Publication No. (SMA) 14-4863. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2014.
- Sullivan, Nicholas, Sytze Elzinga, and Jeffrey C. Raber. "Determination of pesticide residues in cannabis smoke." *Journal of toxicology* 2013 (2013).
- Tennes K, Avitable N, Blackard C, et al. Marijuana: prenatal and postnatal exposure in the human. *NIDA Res Monogr* 1985; 59:48–60.
- Tortoriello G, Morris CV, Alpar A, et al. Miswiring the brain:  $\Delta$ 9-tetrahydrocannabinol disrupts cortical development by inducing an SCG10/stathmin-2 degradation pathway. *EMBO J* 2014;33:668-85.
- U.S. Department of Health and Human Services. *The Surgeon General's Call to Action to Support Breastfeeding.* Washington, DC: U.S. Department of Health and Human Services, Office of the Surgeon General; 2011.
- Valverde O, Noble F, Beslot F, Dauge V, Fournie-Zaluski MC, Roques BP. Delta9-tetrahydrocannabinol releases and facilitates the effects of endogenous enkephalins: reduction in morphine withdrawal syndrome without change in rewarding effect. *Eur J Neurosci* 2001; 13: 1816–1824.
- Varela-Nallar, L et al. Wnt signaling in the regulation of adult hippocampal neurogenesis. *Frontiers in Cellular Neuroscience.* 26 June 2013 | doi: 10.3389/fncel.2013.00100.
- Volkow, Nora et al. Adverse Health Effects of Marijuana Use. *The New England Journal of Medicine.* 2014; 370:2219-27. DOI: 10.1056/NEJMra1402309
- Volkow ND, Compton WM, Wargo EM. The Risks of Marijuana Use During Pregnancy. *JAMA.* 2017;317(2):129-130. doi:10.1001/jama.2016.18612
- Wang X, Dow-Edwards D, Anderson V, Minkoff H, Hurd YL. In utero marijuana exposure associated with abnormal amygdala dopamine D(2) gene expression in the human fetus. *Biol Psychiatry* 2004; 56: 909–915.
- Wang et al. Discrete opioid gene expression impairment in the human fetal brain associated with maternal marijuana use. *The Pharmacogenomics Journal.*

Not to be reproduced without permission. Copyright 2017 Laurel Wilson.

(2006) 6, 255–264.

Wei, Binnian, et al. "Sensitive Quantification of Cannabinoids in Milk by Alkaline Saponification–Solid Phase Extraction Combined with Isotope Dilution UPLC–MS/MS." *ACS Omega* 1.6 (2016): 1307-1313.

Western Australian Centre for Evidence Based Nursing & Midwifery.  
BREASTFEEDING GUIDELINES FOR SUBSTANCE USING MOTHERS. Webpage.  
Written January 2007. Accessed 2/1/2015.  
[https://punkmum.files.wordpress.com/2013/05/infant-feeding\\_guideline.pdf](https://punkmum.files.wordpress.com/2013/05/infant-feeding_guideline.pdf)

Wong et al. SOGC Clinical Practice Guideline: Substance Use in Pregnancy. *J Obstet Gynaecol Can* 2011;33(4):367–384.

Wu, Chia-Shan et al. Lasting impacts of prenatal cannabis exposure and the role of endogenous cannabinoids in the developing brain. *Future Neurol.* 2011; 6(4) pp 459- 480.