Impact of Marijuana on Pregnancy, the Fetus and Neonate

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Disclosures

I have nothing to disclose
Presentation Outline

- Overview of cannabinoids and how they work
- Prevalence and trends of cannabis use in U.S.
- Health and social consequences of cannabis use
- Long term consequences of cannabis use
- Prevalence of cannabis use during pregnancy
  - Impact of cannabis use during pregnancy
    - Longitudinal studies
    - Literature reviews
- CO’s Guidelines and Campaign Materials
Cannabinoids

Three forms of cannabinoids: phyto (plant), endo (within) and synthetic (manufactured)

There are >100 unique phytocannabinoids in the *Cannabis sativa* plant along with terpenes (entourage/ensemble effects) and more than 500 other chemicals when combusted

The most common is the intoxicating THC and the most medically promising for conditions such as epilepsy is cannabidiol (CBD) which is not intoxicating but is psychoactive.
How Cannabis Works

Endocannabinoids (Brain Derived)

Phytocannabinoids (Plant Derived)

Synthetic Cannabinoids (Made in Lab)

Endocannabinoid Receptors: CB1 & CB2

The endocannabinoid system (ECS) is involved in regulating a variety of physiological processes including appetite, pain and pleasure sensation, immune system, mood and memory.
Endocannabinoids are produced on demand. They travel back to the transmitting neuron to dampen further activity.

Anandamide is a partial agonist of CB1. 2-AG is a full agonist of both CB1 and CB2 receptors.

THC is a partial agonist of CB1 receptors.
How Cannabis Works

MENTAL BLOCK: A THC molecule binding to a cannabinoid receptor and suppressing the neuron’s ability to send messages.
Cannabinoid Receptors Are Located Throughout the Brain

How does THC affect behavior? It depends on where the CB receptors are in the brain.

<table>
<thead>
<tr>
<th>Brain Structure</th>
<th>Regulates</th>
<th>THC Effect on User</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amygdala</td>
<td>emotions, fear, anxiety</td>
<td>panic/paranoia</td>
</tr>
<tr>
<td>Basal Ganglia</td>
<td>planning/starting a movement</td>
<td>slowed reaction time</td>
</tr>
<tr>
<td>Brain Stem</td>
<td>information between brain and spinal column</td>
<td>antinausea effects</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>motor coordination, balance</td>
<td>impaired coordination</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>learning new information</td>
<td>impaired memory</td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>eating, sexual behavior</td>
<td>increased appetite</td>
</tr>
<tr>
<td>Neocortex</td>
<td>complex thinking, feeling, and movement</td>
<td>altered thinking, judgment, and sensation</td>
</tr>
<tr>
<td>Nucleus Accumbens</td>
<td>motivation and reward</td>
<td>euphoria (feeling good)</td>
</tr>
<tr>
<td>Spinal Cord</td>
<td>transmission of information between body and brain</td>
<td>altered pain sensitivity</td>
</tr>
</tbody>
</table>

The brain structures illustrated above all contain high numbers of CB receptors.
Cannabinoid Receptors Are Also Located Throughout the Body

Whole Body Distribution of CB1 Receptors (2, 25, and 100 min after injection of 11C-MePPEP)

PET images of [11C]-NE40 (CB2R radioligand)

Terry et al., Eur J Nucl Med Mol Imaging, 2010
Ahmad et al., Mol Imaging Biol 2013
Distribution of THC in the body.
# Clinical Pharmacokinetics of Cannabis

<table>
<thead>
<tr>
<th></th>
<th>Inhaled</th>
<th>Ingested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absorption</td>
<td>10-20%</td>
<td>1-10%</td>
</tr>
<tr>
<td>Onset of action</td>
<td>6-12 min</td>
<td>30-120 min</td>
</tr>
<tr>
<td>Peak effect</td>
<td>20-30 min</td>
<td>2-3 hr</td>
</tr>
<tr>
<td>Duration of effect</td>
<td>1-3.5 hr</td>
<td>5-8 hr or more</td>
</tr>
<tr>
<td>Toxic dose (THC)</td>
<td></td>
<td>15 mg/kg</td>
</tr>
<tr>
<td>Lethal dose (THC)</td>
<td></td>
<td>30 mg/kg</td>
</tr>
<tr>
<td>Half-life</td>
<td></td>
<td>28 hr (56 hr chronic use)</td>
</tr>
</tbody>
</table>
What is marijuana/cannabis?

- Dried flowering heads of the Cannabis sativa or indica plant cross breeds
- Known as: marijuana (in US legislation), cannabis, pot, weed, ganja, dank, 420, grass, dope, bhang, hashish
- Potency of principal psychoactive cannabinoid delta 9 tetrahydrocannabinol (THC) is generally higher than ever before (15-25%) and greatly differs by preparation technique with levels of cannabidiol (CBD) almost bred out of most strains
Synthetic Cannabinoids

First developed in 1980s by chemistry professor John Huffman to enhance understanding of the cannabinoid system (JWH-018)

Known as: spice, K2, fake weed, Yucatan fire, skunk, moon rocks, Black Mamba, crazy clown, Kronic, Kush, Joker

The synthetic cannabinoids are either sprayed on dried, shredded plant material so they can be smoked (herbal incense) or sold as liquids (liquid incense) to be vaporized and inhaled in e-cigarettes or other devices.

- Plant matter itself can potentially be poisonous or hallucinogenic
- Laced with flavors, rat poison, embalming fluids
Synthetic Cannabinoids

How used: 80% inhalation by smoking, 20% ingestion by eating or drinking as tea

7 main structural groups of synthetic cannabinoids:

- Naphthoylindoles (e.g. JWH-018, JWH-073 and JWH-398).
- Naphthylmethylindoles.
- Naphthoylpyrroles.
- Naphthylmethylindenes.
- Phenylacetylindoles (i.e. benzoylindoles, e.g. JWH-250).
- Cyclohexylphenols (e.g. CP 47,497 and homologues of CP 47,497).
- Classical cannabinoids (e.g. HU-210).

Many synthetic cannabinoids, e.g., JWH-018, are full and potent CB1 agonists and have a 4-fold higher affinity for CB1R and 10-fold higher affinity for CB2R, accounting for the higher prevalence of adverse reactions and toxicity.
Synthetic Cannabinoids

**Symptoms of Synthetic Marijuana Use**

**OVERALL SYMPTOMS**
- Increased Agitation
- Paranoid Delusions
- Depression
- Hallucinations
- Exaggerated Thoughts of Suicide
- Feeling of Impending Doom
- Panic Attacks
- Heart Attacks

**“Glazed” expression, red eyes**
- Psychosis
- Inability to Speak
- Body
  - Temperature Fluctuation, Inability to Feel Pain, Seizures
- Increased Blood Pressure and Heart Rate, Heart Attack
- Temporary Paralysis, Cramping
- Kidney Failure
- Vomiting

Please Call 911 IMMEDIATELY if you suspect someone has used Synthetic Marijuana!

Many of these symptoms may be life threatening and may change suddenly.

**Major Adverse Rxns:**
- Heart attack
- Ischemic stroke
- Acute kidney injury
- Generalized tonic-clonic seizures
- Rhabdomyolysis
- Cannabinoid-induced hyperemesis synd.
- Death
  - Prolonged QTc interval

Not detected on standard blood or urine tox screens
Cannabis: Most Commonly Used “Illicit” Drug in the U.S.

- Over **22 million** Americans 12 and older were past month marijuana users
- Approximately **4.0 million** Americans met criteria for cannabis use disorders in 2015
- An estimated **2.6 million** Americans used it for the first time; **1.2 million** were between the ages of 12 and 17
Nearly 6% report daily use of marijuana.
<table>
<thead>
<tr>
<th>Demographic</th>
<th>Past-Month Use Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>White, non-Hispanic</td>
<td>8.4</td>
</tr>
<tr>
<td>African-American</td>
<td>10.7</td>
</tr>
<tr>
<td>Hispanic</td>
<td>7.2</td>
</tr>
<tr>
<td>Asian, non-Hispanic</td>
<td>3.0</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>10.6</td>
</tr>
<tr>
<td>Female</td>
<td>6.2</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
</tr>
<tr>
<td>&lt; HS</td>
<td>8.2</td>
</tr>
<tr>
<td>HS graduate</td>
<td>9.1</td>
</tr>
<tr>
<td>Some college</td>
<td>10.5</td>
</tr>
<tr>
<td>College graduate</td>
<td>5.9</td>
</tr>
<tr>
<td><strong>Family income</strong></td>
<td></td>
</tr>
<tr>
<td>&lt; $10 k</td>
<td>13.6</td>
</tr>
<tr>
<td>$20 k - $29.9 k</td>
<td>9.7</td>
</tr>
<tr>
<td>$50 k - $74.9 k</td>
<td>7.8</td>
</tr>
<tr>
<td>$75 k +</td>
<td>6.6</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>12-17</td>
<td>7.1</td>
</tr>
<tr>
<td>18-25</td>
<td>20.1</td>
</tr>
<tr>
<td>26-34</td>
<td>13.0</td>
</tr>
<tr>
<td>35-49</td>
<td>7.1</td>
</tr>
<tr>
<td>50+</td>
<td>3.9</td>
</tr>
</tbody>
</table>
Trends Among Current **Cannabis** Users: Number of Days Used Cannabis in Past Month

- **42%** used 1 to 2 days
- **23%** used 3 to 5 days
- **15%** used 6 to 19 days
- **20%** used 20 or more days

2014 National Survey on Drug Use and Health
Marijuana Use in Past Month Among People 12 and Older, by Substate Region

Note: For substate region definitions, see the "2012–2014 National Survey on Drug Use and Health Substate Region Definitions" at http://www.samhsa.gov/data/.

Source: SAMHSA, Center for Behavioral Health Statistics and Quality, National Surveys on Drug Use and Health (NSDUHs), 2012 to 2014.
Marijuana Use in Past Month Among People 12 and Older in California, by Substate Region
Marijuana Use in Past Month & Perceived Risk of Great Harm from Use Among People Aged 12 or Older, Los Angeles County, 2012-2014

Marijuana use in past month

<table>
<thead>
<tr>
<th>SPA</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 &amp; 5</td>
<td>9.77%</td>
</tr>
<tr>
<td>2</td>
<td>8.03%</td>
</tr>
<tr>
<td>3</td>
<td>6.18%</td>
</tr>
<tr>
<td>4</td>
<td>10.50%</td>
</tr>
<tr>
<td>6</td>
<td>10.62%</td>
</tr>
<tr>
<td>7</td>
<td>7.00%</td>
</tr>
<tr>
<td>8</td>
<td>9.01%</td>
</tr>
</tbody>
</table>

Perceived great risk of harm from smoking marijuana once a month

<table>
<thead>
<tr>
<th>SPA</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 &amp; 5</td>
<td>21.44%</td>
</tr>
<tr>
<td>2</td>
<td>25.49%</td>
</tr>
<tr>
<td>3</td>
<td>34.66%</td>
</tr>
<tr>
<td>4</td>
<td>30.18%</td>
</tr>
<tr>
<td>6</td>
<td>32.00%</td>
</tr>
<tr>
<td>7</td>
<td>35.10%</td>
</tr>
<tr>
<td>8</td>
<td>27.35%</td>
</tr>
<tr>
<td>Status of State Medical Marijuana Laws</td>
<td></td>
</tr>
<tr>
<td>---------------------------------------</td>
<td></td>
</tr>
<tr>
<td><strong>Operational</strong></td>
<td></td>
</tr>
<tr>
<td>States that have passed laws to remove state-level criminal penalties on the use of medical marijuana by patients who are diagnosed with a debilitating illness. The programs in these states are up and running.</td>
<td></td>
</tr>
</tbody>
</table>

| **Not Yet Operational**                |
| States that have passed medical marijuana laws, but programs are not yet up and running. |

| **CBD-Specific**                      |
| States that have passed laws allowing for the use of cannabis extracts that are high in the non-psychoactive cannabinoid CBD, and low in THC, the psychoactive component of marijuana, to treat severe, debilitating epileptic conditions. |

| **Non-Functional**                    |
| The language of this law calls for a physician's 'prescription', which is illegal under federal law. Consequently, it remains to be seen whether any licensed physicians will agree to participate in the state's program. |
Impact of Medical Marijuana Laws

Illicit cannabis use among adults increased significantly more in states that passed MML than in other states (1.4% more; SE 0.5; \( p = .004 \)), as did cannabis use disorders (0.7% more; SE 0.3; \( p = .03 \))

Medical marijuana may help some; however, changing state laws (medical and recreational) may have adverse public health consequences
State Marijuana Laws

Information is current as of March 23, 2017.

Marijuana Legalization Status
- Medical marijuana broadly legalized
- Marijuana legalized for recreational use
- No broad laws legalizing marijuana
Trends in Routes of Administration

- 40% of 12th grade past-year users reported using cannabis in edible form in MML states vs. 26% in states without MML.

- In WA, an online survey of daily/near-daily users found that 27.5% used edibles, 22.8% used hash resin, and 20.4% “dabbed” in past week.

- In CO’s recreational market, herbal cannabis accounts for 56% of sales and sales of solid concentrates (24%) and edibles(13%) are on the rise.

- In WA, CO, and CA, a “standard dose” of THC is defined as 10 mg; in OR, it’s 5 mg.
Marijuana: Trends in Annual Use, Risk, Disapproval, and Availability
Grades 8, 10, 12

Use
% who used in last 12 months

Risk
% seeing "great risk" in using regularly

2016 Monitoring the Future Study
Average $\Delta^9$–THC Concentration of DEA Specimens by Year

Potency of cannabis judged based on THC content of preparation
Potency > 15% considered to represent “hard drug” in Holland
Cannabidiols lessen the psychoactive effects of THC. This means that a plant with a greater percentage of CBD has a lower potency.

Biol Psychiatry 2016; 79:613-619
Ratio of the Average Concentration of THC to CBD in DEA Specimens by Year, 1995-2014

CBD has been almost bred out of cannabis strains

Biol Psychiatry 2016;79:613-619
How is marijuana consumed?

- **Smoked**
  - cigarette (joint/spliff with or without tobacco)
  - pipe, a water pipe (bong/cone), or a hookah
  - hollowed-out cigar (blunt)

- **Vaporized**
  - heated plant material
  - heated oil or wax (dab)

- **Consumed orally**
  - baked goods or other food products (brownies, cookies, etc.)
  - beverages: tea, milk based products, soda, coffee etc
  - capsules (typically synthetic for pharmaceuticals e.g. dronabinol)

- **Other**
  - Topical
  - Pessaries
Dabbing

- Dabs are concentrated, wax-like doses of cannabis made using a solvent like butane or carbon dioxide.
- Popular because they can contain up to 90% THC.
- Dabs are sometimes called butane honey oil, budder, shatter or wax.
- Dabs are usually smoked using a water pipe (bong).

- Dabs are often placed onto a glass surface heated with blowtorch. The resulting smoke is inhaled.
Marijuana Edibles
An Introduction
Cannabis’ **Acute Effects** (Intoxication Phase)

- Euphoria
- Calmness
- Appetite stimulation
- Altered perception of time
- Heightened sensation
- Impaired coordination and balance
- Red eyes, dry mouth
- Increased heart rate: 20-100%
  - Some evidence of increased risk of heart attack, may be exacerbated in vulnerable individuals (e.g., baby boomers?)

- Orthostatic hypotension initially; then increased BP
- Increased risk of accidents (~2 fold), higher when combined with alcohol

JAMA 2014;370:23
Driving Related Impairments

Cannabis-related impairments detected in a range of skills used in driving:

- Tracking
- Reaction time
- Short-term memory
- Hand-eye coordination
- Time and distance perception
- Decision making
- Concentration
- Selective and divided attention
- Time estimation
- Executive function

Size of impairment dose-related

Impairments for 4+ hours ("don’t drive for five")
Cannabis Use and Overdose Injuries or Deaths

- Moderate evidence of a statistical association between unintentional cannabis ingestion and increased risk of overdose injuries including respiratory distress/failure and temporary coma, among pediatric populations in U.S. states where cannabis is legal. (edibles)

- Insufficient evidence to support or refute a statistical association between cannabis use and death due to cannabis overdose.

- CO law states that a single-serving edible cannabis product should contain no more than 10 mg of THC; however, currently available edible products, such as cookies or brownies, may contain as much as 100 mg of THC.

- Case report of teenager who died after jumping from fourth floor balcony after ingesting a cookie containing 65 mg of THC.

http://www.nap.edu/24625
Cannabis’ **Acute Effects** (Intoxication Phase)

- **Cognition**
  - Impaired short-term memory
  - Difficulty with complex tasks
  - Difficulty learning

- **Executive function**
  - Impaired decision-making
  - Increased risky behavior – STDs, HIV?

- **Mood (especially after high doses or edibles)**
  - Anxiety – panic attacks
  - Psychosis - paranoia
Myth: You can’t become addicted to cannabis

~9% of cannabis users become dependent
- 1 in 6 (17%) who start in adolescence
- 25-50% of daily users
Cannabis Use Disorder

A pattern of cannabis use leading to clinically significant impairment or distress that typically includes (DSM-5):

- Difficulty controlling or cutting down
- Craving
- Using more than intended
- Spending a lot of time on cannabis related activities
- Giving up or reducing activities in favor of cannabis
- Continuing to use despite physical/psychological problems
- Using in high risk situations
- Problems at work, school, and home related to use
- Tolerance
- Withdrawal syndrome upon cessation
Effects of Long-Term or Heavy Use

- Addiction
- Altered brain development*, teenage girls > boys
- Poor educational outcome, with increased likelihood of dropping out of school*
- Cognitive impairment, with lower IQ among those who were frequent users during adolescence*
- Diminished life satisfaction and achievement
- Symptoms of chronic bronchitis
- Increased risk of chronic psychosis disorders (including schizophrenia) in persons with a predisposition to such disorders

* The effect is strongly associated with initial marijuana use early in adolescence
Cannabis Associated Psychosis

Consistent increase in incidence of psychosis in people who have used cannabis

- Ever use increases the risk ~2-fold
  - Dose-response effect
- Age at first use < 15 years increases the risk 4-5-fold
- Heavy use or use of high THC potency increases the risk 6-fold

Continued cannabis use after onset of psychosis is associated with increased relapse rates, length of hospitalizations, and severity of symptoms of psychosis

JAMA Psychiatry 2016;73:1173-1179
Cannabis Associated Psychosis

- Having a close family member with schizophrenia is the strongest known risk factor for schizophrenia.
- Children and young adolescents with such a family history should not initiate cannabis use.
High Rates of Mood & Anxiety Disorders Among Respondents with Cannabis Dependence

J Clin Psychiatry 2006; 67:247-257
MARIJUANA AND PREGNANCY: WHAT'S THE RISK?
Prevalence of Cannabis Use During Pregnancy

- 3.6% rate reported by pregnant women when combining data from 2009 and 2010 (SAMHSA, 2013)
  - 10.7% in first trimester, 2.8% in second and 2.3% in third (SAMHSA, 2013)
- 5.2% of pregnant women aged 15-44 y reported past month use, based on data averaged across 2011 and 2012 National Survey on Drug Use and Health in U.S.
- SAMHSA’s National Survey of Drug Use and Health found that in 2015, 3.4% of pregnant women aged 15-44 had used cannabis in previous month.
- Most of the data reflect cannabis administered by smoking and not cannabis exposure through other routes of administration
Why the Concern about Cannabis Use and Pregnancy?

- THC crosses the placenta
- Most cannabinoids are metabolized in the liver, especially by cytochrome P450 mixed-function oxidases, mainly CYP 2C9
- Endocannabinoids play roles in a broad array of critical neurodevelopmental processes, from early neural stem cell survival and proliferation to the migration and differentiation of both glial and neuronal lineages as well as neuronal connectivity and synaptic function
- THC is secreted in breast milk and can accumulate to high concentrations
The prevalence of marijuana use during pregnancy was statistically higher among women:
- with an **unintended pregnancy** than among women who intended to become pregnant
- with **< HS education** than among women with some college
- **20-24** than among women 25-34 or women 35 and older
There was no statistical differences in marijuana use during pregnancy by race/ethnicity
Marijuana Use During Stages of Pregnancy in the United States, 2002-2015

- 6.44% used in first trimester, 3.34% in second trimester and 1.82% in third trimester
- Marijuana use was more than 2-fold higher among pregnant teens aged 12-17 (14%) than among their nonpregnant peers (6.4%)
Cannabinoids Endanger Fetal Development by Multiple Mechanisms

- Inhalation or ingestion of Cannabis product
  - leads to
  - Prolonged elevation of serum cannabinoid concentration
    - resulting in
      - Embryological or fetal exposure to cannabinoids
        - Which alters:
          - VEGF
          - Folic Acid
          - PCNA
          - MAPK (ERK/JNK/p38)
          - Cellular migration
          - CB1/CB2 activation
          - BDNF Pathway
        - Disrupting
          - Angiogenesis
          - Neurogenesis
          - Replication
          - Cellular development
          - Tissue differentiation
          - Cellular processes
          - Cognitive development

- Causes:
  - Impairment of fallopian motility
  - Ectopic pregnancy
  - Non-hatched or non-viable embryo
  - Decreased uterine receptivity
  - Spontaneous abortion

END RESULT
- Miscarriage
- Low birth weight
- Developmental delay
- Birth defects
- Other unknown complications

Corresponding Reference:
[1] Wang et al., 2006
[21] Pariah et al., 1995
[23] Pariah et al., 2001
[27] Sun and Day, 2008
[31] Wang et al., 2004
[32] Gebeh et al., 2013
[33] Wang et al., 2003
[36] Araujo et al., 2009
[40] Sefaraz et al., 2005
[41] Solinas et al., 2012
[49] Derkinderen et al., 2003
[52] Corson et al., 2003
Impact of Cannabis Use During Pregnancy on Child Development and Behavior

3 prospective longitudinal cohort studies

- Ottawa Prenatal Prospective Study (OPPS)
  Initiated in 1978 & involved a group of Caucasian, predominantly middle-class families (N=698)
  Fried, 2002

- The Maternal Health Practices & Child Development (MHPCD) study
  Commenced in Pittsburgh in 1982, based on a cohort of children of mostly African-American women from low SES (N=564)

- The Generation R study
  Started in 2001, consisted of a multi-ethnic cohort of mothers & children with a predominantly higher SES from Rotterdam (N=220)
  El Marroun, Tiemeier, Steegers, et al, 2009

All 3 studies began when women were pregnant and followed their children into early childhood (Gen R), adolescence (MHPCD), or early adulthood (OPPS)
Impact on Pregnancy, Fetal Development and Birth Outcomes

After controlling for maternal tobacco, alcohol, and other illicit drug use and various demographic covariates:

- No evidence of an association of cannabis use during pregnancy with miscarriage, birth defects, or PTB.
- Significant reduction of ~1 wk in GA of infants born to mothers in OPPS who used ≥6 times/wk
- Hypertelorism and severe epicanthus and 5-fold increase in features consistent with FAS in children of heavy cannabis-using mothers
- No impact on growth measures at birth seen
Impact on Pregnancy, Fetal Development and Birth Outcomes (continued)

In Gen R study maternal cannabis use during pregnancy associated with reduced fetal growth in mid and late pregnancy as well as LBW

A dose-response relationship seen

MHPCD study noted a small but significant negative relationship between cannabis use in first trimester and length of baby at birth.

In a study of a large cohort (n=24,874) of Australian women presenting for public prenatal care at a large hospital between 2000-2006, cannabis use during pregnancy was associated with LBW (OR 1.7; 95% CI 1.3-2.20); PTL (OR 1.5; 95% CI 1.1-1.9); SGA (OR 2.2; 95% CI 1.8-2.7); and admission to NICU (OR 2.0; 95% CI 1.7-2.4)

Hayatbakhsh, Flenady, Gibbons, et al., 2012
Effects on Neurocognitive Functioning

Neurocognitive and Behavioural Effects

<table>
<thead>
<tr>
<th>18 months</th>
<th>3–6 years</th>
<th>9–10 years</th>
<th>14–16 years</th>
<th>17–22 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased aggressive behaviour&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Deficits in:</td>
<td>Deficits in:</td>
<td>Deficits in:</td>
<td>Deficits in:</td>
</tr>
<tr>
<td>Attention deficits (females)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>- Verbal and perceptual skills&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>- Abstract and visual reasoning&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>- Visual-cognitive functioning&lt;sup&gt;a&lt;/sup&gt;</td>
<td>- Executive functioning&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>- Verbal reasoning&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>- Executive functioning&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>- Academic achievement&lt;sup&gt;b&lt;/sup&gt;</td>
<td>- Response inhibition&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>- Visual reasoning&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>- Reading&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>- Information processing speed&lt;sup&gt;b&lt;/sup&gt;</td>
<td>- Visuospatial working memory&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>- Verbal and quantitative reasoning&lt;sup&gt;b&lt;/sup&gt;</td>
<td>- Spelling&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>- Visual motor coordination&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Smoking&lt;sup&gt;ab&lt;/sup&gt;</td>
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<td>- Short-term memory&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>Hyperactivity&lt;sup&gt;ab&lt;/sup&gt;</td>
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<td>Hyperactivity&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>Attention deficits&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>Early initiation of substance use&lt;sup&gt;ab&lt;/sup&gt;</td>
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<td>Attention deficits&lt;sup&gt;ab&lt;/sup&gt;</td>
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<td>Impulsivity&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>Depressive and anxious symptoms&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>Impaired vigilance&lt;sup&gt;b&lt;/sup&gt;</td>
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Porath-Waller, AJ, Canadian Centre on Substance Abuse, 2015

Changes in Marijuana Use Patterns, Systematic Literature Review, and Possible Marijuana-Related Health Effects
# Findings Summary

Effects on exposed offspring of maternal marijuana use during pregnancy and breastfeeding

<table>
<thead>
<tr>
<th>Substantial Evidence</th>
<th>Moderate Evidence</th>
<th>Limited Evidence</th>
<th>Insufficient Evidence</th>
<th>Mixed Evidence</th>
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<td>Psychosis symptoms</td>
<td>Preterm delivery</td>
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<td>Decreased IQ scores in young children</td>
<td>SIDS (evidence of no association)</td>
<td>Breastfeeding and SIDS</td>
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<td>Decreased academic ability</td>
<td>Newborn behavior issues</td>
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<td>Breastfeeding and infant motor development</td>
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<td>Birth defects, including neural tube efeet, gastroschisis</td>
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<td>Frequency of use during adolescence</td>
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CO legalized recreational cannabis in 2012
1. There is no safe amount of marijuana use during pregnancy
2. THC can pass from mother to the unborn child through the placenta
3. The unborn child is exposed to THC used by the mother
4. Maternal use of marijuana during pregnancy is associated with negative effects on exposed offspring, including decreased academic ability, cognitive function, and attention. Effects may not appear until adolescence
5. THC can be passed from the mother’s breast milk, potentially affecting the baby
Marijuana Use During Pregnancy and Lactation

ABSTRACT: *Cannabis sativa* (marijuana) is the illicit drug most commonly used during pregnancy. The self-reported prevalence of marijuana use during pregnancy ranges from 2% to 5% in most studies. A growing number of states are legalizing marijuana for medicinal or recreational purposes, and its use by pregnant women could increase even further as a result. Because of concerns regarding impaired neurodevelopment, as well as maternal and fetal exposure to the adverse effects of smoking, women who are pregnant or contemplating pregnancy should be encouraged to discontinue marijuana use. Obstetrician–gynecologists should be discouraged from prescribing or suggesting the use of marijuana for medicinal purposes during preconception, pregnancy, and lactation. Pregnant women or women contemplating pregnancy should be encouraged to discontinue use of marijuana for medicinal purposes in favor of an alternative therapy for which there are better pregnancy-specific safety data. There are insufficient data to evaluate the effects of marijuana use on infants during lactation and breastfeeding, and in the absence of such data, marijuana use is discouraged.
ABM Clinical Protocol #21: Guidelines for Breastfeeding and Substance Use or Substance Use Disorder, Revised 2015

Sarah Reece-Stremtan,1,2 Kathleen A. Marinelli,3,4 and The Academy of Breastfeeding Medicine

A central goal of The Academy of Breastfeeding Medicine is the development of clinical protocols for managing common medical problems that may impact breastfeeding success. These protocols serve only as guidelines for the care of breastfeeding mothers and infants and do not delineate an exclusive course of treatment or serve as standards of medical care. Variations in treatment may be appropriate according to the needs of an individual patient.
Is it dangerous to use marijuana during pregnancy?

Just as alcohol crosses the placental barrier, so does THC. But does THC exposure damage the fetus?

The answer is: we don't know enough yet to be certain about all of the possible risks.

One thing that scientists do believe, however, is that regular marijuana use during pregnancy leads to babies born with reduced weight. Scientists are still looking into some other possible risks to the baby, including behavioral and developmental delays during the baby's first few months that may persist into childhood and adolescence.

During breast feeding, marijuana consumed by the mother is also consumed by the baby through mother's milk and may be harmful.

There's another possibility -- one having to do with the parents. For some people, getting high appears to interfere with their ability to reproduce.

DON'T RISK IT! Though we still have many unanswered questions about the risk of exposing your baby to marijuana, the risk is too great. Just don't do it -- don't get high if you're pregnant and don't get high while you are breastfeeding. Also, if you and your partner are unsuccessful in trying to get pregnant and either or both of you are getting high regularly, pot use might be getting in your way.

For more, see our Factsheet on Marijuana and Reproduction/Pregnancy.


Conclusions for Prenatal, Perinatal, and Neonatal Exposure

- There is **substantial evidence** of a statistical association between maternal cannabis smoking and:
  - Lower birth weight of the offspring
- There is **limited evidence** of a statistical association between maternal cannabis smoking and:
  - Pregnancy complications for the mother - anemia
  - Admission of the infant to the NICU
- There is **insufficient evidence** to support or refute a statistical association between maternal cannabis smoking and:
  - Later outcomes in the offspring (e.g., SIDS, cognition/academic achievement, and later substance abuse)
- The committee did not identify enough quality literature to comment on associations between breastfeeding and cannabis use

http://www.nap.edu/24625
Need More Contemporary Data!

Most studies done when potency of THC was much lower

- Now the average potency of THC in CO is 20% and rising
- Cannabis is stored in fat; we have an obesity epidemic

Impact of edibles?

Impact of synthetic cannabinoids on pregnancy unknown

- Longer half-life, higher affinity for receptors
- Could result in much higher levels in fetus

Impact of breastfeeding?
Synthetic Cannabis Use During Pregnancy

Anencephaly
Attention deficit hyperactivity disorder
Learning disabilities and memory impairment in toddlers and 10 yr olds
Neuropsychiatric conditions, such as depression, aggression, and anxiety in teens
Clinical Practice Guidelines
Marijuana Pregnancy and Breastfeeding Guidance for Colorado Health Care Providers

Pediatric exposure Prevention Clinical Guidance for Colorado Health Care Providers for Discussions with Children/Adolescents 9-20

Pediatric Exposure Prevention Clinical Guidance for Colorado Health Care Providers for Discussions with Parents/Guardians of Children/Adolescents Ages 0-20
CO Offered Free Training for Their Professionals

Welcome to TRAIN, the premier learning resource for professionals who serve the citizens of Colorado. A free service of the Public Health Foundation, www.train.org is part of the newly expanded TrainingFinder Real-time Affiliate Integrated Network (TRAIN).

Through this site, you can:

- Quickly find and register for many courses listed on Train.org and participating TRAIN affiliate sites,
- Track your learning with personal online transcripts,
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CO.TRAIN - LMS Software by KMI Learning
“Women trust YOUR knowledge”

Healthcare providers and the internet are the most trusted sources for information about marijuana use during pregnancy or while breastfeeding.

What Women Want to Know:
1. Side effects as far as development and growth
2. Long-term health effects for their babies
3. How THC is passed/stored in their baby’s body
Colorado’s Recommendations

- Screen for marijuana use at all well woman visits, prenatal visits, delivery and postpartum visits
- Talk about marijuana use and encourage cessation before pregnancy or early in pregnancy
  - Educate patients on potential risk
- Discuss plans for breastfeeding early in pregnancy
Motivational Interviewing

Can you tell me about why you are using marijuana? How does it help you?
Do you want to stop using marijuana?
How difficult do you think it will be to stop using marijuana?
Do you think you can stop?
Talking to Patients: Effects

No known safe amount of use during pregnancy

Associated with negative effects on exposed children:

- Decreased cognitive function
- Decreased attention
- These effects may not appear until adolescence

Language for patients:

*Using marijuana while pregnant may harm your baby. It may make it hard for your child to pay attention and learn, and make it harder for him to do well in school.*
Talking with Patients: Medical Marijuana

The decision to continue medical marijuana use during pregnancy and/or breastfeeding is based on whether the benefits outweigh the potential risks to the baby

If using marijuana to treat a medical issue:
- Talk to your patients about safer treatments

If patient is using marijuana for nausea, anxiety, or sleep:
- Talk to your patients about safer ways to deal with these issues
Testing

Marijuana is legal for adults over 21 – but this doesn’t mean it is safe for pregnant moms or babies.

Some hospitals test babies after birth for drugs. If your baby tests positive for THC at birth, Colorado law says child protective services **must** be notified.

If you are concerned about a patient’s substance use, you can recommend testing a mother during prenatal care and/or delivery.

**Testing Information**

- Meconium testing generally identifies maternal marijuana use after 24 wk GA.
- Urine testing generally identifies maternal marijuana use after 32 wk GA.
- Umbilical cord testing generally identifies maternal marijuana use after 24 wk GA.
Colorado’s Recommended Practice Flow

Incorporate marijuana screening into alcohol, drug, and tobacco screening practice flow

Screen at every visit:
- Patient’s use
- Partner’s use
- Caregiver’s use
- Safe use and storage

Based on patient response, counsel on safe alternatives, treatment resources, and/or safety

Determine appropriate f/u based on screening results and discussion

For CPT and ICD-10 codes see Billing attachment

Safe Alternatives

- If using for nausea, try:
  - Change type of food or eating schedule; multiple forms of ginger and lemon; lemonade; drink plenty of water; anti-nausea compression bands; acupuncture

- If using for anxiety/depression:
  - Medication; professional talk therapy; yoga; breathing exercises; acupuncture

- If using for sleep, try:
  - Relaxation techniques, aromatherapy; pillows; well-timed food and exercise; supplements that support sleep

Treatment

- SBIRT: screening, brief intervention, referral to treatment
- CUDIT-R: cannabis use disorder identification test – revised
- CRAFFT: cannabis assessment for youth < age 21

- CO Substance Use Disorder Treatment Referral Line
Finding Drug/Alcohol Treatment

Nationally

Los Angeles County

- Call Community Assessment Service Center at **1-800-564-6600**
- There is at least one CASC in each SPA
- Specify if patient is pregnant so she can be referred to a Perinatal Program

New Drug Medi-Cal system starts **7/1/17**.

https://findtreatment.samhsa.gov/
Marijuana was the primary drug of concern for 17% of TEDS (treatment episode data set) admissions aged 12 and older in 2012.

The average age at admission for primary marijuana admissions was 25 yr, the most common age at admission for both genders in all race/ethnicities was 15-17 yr.

39% of marijuana admissions were under age 20 (vs. 10% of all admissions).

- 27% first used marijuana by age 12 & 32% by age 14.

85% received ambulatory treatment compared with 61% of all admissions combined.
CO Public Education Campaign

Campaign objectives

Provide **educational information** about health effects and risk associated with using retail marijuana during pregnancy and breastfeeding to empower women to make informed decisions.

Help **encourage conversations** between women and their healthcare providers and provide resources to support a positive, open and honest conversation.
Spectrum of Risk

- Salty foods
- Going in a hot tub
- Caffeine
- Lifting heavy items
- Sugar
- Impact sports
- No sleep
- Stress
- Minimal prenatal care
- Poor diet
- Heat
- Marijuana
- Domestic violence
- Tobacco
- Hard drugs
- Alcohol

Low Risk

High Risk
Be safe. Be educated. 
BE RESPONSIBLE.

Marijuana is legal in Colorado.
But if you choose to use, there are a few things you need to know.

LEARN BEFORE YOU USE
LEARN the LAWS

Marijuana in Colorado is legal. But that doesn't mean you can use it anywhere you want.

You must be over 21

In order to purchase, possess or use retail marijuana in Colorado, you must have a valid ID proving you're 21 or older. It's that simple.
Safe storage of marijuana products, especially edibles!
How Marijuana Affects Pregnant & Breastfeeding Women

Here's what you need to know in order to make the healthiest choices for you and your baby.
Fact sheets for patients, clients

Fact sheets available in multiple languages

Download at Colorado.gov/marijuana

- Spanish
- Korean
- Vietnamese
- Chinese
- Somali
- Arabic

MARIJUANA AND YOUR BABY

Marijuana is now legal for adults over 21. But this doesn't mean it is safe for pregnant or breastfeeding moms and babies. There is no known safe amount of marijuana use during pregnancy. You should not use marijuana while you are pregnant, just like you should not use alcohol and tobacco. Tetrahydrocannabinol (THC) is the chemical in marijuana that makes you feel “high.”

Using marijuana while you are pregnant passes THC to your baby.

KNOW THE FACTS

Marijuana and pregnancy

IS SMOKING MARIJUANA BAD
Brief Review

- Overview of cannabinoids and how they work
- Prevalence and trends of cannabis use in U.S.
- Health and social consequences of cannabis use
- Long term consequences of cannabis use
- Prevalence of cannabis use during pregnancy
- Impact of cannabis use during pregnancy
  - Longitudinal studies
  - Literature reviews
- CO’s Guidelines and Campaign Materials
QUESTIONS?