Marijuana and pregnancy – our local experiment

What is marijuana?
Types Of Weed

Marijuana and pregnancy – our local experiment

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What is marijuana?

SATIVA

INDICA

RUDERALIS

These are the 5 main cannabinoids found in marijuana (out of 85)

Cannabinoid receptors
and Placenta…..

Endogenous cannabinoids

Mechanism of action

The Human Endocannabinoid System

CB1 receptors
mainly localized in the brain (hippocampus, cerebellum and cerebrum)

CB2 receptors
mainly situated in the periphery (spleen, tonsil and immune cells)

Endogenous cannabinoids

Neurotransmitters

Activity

Receptor

CB1

CB2

THC

2-AG

Andromedan

CBDA

CBN

THCA

CBD
Passage to fetus and breast milk

- In bloodstream within seconds and brain within minutes of inhalation
- Highly lipophilic with a tissue half life of 7 days
- Cord blood levels found positive (3-6 times lower than maternal)
- Fetus receives a proportionally smaller dose than mother and neonatal urine tests positive
- Bound to proteins in breast milk
- Neonatal exposure 0.8% of mother’s exposure

Fetal implications

- In animal studies fetal levels of THC are 10% lower than maternal levels (90% of maternal levels)
- Repeated dosing results in progressively higher levels in the fetus (concentration)
- CB1 receptors found in fetal brain in embryological period

Potential concerns

Box 3
Possible pregnancy-related effects of prenatal marijuana use

- Decreased male fertility
- Decreased ovulation
- Altered hormones (prolactin, follicle-stimulating hormone, luteinizing hormone, estrogen)
- Altered placental transport, embryo implantation, and maintenance of pregnancy
- Altered placental blood flow
- Intrauterine growth restriction
- Decreased gestational age
- Decreased birth weight

Youth Risk Behavior

Prevalence in the pregnant population

<table>
<thead>
<tr>
<th>Year</th>
<th>Total</th>
<th>Marijuana</th>
<th>Reporting</th>
<th>MDA</th>
<th>End</th>
<th>Start</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>537</td>
<td>106</td>
<td>39</td>
<td>36</td>
<td>12</td>
<td>219</td>
<td>537</td>
</tr>
<tr>
<td>2011</td>
<td>410</td>
<td>87</td>
<td>29</td>
<td>25</td>
<td>4</td>
<td>174</td>
<td>410</td>
</tr>
</tbody>
</table>

5.2% = 115,000 pregnant women using marijuana annually 2011-2012

More women using marijuana are seeking and receiving substance abuse treatment in pregnancy


Effect of legalization

- States that have legalized MMJ have higher usage rates
- Home growth is correlated with higher heavy usage rates
- Seen as “safe” compared to alcohol and tobacco
- As price falls we can expect to see even greater usage

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Prevalence and patterns of marijuana use among pregnant and non-pregnant women of reproductive age – AJOG 2015

- More than 1 in 10 pregnant and non-pregnant women reported using marijuana in the past 12 months.
- A considerable percentage of women who used marijuana in the past year were daily users, met abuse and/or dependence criteria, and were poly-substance users.
- Comprehensive screening, treatment for use of multiple substances, and additional research and patient education on the possible harms of marijuana use are needed for all women of reproductive age.

Why would a pregnant mom use marijuana?


<table>
<thead>
<tr>
<th>Table 4. Reasons for marijuana use¹</th>
<th>Ever users</th>
<th>Current users</th>
<th>Past users</th>
</tr>
</thead>
<tbody>
<tr>
<td>To help with depression/boredom</td>
<td>35%</td>
<td>63%</td>
<td>28%</td>
</tr>
<tr>
<td>To help with pain</td>
<td>29%</td>
<td>60%</td>
<td>21%</td>
</tr>
<tr>
<td>To help with nausea/vomiting</td>
<td>23%</td>
<td>48%</td>
<td>17%</td>
</tr>
<tr>
<td>For fun/recreation</td>
<td>59%</td>
<td>39%</td>
<td>65%</td>
</tr>
<tr>
<td>Other reason</td>
<td>16%</td>
<td>14%</td>
<td>16%</td>
</tr>
</tbody>
</table>

¹Other reasons (write in responses) included: sleep, cancer, seizures, migraines, and increased appetite. A couple of direct quotes from respondents were:

"To help with nausea and vomiting in first trimester of pregnancy"  
"All the reasons above and plus when I was pregnant, it helped me want to eat..."

44% of self reporting low income women reported that marijuana costs less than cigarettes

Average amount spent $6 to $10 per day

Easy to get and seen as safe...
Marijuana and Pregnancy - Martin Walker

**It's not your mother's marijuana**

- 1970’s to 2000: 6 to 7 fold increase in potency of seized MMJ (%THC)
- 1993 to 2008: Mean concentration of THC rose from 3.4% to 8.8%
- Consumption has increased as joints are replaced by blunts (Swisher Sweets skins filled with weed): 1.5 x more MMJ than a joint and 2.5 x more MMJ than a pipe

**Relatively unstudied**

- The Ottawa Prenatal Prospective Study (OPPS). 1978. Middle class, low risk, Caucasian population.
- N=698
- Recruited mostly in second trimester
- Data collected on ETOH, tobacco and cannabis use during pregnancy

**The Ottawa Prenatal Prospective Study**

- Initiated in 1970’s
- Sample: Low risk, European-American, middle class
- N=698
- Recruited mostly in second trimester
- Data collected on ETOH, tobacco and cannabis use during pregnancy
- Of the original cohort two comparative groups were selected for follow up:
  - 140 with any use of cannabis or .85 oz of ETOH or at least 16mg nicotine per day
  - 50 with no substance use in pregnancy
Marijuana and Pregnancy - Martin Walker

**OPPS Cannabis use**
- Cannabis use
  - None
  - Mild/moderate: up to 6 joints per week (n=37)
  - Heavy: at least 6 joints per week (n=25)

**OPPS follow up**
- Follow up to 18-22 years of age
- N=49 of any cannabis exposed offspring left by 18-22

**Maternal Health Practice and Child Development Study**
- Initiated 1982
- High risk, low SEC, mixed ethnicity
  - 57% African American
  - 71% single
- N=1360 women in the 16th week interviewed at inner city clinic in Pittsburgh
- Women using 2 or more joints per week selected for study
- Equal number of randomly selected women from the remainder chosen as a comparison group
- Total n=564

**MHPCD Cannabis use**
- Expressed as average daily joints for each trimester.
  - Heavy use: 1 or more joints per day
    - First trimester n=103
    - Second trimester n=54
    - Third trimester n=37
  - Light to moderate use: 1 to 6.9 joints per week
    - First trimester n=176
    - Second trimester n=180
    - Third trimester n=93
- Follow up to age 14 (including 79 of the heaviest first trimester exposed fetuses)

**Generation R Study**
- Initiated in 2001
- Multi-ethnic (Dutch, Surinamese, Turkish, Moroccan
- Rotterdam
- 9778 mothers enrolled
- Follow up to age 6 yrs: >80%
- 220 women used cannabis in pregnancy
  - 177 first trimester only
  - 44 throughout pregnancy
  - 30% daily use (= heavy use)
  - 25% weekly use (= moderate use)
  - Compared to tobacco exposed and non exposed
  - Highest levels of THC

**Confounding issues**

<table>
<thead>
<tr>
<th>Prenatal drug use</th>
<th>Socioeconomic status</th>
<th>Mental status</th>
<th>Parity</th>
<th>Prenatal care</th>
<th>Psychological distress</th>
<th>Quality of home environment</th>
<th>Race</th>
<th>Cognitive ability</th>
<th>Years of education</th>
</tr>
</thead>
</table>
Marijuana and Pregnancy - Martin Walker 9/14/15

Self reported current substance abuse

Teratogenicity

- Early reports suggested association with anencephaly
- No evidence of marijuana associated fetal teratogenicity

Growth

- 2005 termination 17-22 weeks. No association of prenatal MMJ with smaller HC or AC measurements
- Gen R study: Reduced fetal growth from T2 onwards – dose related
  - 156g average – T1 only
  - 277g average – throughout pregnancy
- OPPS: Reduced gestational age (5.6 days) but no effect on weight
- MPHCD: Increased BW after T3 exposure (142g)

Inconsistent findings though fetal growth may be reduced from mid-pregnancy onwards – especially with higher THC

Neonatal behavior

- Withdrawal has not been reported
- OPPS: Increased startle and tremor 1st week of life
- MHPCD: Altered sleep patterns
- Gen: No effect
- No consistent pattern of adverse effect

Infant behavior and development

- OPPS
  - did not yield significant association between exposure and 24m development
  - Memory and some verbal scores lower in heavily exposed infants at 48m
  - Motor skills more advanced in moderately exposed infants at 36m
- MPHCD
  - No relation between exposure and motor and mental development at 19m
  - In African Americans only, prenatal exposure related to lower scores on short term memory functioning and verbal reasoning
- Generation R
  - No evidence of association between exposure and non-verbal cognition scores at 18m and 36m
  - Girls only at 18m had higher aggression and inattention scores

Little evidence for a negative effect

Child behavior and development

- OPPS and MPHCD: worse scores on memory and verbal scores
- OPPS: negative effect on attentiveness
- MPHCD: increased impulsivity

Box 4
Finding in areas of development in prenatal marijuana exposure
1. Minimal, inconsistent effect on general cognition[5, 76]
2. Altered sleep patterns[7]
3. No effect on language[59, 41, 47]
4. Minimal effect on motor development[5, 44, 18, 78, 79]
5. Minimal effects on growth and puerperal development[47, 79]
Child behavior and development

- OPPS and MHPCD are only studies analyzed beyond infancy
- More symptoms of externalizing behavior at age 6yr and 10yr
- More delinquency in the high risk MHPCD group

Asking patients about marijuana
The Law

- 17 states consider substance abuse during pregnancy to be child abuse
- 3 states consider it grounds for involuntary commitment

Lactation

- Not much data. No long term studies
- MMJ excreted into breast milk in levels up to 8 times higher than maternal blood
- Delta 9-THC inhibits gonadotrophin, prolactin, growth hormone and TSH and thus may inhibit breast milk production
- AAP recommend against breastfeeding
  - (AAP Committee on Drugs. Pediatrics 1994)
Genetic susceptibility

- Animal evidence of genetic susceptibility
- Chronic use before 16 years of age changes volume of caudate nucleus in users with specific catecholamine-O-methyl transferase gene polymorphisms
- Neuropsychopharmacology 2012
- Area for future research.....

Anesthetic implications

- Biphasic effect on autonomic nervous system
  - Low/moderate
    - Increased sympathetic activity
    - Tachycardia
    - Increased cardiac output
  - High doses
    - Increased parasympathetic activity
    - Bradycardia
    - Hypotension
- Reversible ST segment and T wave abnormalities reported as well as myocardial depression
- Adverse interactions with propranolol and physostigmine reported

Summary

- Evidence is inconclusive
- Subtle effects on attention, executive functions and behavior especially in adolescence
- Increasing potency and usage will need ongoing evaluation
- Criminalization and the converse assumption of safety complicates counseling

Professional Recommendations

- Evidence is inconclusive
- Subtle effects on attention, executive functions and behavior especially in adolescence
- Increasing potency and usage will need ongoing evaluation
- Criminalization and the converse assumption of safety complicates counseling

Colorado WIC MJ use

Table 3. Timing of marijuana use during most recent pregnancy among ever, current, or past marijuana users

<table>
<thead>
<tr>
<th></th>
<th>Ever users</th>
<th>Current users</th>
<th>Past users</th>
</tr>
</thead>
<tbody>
<tr>
<td>Used marijuana during pregnancy</td>
<td>10.9%</td>
<td>35.8%</td>
<td>4.5%</td>
</tr>
<tr>
<td>Used marijuana since the baby was born</td>
<td>9.8%</td>
<td>41.3%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Used marijuana while breastfeeding</td>
<td>3.0%</td>
<td>13.7%</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

1 Percent of WIC mothers in the marijuana user group
Use in adults in CO and surrounding states

<table>
<thead>
<tr>
<th>State</th>
<th>Estimate</th>
<th>95% CI</th>
<th>Estimate</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorado</td>
<td>14.79</td>
<td>14.08-15.50</td>
<td>7.43</td>
<td>7.12-7.77</td>
</tr>
<tr>
<td>New Mexico</td>
<td>12.71</td>
<td>12.01-13.41</td>
<td>7.64</td>
<td>7.21-8.08</td>
</tr>
<tr>
<td>Utah</td>
<td>9.95</td>
<td>8.37-11.53</td>
<td>5.81</td>
<td>4.96-6.64</td>
</tr>
<tr>
<td>Idaho</td>
<td>12.70</td>
<td>11.92-13.48</td>
<td>6.46</td>
<td>5.71-7.21</td>
</tr>
<tr>
<td>Montana</td>
<td>8.38</td>
<td>7.41-9.36</td>
<td>3.98</td>
<td>3.50-4.46</td>
</tr>
</tbody>
</table>

Marijuana Use During Pregnancy and Breastfeeding
Systematic Literature Review

Retail Marijuana Public Health Advisory Committee
Final Approval: January 12, 2015

Public Health Statements
Public health statements are plain-language translations of the major findings (Evidence Statements) from the systematic literature review. These statements have been officially approved by the Retail Marijuana Public Health Advisory Committee.

1. There is a known fetal exposure 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 the newborn and breastfeeding.
5. These effects may be seen as early as adolescence.
6. Marijuana use during pregnancy increases the risk of heart defects in the child.
7. There is insufficient evidence for whether or not marijuana use during pregnancy is associated with increased risk of stillbirth.
8. There are negative effects of marijuana use during pregnancy on the newborn and breastfeeding.
9. There are negative effects of marijuana use during pregnancy on the newborn and breastfeeding.
10. THC may be passed from the mother’s breast milk, potentially affecting the baby.
Figure 1: Rates of Hospitalizations (HD) and Emergency Department (ED) Visits with Perinatal Marijuana Exposure* in Children Up to 9 Years Old Out of 100,000 HD and ED Visits in Children Under 9 Years Old by Time Period in Colorado.

- HD Visits
- ED Visits

<table>
<thead>
<tr>
<th>Time Period</th>
<th>HD Visits</th>
<th>ED Visits</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>1.2</td>
<td>NA</td>
</tr>
<tr>
<td>2001-2009</td>
<td>1.3</td>
<td>NA</td>
</tr>
<tr>
<td>2010-2013</td>
<td>5.9</td>
<td>7.0</td>
</tr>
<tr>
<td>Jan-Jun 2014</td>
<td>5.5</td>
<td>26.4</td>
</tr>
</tbody>
</table>

*Perinatal marijuana exposure includes exposure to marijuana before or during pregnancy.