Substance Use in Pregnancy and Breastfeeding

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- Colleagues from PRIMA (Pregnancy Related Issues in the Management of Addiction)

- Patients and their families
Objectives

- Identify the evidence related to substance use in pregnancy and breastfeeding focusing on cannabis, cocaine and opiates

- Discuss challenges in addressing substance use in pregnancy and breastfeeding focusing on cannabis, cocaine and opiates

- Apply techniques learned in day to day clinical care of women of reproductive age focusing on cannabis, cocaine and opiates
Marijuana Use in Women

SAMSA, NSDUH, 2013; Statistics Canada, 2015

- **US data: 2013 NSDUH study**
  - Non-pregnant (past-month 15-44): 8.9%
  - Pregnant (past-month 15-44): 4.9%

- **Canadian data: 2013 Canadian Tobacco, Alcohol and Drugs Survey (CTADS) study**
  - All Canadians (Past year use; 15+): 10.6%
  - Youth (Past year use: 15-19): 22.4%
  - Young adults (Past year use: 20-24): 26.2%

- Approximately 28% of Canadians aged 15 and older who used cannabis in the past three months reported that they used this drug every day or almost every day.
The THC & CBD Debate

*Zuardi, 2012; **Nagarkatti, 2009; Esposito, 2013

- Δ-9-Tetrahydrocannabinol (THC)
  - Binds to CB1 and CB2 receptors
  - ↑Dopamine – which reinforces use
  - Stimulant & depressant, some pain relieving
  - Psychotropic – psychosis, paranoia, anxiety
  - Produces a withdrawal syndrome in 25% of people

- Cannabidiol (CBD) – not psychoactive
  - Protective against psychosis*
  - Anti inflammatory**
  - As THC content goes up, CBD goes down
  - In 1960s marijuana had 2-3% THC and CBD
  - Now THC can be up to 25%+ & CBD near 0

- NO quality control on THC or CBD at dispensaries or off the street, and only on THC(9%) when federally endorsed source

Adapted from Rieb, 2017
Label Accuracy in Edible Medical Cannabis Products: Buyer Beware
Vandrey et al., JAMA 2015

- 75 products randomly selected & tested 47 brands in shops in LA, SF, and Seattle

- THC accurately labeled in 17%
  - 60% over-labeled, 23% under-labeled

- 44 products had detectable CBD on testing
  - 13 of these were labeled

- CBD accurately labeled in 0%
  - 4 products over-labeled, 6 under-labeled

- Mean THC:CBD ratio was 30:1

Adapted from Rieb, 2017
<table>
<thead>
<tr>
<th>Intoxication</th>
<th>Withdrawal</th>
<th>Route</th>
<th>Fetal/ Neonatal/ Child</th>
<th>Breastfeeding</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachycardia</td>
<td>Fatigue</td>
<td>Inhaled - joint - pipe - bong</td>
<td>Teratogenicity*</td>
<td>Contra-indicated</td>
<td>Abstinence</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>Yawning</td>
<td>Oral - food - tea</td>
<td>Decreased fetal growth</td>
<td>(no safety data available)**</td>
<td>Nabilone (Cesamet®)</td>
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<tr>
<td>Hypertension</td>
<td>Hypersomnia</td>
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<td>Preterm birth</td>
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<td>(harm reduction)</td>
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<td>Red eye</td>
<td>Psychomotor retardation</td>
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<td>Miscarriage</td>
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<tr>
<td>Dry mouth</td>
<td>Anxiety/Depression</td>
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<td>Stillbirth</td>
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<tr>
<td>Increased appetite</td>
<td>Hypersomnia</td>
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<td>Neonatal tremors</td>
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<tr>
<td>Slurred speech</td>
<td>Weight loss</td>
<td></td>
<td>Increased startle</td>
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<tr>
<td>Ataxia (gait)</td>
<td>Anger/Irritability</td>
<td></td>
<td>Memory/Development</td>
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<tr>
<td>Dysphoria/Panic</td>
<td>Strange dreams</td>
<td></td>
<td>*five-fold increase in distorted facial features consistent with FASD</td>
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<tr>
<td>Paranoia</td>
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<td>Impaired</td>
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<tr>
<td>Cognition &amp; Psychomotor</td>
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Effects on Neurocognitive Functioning

- Three studies have contributed to our understanding
  - OPPS
  - MHPCD
  - Generation R

- All studies were longitudinal

- Controlled for
  - gender,
  - ethnicity,
  - home environment,
  - maternal SES,
  - prenatal alcohol
  - tobacco exposure
  - current maternal substance use
Neonatal Neurocognitive Effects of Cannabis

- 5-fold increase in distorted facial features compared to FASD babies

- Deficits in:
  - memory, verbal and perceptual skills (age 3-4+)
  - verbal and visual reasoning (age 3-4+)

- Impaired performance in:
  - reasoning and short-term memory (age 6+)
  - reading, spelling and achievement (age 9+)

- Effects on behaviour:
  - attention deficit, increased hyperactivity and impulsivity.

- Increased likelihood of smoking, substance abuse and delinquency among adolescents

- Canadian Centre on Substance Abuse, 2015
Fetal Growth Effects from Cannabis

Canadian Centre on Substance Abuse, 2015
**El Marroun, 2009

- Growth restriction: especially T2/T3
- Lower birth weight
- Dose response effect present
- Both independent of socioeconomic and lifestyle factors**
- Cannabis stays in system up to 30 days
  - Transfer through placenta potentially for 30 days after single use
  - UDS + for 30 days
### Neurocognitive and Behavioural Effects

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

<sup>a</sup> OPPS  <sup>b</sup> MHPCD  <sup>c</sup> Generation R
More than just cannabis

- Current cannabis often contains contaminants that can include:
  - Cocaine (abruption risk)
  - Fentanyl (overdose risk)
  - Methamphetamine (abruption risk)
  - Benzodiazepines (cleft lip/palate risks)

- Tobacco can be mixed with cannabis
  - Adds impact of tobacco to that of cannabis
  - More challenging to stop when combined together
  - Often needs combined smoking cessation and cannabis cessation techniques
### Reduction / Abstinence

<table>
<thead>
<tr>
<th>Weigh your cannabis</th>
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<tbody>
<tr>
<td>Separate out tobacco and cannabis</td>
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<tr>
<td>Reduce by 10% of daily amount each week</td>
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</table>

- From alcohol research, do not accurately assess harm.
- Gives a better understanding of potential harm.
- Start NRT with both patches + gum.
- Will need higher doses than non-smokers.
- Expect to be more accoutable with options to increase.
- Set goals (written).
- Consider starting realine for anxiety.
- 25 mg daily to start and titrate up by 25 mg weekly.
- Set written goals for cannabis and tobacco reduction by 10% of daily amount each week.
SOGC: Marijuana use during pregnancy

- Evidence-based data has shown that cannabis use during pregnancy can adversely affect the growth and development of the baby, and lead to long-term learning and behavioural consequences.

- There have been sufficient studies with comparable results, showing that cannabis use during pregnancy raises concerns of impaired neurodevelopment of the fetus, in addition to the adverse health consequences related to maternal and fetal exposure to the effects of smoking.

- Pregnancy is a critical time for the brain development of the baby and the adverse effects caused by cannabis exposure can be life-long.

- The SOGC recommends that women who are pregnant or contemplating pregnancy should abstain from cannabis use during pregnancy.

ACOG: Marijuana Use During Pregnancy and Lactation (Oct 2017)

- Women reporting marijuana use should be counseled about concerns regarding potential adverse health consequences of continued use during pregnancy.

- Women who are pregnant or contemplating pregnancy should be encouraged to discontinue marijuana use.

- 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.
Breastfeeding

- Literature is variable, but the prudent choice is to avoid marijuana use while breastfeeding
- Organizations that do not support breastfeeding with marijuana use are: ACOG, MOTHERISK, ABM, AAP, SOGC
- ACOG statement: “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.”
- Possible increased risk of SIDs that may vary with amount in breastmilk and method of use (smoking vs. edibles)
American Academy of Breast Feeding Medicine: 2015

- Strongly advise mothers found with a positive urine screen for THC to discontinue exposure while breastfeeding and counsel them as to its possible long-term neurobehavioral effects.

- When advising mothers on the medicinal use of marijuana during lactation, one must take into careful consideration and counsel on the potential risks of exposure of marijuana and benefits of breastfeeding to the infant.

- The lack of long-term follow-up data on infants exposed to varying amounts of marijuana via human milk, coupled with concerns over negative neurodevelopmental outcomes in children with in utero exposure, should prompt extremely careful consideration of the risks versus benefits of breastfeeding in the setting of moderate or chronic marijuana use.
Intrapartum & Immediate Postpartum

- Adequate pain control needed; pain perceptions may be different with women who are cannabis dependent/using
  - Epidural, if available is the best option

- Nicotine replacement therapy (NRT) for women with concurrent tobacco use
  - # of cigarettes = # mg of nicotine needs (7 mg, 14 mg and 21 mg patch)

- Acute cannabis withdrawal can occur post-partum
  - may look like someone is “high”
  - Nabilone could be consider for acute withdrawal (off label)

- Monitor baby for withdrawal
  - No need to use Finnegan Scale since opioid-specific

- Provide supportive care for baby
  - keep in hospital for at least 48 hours (no early discharge)
  - ensure feeding well; co-ordinates sucking well, parents able to soothe
Postpartum

- CAS issues;
  - Advocate on behalf of woman and child
  - Both should receive additional supports

- Discuss ability to parent while impaired
  - Who is the designated parent?
Cocaine

- Stimulant - a vasoconstrictor

- Routes: injected, snorted (powder), smoked (crack "rock")

- Blocks presynaptic uptake of dopamine and catecholamines

- Intense euphoria x 20 minutes

- With chronic use, brief euphoria followed by agitation, paranoia
Cocaine: Withdrawal

- Symptoms primarily psychological:
  - Heavy sleep followed by insomnia
  - Anxious, fatigued, irritable, depressed
  - Increased appetite
  - Cravings and drug dreams

- Main risks: relapse, suicide

- No specific medical therapy
Cocaine: Obstetrical Outcomes

Risk of:

- Spontaneous abortion (SA) (miscarriage)
- Intrauterine growth restriction (IUGR)
- Prematurity - premature rupture of membranes and preterm labour
- Stillbirth - placental abruption a risk
- Intrauterine cerebral infarction

Neurodevelopmental effects*:
- Expressive language, Verbal comprehension delay
- Behaviour problems at school

*New data suggests less impact than previously shown due to improved neonatal interventions
Management of Pregnant Women Dependent on Cocaine

- Safe to stop cocaine suddenly
- No specific therapy- occasionally short term benzodiazepines are used to treat anxiety & insomnia but this may lead to dependence so use only if necessary
- Encourage treatment program attendance
- Ongoing counseling to support the woman
- Offer comprehensive prenatal care
- Ensure safe housing safe housing, adequate food
Cocaine: Postpartum Issues

- If woman is intoxicated at time of delivery, neonate may have mild central nervous system effects such as poor feeding and sleepiness.

- Baby should be treated like any other neonate: rooming in, cuddling.

- Cocaine enters breast milk so it is best to avoid breastfeeding within three days of use (consider pump and discard).
Cocaine: Limitations of Neurodevelopmental Studies

- Several showed a dose-response relationship

- Hard to control for confounders: poverty, poor diet, smoking, other drug use

- Further long-term studies are required
Opioids
Effects of Dependence

- Tolerance: no longer gets ‘high’

- Frightened of withdrawal

- Significant amount of time devoted getting and taking the drug

- Little time or energy for family, friends

- Survival sex (using sex to pay for her drugs)
Risks of Opioid Dependence

- Opioid dependence during pregnancy has been associated with numerous adverse fetal outcomes secondary to the drug itself, as well as, secondary to poor nutrition and inadequate prenatal care.

- Poor neonatal outcomes such as:
  1. Intrauterine growth restriction
  2. Lower birth weight
  3. Preterm prelabour rupture of membranes
Risks of Opioid Dependence

- Opioid withdrawal can trigger uterine contractions leading to an increased risk of spontaneous abortion (miscarriage) in the first trimester, premature labour in the third trimester.

- Maternal complications include pre-eclampsia (pregnancy related high blood pressure) and antenatal bleeding.

- Heroin can lead to intrauterine growth restriction.
Tolerance to Opioids

- Most women on prescription opioids don’t develop dependence – may stay on the same dose for years
- Neurobehavioural adaptation
- Tolerance to analgesic effects develops slowly
- Rapid tolerance to psychoactive effects
- Highly tolerant women can function on massive amounts of opioids
- Tolerance disappears within days (resuming usual dose after a period of abstinence can be lethal)
Opioid Withdrawal

Psychological
- Intense anxiety, agitation
- Intense craving for opiates
- Restlessness, insomnia, fatigue

Physical
- In pregnancy: uterine irritability
- Muscle aches, flu-like symptoms “dope sick”
- Nausea, vomiting, cramps, diarrhea
- Sweating, goose bumps
- Dilated pupils
- Runny eyes
Opioid tapering during pregnancy

- Some OB providers taper patients off opioids to avoid neonatal abstinence syndrome

- **Slow tapering** may be attempted in non-addicted patients on low to moderate doses

- However, this is rarely successful in **opioid-addicted** patients:
  - They usually relapse because they can’t tolerate the severe withdrawal symptoms that accompany tapering
  - Relapse during pregnancy can have catastrophic consequences – child apprehension, family break-up etc

- Therefore best to start opioid-addicted pregnant patients on **buprenorphine/naloxone or methadone**

- Maintain them on their prescription opioid until this can be arranged
Methadone Maintenance Therapy in Pregnancy

- Methadone is a long-acting opioid with a half-life of 24- to-36 hours
- Can be initiated in hospital or in an outpatient setting
- Women on methadone are less likely to experience withdrawal symptoms and drug cravings
- Methadone-maintained pregnancies have reduced obstetrical complications and improved outcomes
Buprenorphine and pregnancy

  - Patients taking buprenorphine/naloxone during pregnancy had higher birthweight babies and less exposure to marijuana than patients taking other opioids during pregnancy

- MOTHER trial (Jones, Fischer, Heil, Kaltenback, Martin, Coyle, et al 2012): Buprenorphine associated with good maternal outcomes, and shorter and milder neonatal abstinence syndrome than methadone

- SOGC guideline (2017) cautions that literature around safety of Buprenorphine/naloxone is still early

- Pregnant patients who do not get adequate relief of cravings and withdrawal from buprenorphine should be switched to methadone
Neonatal Withdrawal

- Not related to methadone/buprenorphine/naloxone dose
- Occurs 2-4 days after birth, can last a couple of weeks
- Poor feeding, irritability, mottled skin, crying, jitteriness, inability to gain weight
- Comfort measures usually sufficient, morphine may be necessary
- Remember to look for other serious problems: sepsis, hypoglycemia, etc. in an unstable infant - do not assume signs due to neonatal withdrawal
- Suggest neonatology/pediatrics consult in hospital with at least Level II capabilities if infant is unstable
Breastfeeding

- Safe to breastfeed on methadone/buprenorphine/naloxone regardless of dose
- Ensure close follow-up of mother and baby
- Rooming-in is the best option to encourage attachment and good parenting
- If baby needs to go to the nursery, parents should accompany and be encouraged to hold and cuddle infant 24/7 if possible
Postpartum Care

- Assess social support, ensure community supports in place before discharge
- Provide ongoing care for substance use/Continue to provide care to women
- Ensure safety, food, shelter, baby supplies
- Regular ongoing support by stable team of caregivers is best predictor of good outcome
- Link parents to community supports and parenting resources
Take-home naloxone

- Important for naloxone to be given at the **point of care**:
  - Patients may not be motivated to follow up at a pharmacy
  - Pharmacy may not be open when patient is ready to get a kit
  - Not all pharmacies are stocked with naloxone
  - It is safe, easy to use, and not a drug of abuse
Thank you