Marijuana Update – From Antepartum to Adolescence

Elizabeth Meade, MD, FAAP
Chief of Pediatrics, Swedish Medical Center
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Disclosures

• No financial disclosures
• Brief discussion of off-label use of cannabinoids
Objectives

• Review trends in legalization and use
• Review current AAP policy statement
• Discuss recent literature on exposure across the age spectrum
• Update on newer synthetic cannabinoids
• Brief discussion of recent case reports and of medical indications
The Legal Landscape

CA – MM 1996
WA – recreationally legal since 2014
2017 changes:
• NH decriminalized
• WV medical use
Suspected in 2018:
• Vermont
• New Jersey
• Michigan
Trends In Use

• Most commonly used illicit drug
• National (2014):
  • 7.5% of those ≥12 years within last month
  • 7,000 new users each day
  • Increased use in adults, but not adolescents
  • Past-year use: 9.4% of 8th graders, 23.9% of 10th graders, 35.6% of 12th graders (6% daily)
  • Teen perception of risk of using steadily decreased over last 10 years
• Washington:
  • Similar <18y usage; but increase in all groups >18y
  • 21% of 18-24y report current use
  • 73% increase in related poison control calls from 2011-13 to 2014-16 (40% pediatric)
• Colorado:
  • Same usage but >2x ED/UC visits in <18y
AAP Policy

- Opposes use by children/adolescents
- Opposes use outside of the FDA process
  - Recognizes option for life-limiting or severely debilitating conditions and inadequate current therapies
- Advocates for more research & development of cannabinoid pharmaceuticals
- Advocates against legalization, but for decriminalization
“Studies have shown that the babies of cannabis-consuming mothers are more advanced and less irritable than the babies of mothers who do not use cannabis… [it] is also extremely nutritious… as a food source… In the future (when real research is allowed) cannabis supplements will be as common for pregnant women as prenatal vitamins.” – Serra Frank, Founding Director of www.momsformarijuana.org

PRENATAL EXPOSURE
Prenatal Exposure

• Most common illicit drug used in pregnancy
• Existing US data:
  – 2002-2014, self-reported past-month use increased 2.4% → 3.9%
  – 14.6% of pregnant adolescents
• Kaiser Permanente Northern California 2009-2016:
  – Pregnant females ≥ 12y (310,085 pts)
  – Use increased from 4.2% → 7.1%
    • Highest in 12-24y - ~10% → ~20%
  – Higher based on toxicology than self-report
  – This was after medical use legalized, but before recreational use!
• 79% of pregnant women 2007-2012 reported perceiving little to no harm
Risks of Prenatal Exposure

- Alters neurotransmitters, decreases synthesis of protein/nucleic acid/lipids
- Smoking – may alter fetal oxygenation and uterine blood flow (>cigarettes)
- Increased tremor/startle in newborns, inattention/impulsivity at age 10, academic underachievement
2016 meta-analysis

- 24 studies; various outcomes (maternal, fetal, neonatal) up to 6 weeks postpartum
  - 1.4x risk of anemia
  - 1.77x risk of low birth weight
  - 2x risk of NICU admission
- Difficult to determine cannabis-only effect given frequent co-use of tobacco/EtOH
- Small studies with unique outcomes
- Often relies on self-report
Spontaneous Preterm Birth

- International study – 2004-2011 (5588 women)
  - Excluded high risk of pre-eclampsia, SGA, or preterm birth
- Interviewed at 15 and 20 weeks
- Categories: never, quit prior to pregnancy, quit prior to 15 weeks, still using at 15 weeks, still using at 20 weeks
- 5.6% using marijuana, 26.4% using tobacco
- Over 2x risk of PTB with any MJ use three months prior to/during pregnancy – regardless of cigarette use
  - Especially true if using past 20 weeks (5x risk)
THC and Breastfeeding

• AAP considers chronic/heavy use to be a contraindication (accumulates in human milk)
• Infants exposed to marijuana through breastmilk tested + in urine for 2-3 weeks
• Reported effects include:
  – Increased tremor
  – Poor suck
  – Decreased feeding time/slow weight gain
  – Changes in visual responses
  – Delayed motor development
• Other studies have not shown differences, especially among infrequent/light users
YOUNG CHILDREN
Not your grandma’s pot…

- Potency (% of THC) in 1978 – avg 1.37%
  - 1998 – avg 4.43%
  - 2009 – avg 8.52%
  - 2014 – avg 12%
  - CBD declining

- **Edibles**
  - Delayed onset
  - Potential for accidental ingestion

- **Vaping**
  - Concentrates can be up to 90% THC

- **Synthetics**
Young Children

• Where legalization does = increased “use”
  – CO: no reported toddler ingestion <2009
  – 2009-2015: 81 reported, 21% admitted, 15% PICU
Marijuana Exposures in WA for 2011-2016

Marijuana Exposure by Age in WA for 2015-2016

Among exposures in 0-5 year olds for 2016, 73% of exposures occurred in 1-3 year olds.
OLDER CHILDREN
Mental Health

• Previous studies:
  – 2012 large prospective study NZ – decrease 6-7 IQ points if use started in adolescence
  – 2014 case control study Sweden – increased risk of schizophrenia with prior cannabis abuse (even among sibling/twin pairs)
  – Onset of use < age 16 → poorer attention, executive functioning, memory performance, verbal IQ
  – Elevated risk of developing other substance use disorders
  – Subclinical psychotic symptoms (even after 1 year abstinence)
  – Poor school performance and leaving school early
Hypomania

• 2017 study in UK
  – Birth cohort study; 3370 participants
  – Cannabis use at age 17 associated with hypomania at age 22-23
    • Dose-response relationship – any use (OR 1.82) vs 2-3x weekly (OR 2.87)
    – Predicted depression (OR 2.48) & psychotic symptoms (OR 3.33)
  – Dose-response relationship
    – Independent of gender, environmental risk factors, alcohol/other drug use, depression, psychotic symptoms at age 18
• Observational study, self-reporting
• Dopaminergic signaling increases during adolescence – cannabis may compound this, leading to hypomania
Case

- 18 y/o healthy male found agitated and diaphoretic at a party → aggressive in the ED
- T 37.6, HR 131, RR 24, BP 131/89, O2 98%
- Pupils 3-4mm, sluggishly reactive. Mild conjunctival injection. Nonfocal physical exam.
- Utox, EtOH negative. Lytes normal.
- Returned to baseline over several hours
Synthetic Cannabinoids

- K2, Spice, Aroma, Mr. Smiley…
- Plant/herbal materials sprayed with active chemical
- Recently classified as schedule 1 substances
- Similar to marijuana + diaphoresis, agitation, restlessness
- Do not result in + THC screen
- Treat with benzos (+ diphenhydramine if dystonic)
- Reports of association with immunomodulation, carcinogenicity, memory loss, psych disease, dependence
Synthetic Cannabinoids

• Who’s using them?
  – 2.9% of HS seniors, currently
  – 1.4% of HS seniors ≥3 days in past month

• More likely to use LSD, cocaine, heroin, and/or nonmedical use of opioids (compared to marijuana-only users) – and to engage in other risky behaviors

• Risk factors: depressive symptoms, marijuana use, EtOH use
Marijuana admissions by age, statewide

Less than 18  18–29  30–44  45+

SWEDISH PEDIATRICS
Extraordinary care. Extraordinary caring™

SWEDISH CARES FOR KIDS
Why are teens so at risk?

• Period of rapid brain development – well into 20s
• Earlier onset of use = higher rates of addiction
  – Overall – 9%
  – Starting in adolescence – 17%
  – Teens who smoke daily – 25-50%
• Episodes of lifetime use correlated with lower cognitive functioning
• Mental health – already tricky time
• Decreased odds of H.S. completion/degree attainment
• Increased risk of use of other substances and suicide attempts
CASE REPORTS
Myocarditis and Death

- 11 m/o male in CO presented with CNS depression → cardiac arrest → unable to resuscitate
- Preceded by 24-48 hours irritability, decreased activity
- Workup significant only for + THC
- Autopsy – severe, diffuse, lymphocytic myocarditis and no infection
- Motel living; parental disclosure of drug possession
- Myocardial complications and cannabis toxicity well-documented in adolescents/adults
“Cookie death”

• 19 y/o in CO (visiting from WY – exchange student from Republic of Congo)
• No h/o drug use or mental illness
• Died after eating 6x recommended dose of marijuana cookie → jumped off 4th story
• 1 cookie was 6 servings
• Inexperienced users, unclear packaging, latency of onset = trouble
MEDICAL USE
Washington State

• Medical marijuana
  – <18, requires parent and physician authorization
    • Terminal/debilitating conditions
  – >18, requires physician authorization (no parent)
  – >21y legal recreationally
<table>
<thead>
<tr>
<th>Products Generic (Brand)</th>
<th>Cannabinoid Content</th>
<th>Administration Formulation and Dosage</th>
<th>FDA Approval</th>
<th>Indications</th>
<th>Approved Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dronabinol (Marinol and Syndros)</td>
<td>Synthetic δ-9-THC</td>
<td>Oral capsule or solution 5–15 mg/m² per dose, up to 6 doses daily</td>
<td>Approved in 1985, Schedule III controlled substance</td>
<td>CINV (pediatric and adult), anorexia associated with weight loss in AIDS (adult)</td>
<td>United States, Australia, Germany, New Zealand, and South Africa</td>
</tr>
<tr>
<td>Nabilone (Cesamet)</td>
<td>Synthetic δ-9-THC</td>
<td>Oral capsule 1 or 2 mg twice a day, up to 6 mg daily (adult)</td>
<td>Approved in 1985, Schedule II controlled substance</td>
<td>CINV</td>
<td>United States, Canada, Ireland, Mexico, and United Kingdom</td>
</tr>
<tr>
<td>Nabiximols (Sativex)</td>
<td>Ratio of 2.7 δ-9-THC to 2.5 CBD, plant derived</td>
<td>Oromucosal spray 1 spray daily, up to 12 sprays daily with at least 15 min between sprays (adult)</td>
<td>Phase III trials</td>
<td>Neuropathic pain, cancer pain, multiple sclerosis spasticity</td>
<td>Canada, Czech Republic, United Kingdom, Denmark, Germany, Poland, Spain, and Sweden</td>
</tr>
<tr>
<td>CBD (Epidiolex)</td>
<td>CBD, plant derived</td>
<td>Oral solution 2 up to 50 mg/kg per d (research trials)</td>
<td>Phase III trials, fast-track designation</td>
<td>Epilepsy</td>
<td>None</td>
</tr>
<tr>
<td>Cannabis plant products (eg, marijuana and oral cannabis extracts)</td>
<td>Varying concentration of plant-derived THC to CBD</td>
<td>Includes smoking (marijuana) and oral (cannabis extracts)</td>
<td>None, Schedule I controlled substance</td>
<td>None approved</td>
<td>Medically and recreationally legal in certain states via physician certification</td>
</tr>
</tbody>
</table>

Medical Use

- Adult patients - use in nausea/vomiting from chemo, reducing pain in chronic neuropathic pain
- 2017 systematic review peds literature
  - 2743 citations → 22 studies met criteria (795 pts)
    - Seizures (11) – strongest evidence in Dravet syndrome; promising data in smaller studies of refractory epilepsy, Sturge-Weber,
    - CINV (6) – reduced CINV across multiple trials
    - Spasticity (2)
    - Tics (1)
    - PTSD (1)
    - Neuropathic pain (1)
- Adult patients – use in nausea/vomiting from chemo, reducing pain in chronic neuropathic pain
Our Role

- Counteract perception of use as “benign”
  - Tobacco literature: teens alter use with detrimental association between use and current health, cost, athletic performance
  - Recommend avoidance until mid-20s
- Minimize collateral damage (ingestions, secondhand smoke)
- Know alternatives/synethetics
- Screen adolescents – AAP recommends SBIRT assessment as part of routine care
  - 2017: <1/3 adolescents reported being asked by MD/RN
- Address use/dependence/addiction
- Provide guidance on medical use
Now we need…

- More research, especially in pregnancy/breastfeeding
- Improved packaging/warnings
- Continue to collect case reports/data
References