

# Cannabis and the Pediatric Population

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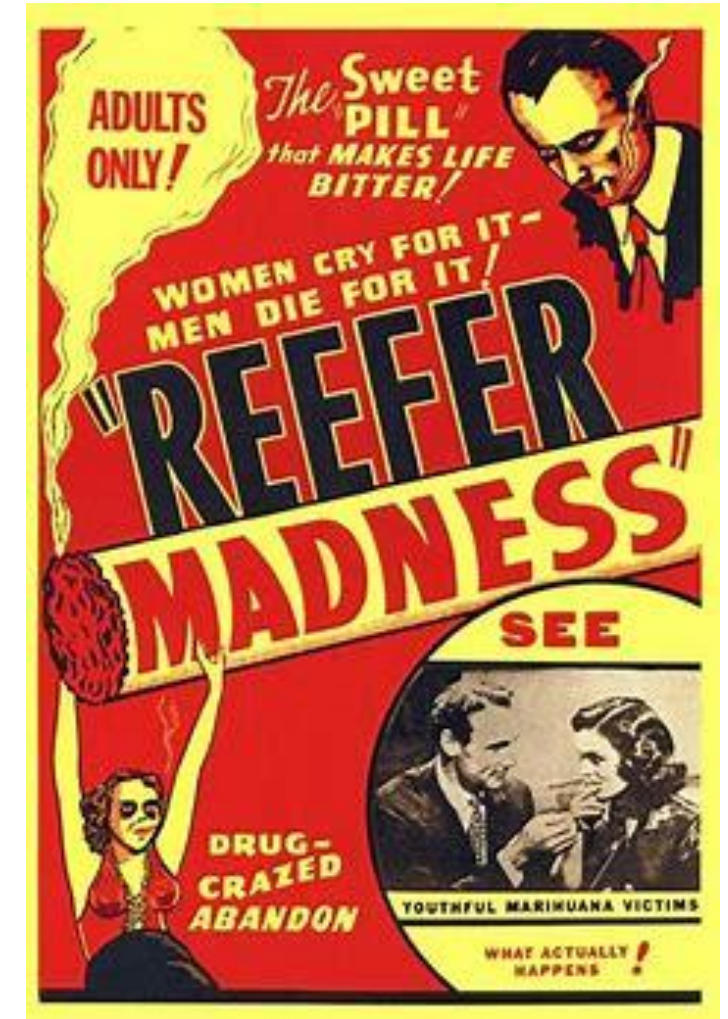
There are no relevant financial relationships to disclose.



Maine Pediatric  
& Behavioral Health  
Partnership



- Passage of laws in many states making both medicinal and recreational use legal
- Increase of tetrahydrocannabinol (THC) content by six or sevenfold in today's products
- Explosion of options for ingesting marijuana
- Lack of FDA oversight
- General view of the public that marijuana is safe and 'natural'
- General lack of public health information that examines marijuana usage and risks and benefits



# CDC Youth Risk Behavior Survey 2017

- Ever used marijuana: 35.6% (compared to peak rate of 47.1 % in 1997)
- Currently use marijuana: 19.9%
- Tried marijuana before 13 yo: 6.5%
  
- Currently use alcohol: 29.8%
- Tried alcohol before 13 yo: 15.5%
  
- Ever tried cigarettes: 28.9%
- Ever vaped electronic products: 42.2%
- Currently vape electronic products: 13.3%
  
- Ever used illicit drugs (heroin, cocaine, meth, etc): 14.0%
- Ever took pain pills not prescribed: 14.0%



# Varying Use

- African-American students: 42.8%
- Latino students: 42.2%
- White students: 32%
  
- LGTBQ students: 30.6%
- Heterosexual students: 19.1%
- 'not sure' students: 18.9%
  
- 9<sup>th</sup> graders: 13.1%
- 10<sup>th</sup> graders: 18.7%
- 11<sup>th</sup> graders: 22.6%
- 12<sup>th</sup> graders: 25.7%
  
- Youth who engage in substance use in later years (>17 yo) less likely to develop substance use disorders
- Positive attitudes towards school, parental monitoring and strong disapproval of peer substance use also protective



# Cannabis 101

- Cannabis products contain terpenes, flavonoids, alkaloids, and >100 cannabinoids
- Phytocannabinoids, plant-derived cannabinoids, have several classes
  - tetrahydrocannabinol (THC) and cannabidiol (CBD) are the most abundant and studied forms
  - THC is considered the main psychoactive component of the plant
- there is no 'standard' form of cannabis; each extract or product has varying forms of ingredients
- There is no general regulating body of these products, much like supplements
- THC content can range from 17%-95%, compared to 4% from 20 years ago
- Average THC content of MJ sold legally in Colorado is 18%



# Endocannabinoid System

- Endocannabinoids and endocannabinoid receptors are widely distributed in the brain and spinal cord (lipophilic)
- Regulatory role in many processes:
  - inflammation
  - appetite regulation
  - immune function
  - cardiovascular function
  - connective tissues
  - neural development
  - pain
  - sleep and wake cycle
  - psychiatric functions
  - GI functions
- Endocannabinoids interact with endocannabinoid receptors CB1 and CB2
- Phytocannabinoids interact with the body through these receptors
- CB1:
  - CNS: prefrontal cortex, basal ganglia, hippocampus, amygdala, hypothalamus, and cerebellum
  - also smooth muscle, myocardium, adipocytes, and preganglionic sympathetic neurons
- CB2: peripheral blood mononuclear cells, adipocytes, smooth muscle, myocardium, and vascular endothelium

# THE BODY'S ENDOCANNABINOID SYSTEM

## Central Nervous System

Facilitates the generation of new neurons and involved in neuroprotection, regulation of motor activity, synaptic plasticity, and control of certain memory processing.



## Immune System

Regulates immune system by suppressing proinflammatory cytokine production.



## Gastrointestinal System

Helps protect GI tract from inflammation and abnormally high gastric and enteric secretions.



## Metabolism

Maintains balance by controlling food intake and metabolic functions such as energy storage, nutrient transport, and modulating insulin sensitivity.



## Hormones

Plays a significant role in the hypothalamic function which regulates metabolism, reproduction, and responses to stress.



## Muscles

Enhances stamina by regulating blood sugar and encourages 'runner's high'.



## Bones

Plays an important role in regulating bone mass and bone regrowth.



● Cannabinoid Receptor 1 (CB1)

● Cannabinoid Receptor 2 (CB2)



# Marriage of Endocannabinoids and Phytocannabinoids

- THC an agonist at CB1 and CB2 sites and reduces neurotransmission, effecting:
  - learning and memory
  - gut motility
  - thyroid levels
  - attention
  - heart rate and blood pressure
  - analgesia
  - anti-inflammatory effects
- Metabolism of THC through the liver by the cytochrome P450 system
- Can decrease efficacy of certain drugs (i.e. risperidone)
- Synthetic cannabinoids (i.e. Dronabinol, Nabilone) work like THC
  - approved for nausea, vomiting, anorexia assoc. with chemotherapy
- CBD has weak affinity to CB1 receptors and does not bind directly to CB2 receptors
- Activates TRP1 receptors that control pain perception, body temperature, inflammation
- CBD also inhibits fatty acid amide hydrolase (FAAH), which increases feelings of well-being
- CBD inhibits cytochrome oxidases and interferes with metabolism of many common medications (i.e. increasing levels of anti-epileptic medications)
- CBD has a regulatory effect on THC and may inhibit some adverse effects (tachycardia, anxiety, sedation)
- Most studies for CBD have been on adults
- Is approved for some juvenile epilepsy conditions



# Medical Uses of Cannabis- some data

- Lennox-Gastaut syndrome (children- 2<sup>nd</sup> line)
- Dravet syndrome (children- 2<sup>nd</sup> line)
- Chronic pain (adults)
- Antiemetics (adults)
- Spasticity in multiple sclerosis (adults)
- Irritable bowel syndrome (adults- weak evidence))
- Social anxiety (CBD)
- Sleep and PTSD (weak evidence)
- No benefit found for depression (Sams, 2020)

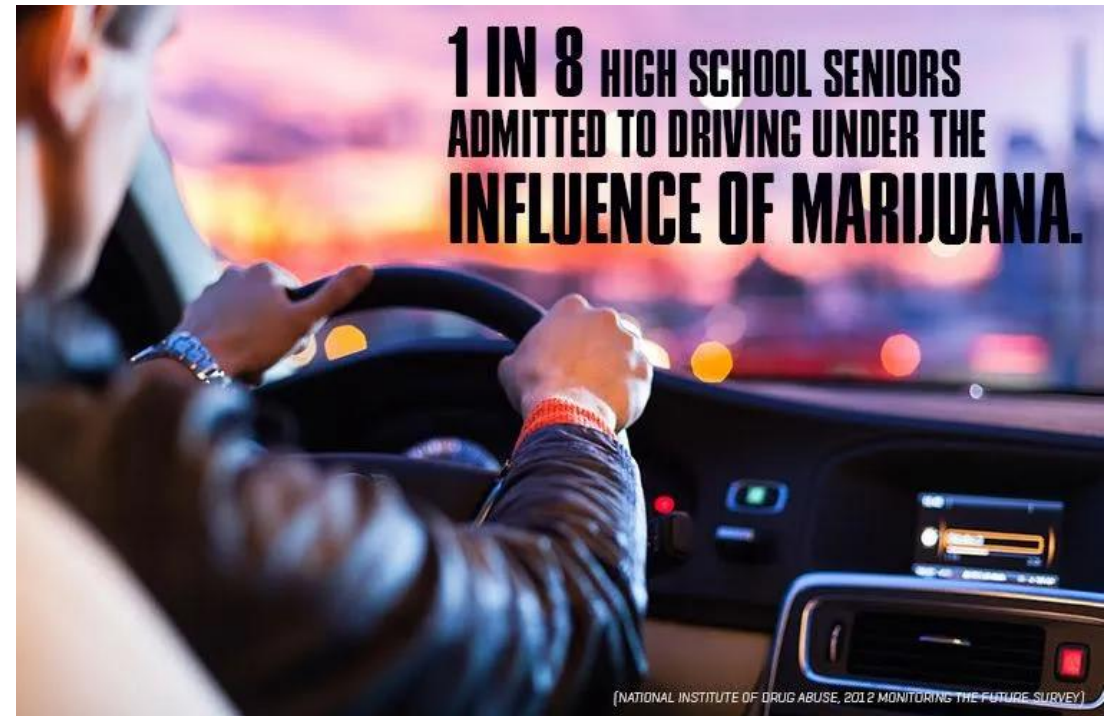


# Neurocognitive Adverse Effects

- Because of role in the prefrontal cortex and hippocampus, maturation of circuits regulating attention, executive functioning, and memory can be affected by cannabis use during adolescence (Rubino, 2009)
- Persistent neurocognitive changes and lower functioning even after abstaining from cannabis use, even after a year (Meier, 2012)
- Cannabis use was adverse effects on IQ and executive functioning and declines in neural connectivity (Camchong, 2017)
- Those who start using before 17 yo have reduced odds of high school graduation, more likely to have cannabis use disorder, more likely to use other illicit substances and tobacco, and more suicide attempts (Silins, 2014)

# Cannabis Use and Sequellae

- Most adolescents do not perceive MJ use as harmful or addictive
- As opposed to ETOH, drivers feel MJ is safer to use while driving, yet do not understand the effects (Keyes, 2016)
- Animal studies show MJ does prime the brain to the effects of other substances
- Those who use MJ have a 2.78 increased risk of opiate use disorder, as well as increased risk of stimulants, cocaine, and injection drugs (Olfson, 2018)
- 8-12% of MJ users will develop moderate to severe cannabis disorders
- Withdrawal is not fatal, but within a week of stopping can be linked to irritability or aggression, anxiety, decreased appetite, depressed mood, abdominal pain, tremor, fever chills and headaches



# Marijuana and Psychosis

- Daily marijuana use and high-potency marijuana (THC>10%) are strongest predictors of a psychotic episode
- Individuals with high potency MJ 1.6 times more likely to develop psychosis than non-users
- High potency and daily use 5 times more likely to develop psychosis than non-users



# Cannabis and Bipolar Disorder



- Relatively well-known association between marijuana and psychotic spectrum illnesses
- Several articles have shown that marijuana may worsen manic symptoms in those with bipolar disorder
- Cannabis may also be a causal risk factor, with an increased incidence of up to three-fold
- *Cannabis use and mania symptoms: a systematic review and meta-analysis, Gibbs, M, et al; J Affective Disord Jan 2015*

# Cannabis and Depression

- Meta-analysis of 11 studies and 23,317 individuals
- OR of developing depression in MJ users vs non-users is 1.37 (95% CI 1.16-1.62)
- OR of anxiety not statistically significant 1.18 (95% CI 0.84-1.67)
- OR of suicidal ideation of 1.50 (95% CI 1.11-2.03)
- OR for suicide attempt of 3.46 (95% CI 1.53-7.84)

*(Gobbi, 2019)*



# Marijuana and Anxiety



- Anxiety is often cited by adolescence as a reason they use marijuana
- Anxiety is one of the most common disorders
- Acute use of MJ can either mitigate or cause anxiety; CBD often cited as being more helpful
- Anxiety returns when person is no longer using, having not learned any skills
- 27 adolescent studies: 67% found a positive relationship between anxiety and MJ use, but relationship was unclear (causal or incidental)

(Cancelliere, 2018)

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