CANNABIS

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2022 CSAM Conference - Test Taking Track

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Educational Objectives

After attending this presentation, participants will be able to:

1. Summarize the clinical manifestations and diagnostic criteria for cannabis use disorder, cannabis withdrawal, and cannabis intoxication
2. Understand the basic pharmacology of cannabinoids, in particular THC and CBD
3. Describe current epidemiologic trends in cannabis use and cannabis use disorder

Conflicts of Interest

Consultant for Roche, ended 07/2021

Stocks in Intuitive Surgical

I will be discussing “off label” use of drugs in this presentation

- *Gabapentin, dronabinol for cannabis withdrawal*

Need To Know

1. Function of the endocannabinoid system
2. Cannabis pharmacology
3. Epidemiology of cannabis use
4. Cannabis intoxication and withdrawal
5. Cannabis drug testing
6. Synthetic cannabinoids
7. Negative effects from cannabis use
8. FDA-approved cannabinoids

Question 1

Which of the following statements is true?

A. Δ^9-tetrahydrocannabinol (THC) is the main psychoactive component of cannabis and exerts its behavioral effects through the CB_2 receptor.

B. Cannabidiol (CBD) is the main psychoactive component of cannabis and exerts its behavioral effects through the CB_2 receptor.

C. Cannabidiol (CBD) is the main psychoactive component of cannabis and exerts its behavioral effects through the CB_1 receptor.

D. Δ^9-tetrahydrocannabinol (THC) is the main psychoactive component of cannabis and exerts its behavioral effects through the CB_1 receptor.

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Cannabinoids and the Endocannabinoid System

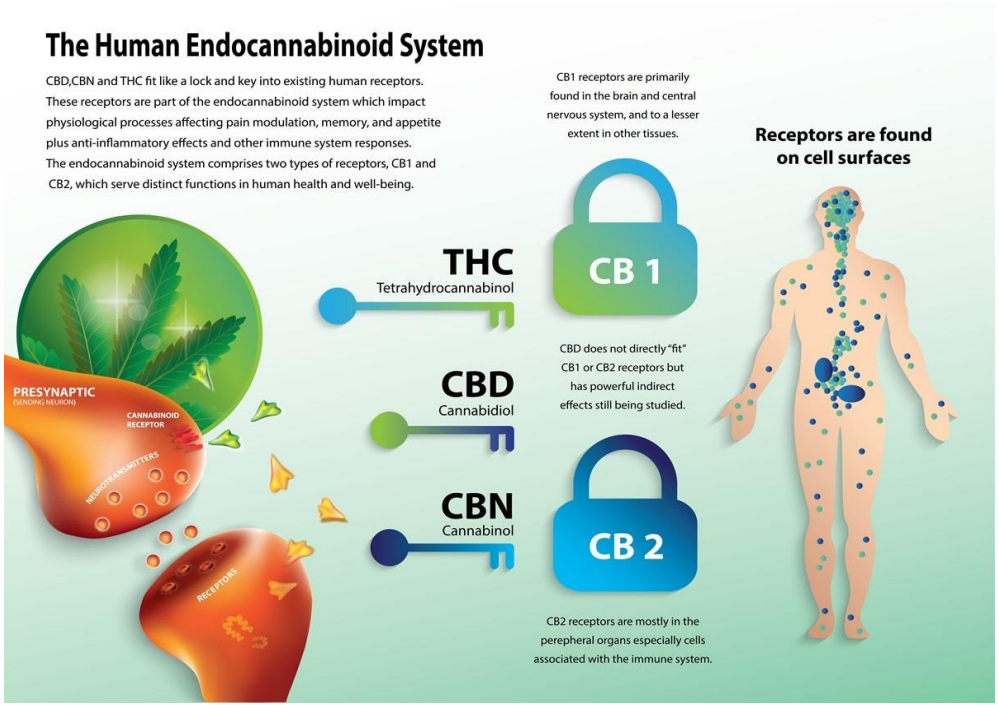

Image from News-Medical.net

Cannabis sativa and indica

113 cannabinoids *Gulk and Moller, 2020*

- ***Δ9-THC***
- Δ8-THC
- **Cannabidiol (CBD)**
- Cannabinol (CBN)

Question 2

Which of the following is true regarding the endocannabinoid system?

A. The CB1 receptor is tonically inactive

B. The CB1 receptor is a G-protein coupled receptor

C. The CB1 receptor is a voltage gated sodium channel

D. THC is a full agonist with a high binding affinity at the CB1 receptor

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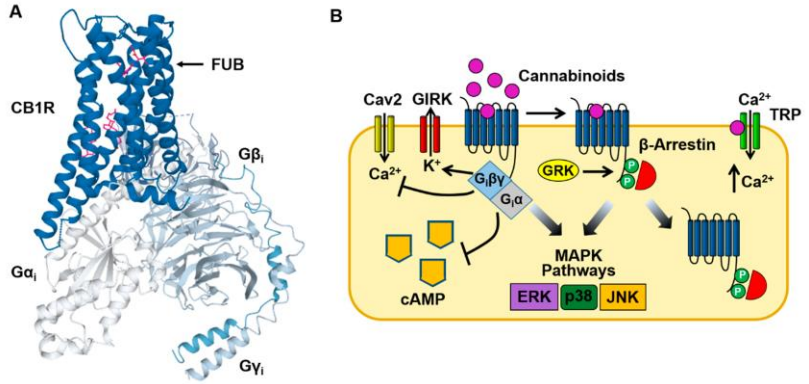
Cannabinoid Pharmacology



Walsh and Andersen, Int. J. Mol. Sci. 2020

- CB1 receptor is a **GPCR**
  - EC activation decreases cAMP → decrease neuronal excitability
- Intrinsic activity, **tonically active**
  - Off-balance by exogenous cannabinoids
- THC: **partial agonist** → ~20% CB1R activation
  - Synthetic cannabinoids are often full agonists, activate CB1R ~100%

Question 3

According to the 2020 National Survey on Drug Use and Health (NDSUH), which age group had the highest prevalence of cannabis use disorder in 2020?

A. 12 to 17

B. 18 to 25

C. 25 to 65

D. 65 and older

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Cannabis Use and Use Disorder Epidemiology

- **Cannabis use** is most prevalent in **young adults (18-25): 34.5%**, 11.6 million
  - *Adults (26+) 16.3%, adolescents (12-17) 10.1%*
- **Cannabis Use Disorder: 13.5% of young adults**
  - *5.1% of 12+ US population, 4.1% in adolescents, 4.0% in adults*
- Perceived risk of cannabis use continuing to decrease
- CUD Risk Factors
  - *Patterns of use: early onset, heavy/frequent use, potent forms*
  - *Heritability*
  - *Psychiatric comorbidities, comorbid SUDs, male sex, less education*

2020 NSDUH
Monitoring the Future 2021
Cougle et al. 2016

DSM-5 Cannabis Use Disorder

A. Problematic pattern of cannabis use causing impairment/distress
    1. *11 possible criteria, e.g., using larger amount/for longer periods, difficulty cutting down or controlling use, cravings, social problems, physically hazardous use, tolerance, withdrawal, etc.*
    2. ***3 C's: control, consequences, cravings***
B. Severity: 2-3 = mild, 4-5 = moderate, 6+ = severe
C. Remission: 3 month = early, 12 month = sustained

Question 4

A patient is admitted to the emergency department with several hours of anxiety and panic attacks. Family also brings in a glass pipe as shown to the right. Physical exam is only notable for periodic coughing, conjunctival injection, and tachycardia (105 bpm). UDS is +cannabinoid only. Labs and EKG are unremarkable. ***Which of the following is the most appropriate diagnosis?***

A. Cannabis intoxication

B. Cannabis withdrawal

C. Cannabis use disorder

D. Cannabis was laced with a stimulant such as methamphetamine or cocaine

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DSM-5 Cannabis Intoxication

A. Recent cannabis use

B. Clinically significant problematic behavior or psychological changes (motor incoordination, euphoria, anxiety, changes in time perception, impaired judgment, social withdrawal)

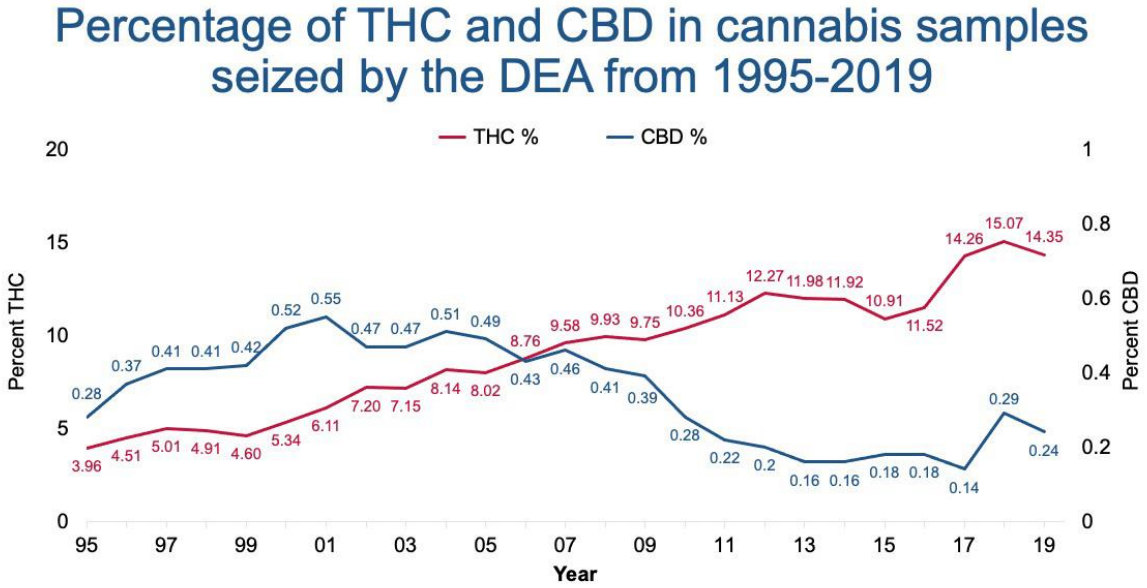
C. Two or more of following signs or symptoms within 2 hours of use:
   1. Conjunctival injection
   2. Increased appetite
   3. Dry Mouth
   4. Tachycardia

Cannabis Preparations and Intoxication

- Cannabis plant (5-30+% THC) < concentrates (as high as 90+% THC)
  - Potency today far greater than in the 90s

    (4% vs 17-28%) *ElSohly Biol Psychiatry 2016*
- Smoked cannabis: faster onset and more intense high
- Edible cannabis: slower onset, longer duration
- Potency of THC associated with adverse neuropsychiatric effects in a dose dependent manner
- Treatment of intoxication: supportive and symptom-targeted

Cannabis and THC/CBD potency over time



NIDA, 2021

Question 6

Regarding cannabis withdrawal, which of the following is FALSE?

A. Cannabis withdrawal is defined in the DSM-5

B. Chronic heavy cannabis use causes a reduction in CB1 receptors that reverses as cannabis withdrawal resolves

C. Cannabis withdrawal is equally likely to occur from use of CBD as it is from use of THC

D. There are no FDA approved treatments for cannabis withdrawal

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DSM-5 Cannabis Withdrawal

A. Cessation of heavy and prolonged cannabis/THC use (daily to near-daily)

B. 3+ of following within 1 week of cessation:
   1. Irritability, anger, or aggression
   2. Nervousness or anxiety
   3. Sleep difficulty
   4. Decreased appetite or weight loss
   5. Restlessness
   6. Depressed mood
   7. At least 1 physical symptom: abdominal pain, tremors, sweating, fever, chills, headaches

Cannabis Withdrawal

- Prevalence 47% with cessation of daily cannabis/THC use *Bahji et al 2020*
- Peaks at day 4 in most, resolves by day 16
- On PET, CB1R expression reduced with chronic heavy use *D'Souza et al 2017*
  - *Reverses with abstinence*
- Time-limited, symptom-targeted pharmacotherapy
  - *No FDA-approved options*
  - *Some evidence for dronabinol, gabapentin* *Werneck et al., 2018; Brezing and Levin, 2017; Mason et al., 2012*
- Rule out other substance use/withdrawal, psychiatric comorbidities
  - *Those with co-occurring depression and anxiety may have a prolonged course*

Question 7

A patient with a history of heavy, daily cannabis use reports abstinence for three weeks. His urine drug screen results as +cannabinoid. The patient adamantly denies use.

Which of the following is FALSE?

A. With heavy cannabis use, THC metabolites can be detected for weeks or even a month after last use.
B. Cannabinoid urine drug screens primarily detect THC metabolites such as 11-nor-9-carboxy-Δ-9-THC (carboxy THC).
C. If the patient was poorly hydrated, urine THC metabolite concentration would increase.
D. Pure CBD would be expected to yield a positive cannabinoid urine drug screen.

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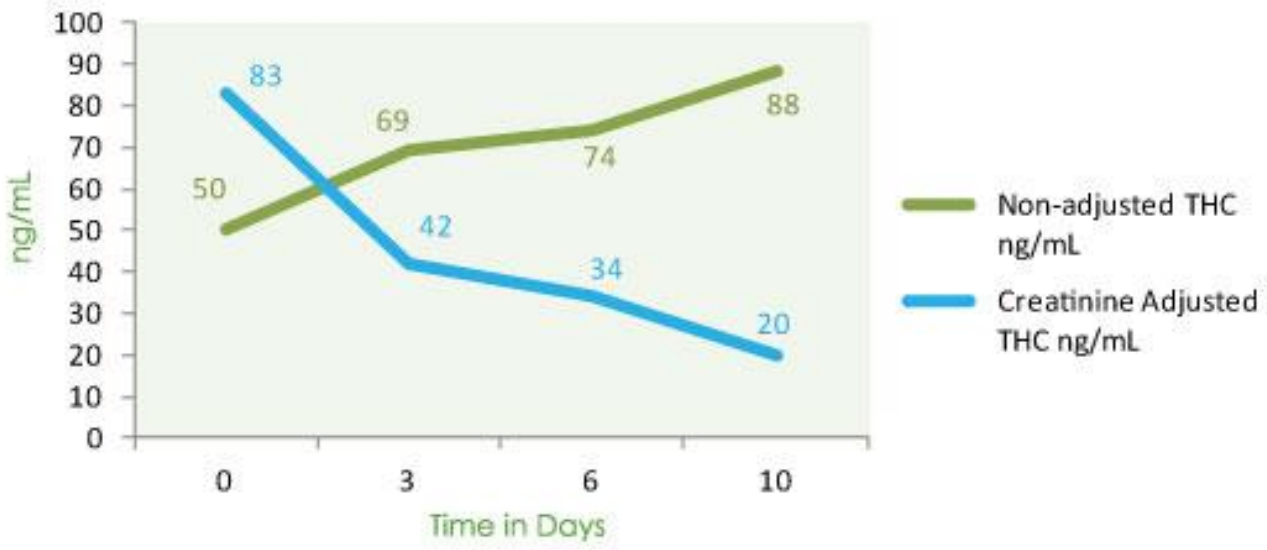
Cannabis Drug Testing

- Detection of THC/metabolites, 11-nor-9-carboxy-Δ-9-THC (carboxy THC)
- Urine Immunoassay (urine)
  - *Sensitive and specific*
  - *Single use detected 2-4 days*
  - *More frequent use 1-2 weeks*
  - *Chronic heavy use 20-30 days, rarely longer*
  - *THC concentrations in hemp (CBD products) too low, as is passive/ second-hand inhalation*
  - *Rare false positives: efavirenz, PPIs (pantoprazole)*

ASAM Principles of Addiction Medicine, 6th Ed.
URUP Laboratories. (2019). Drug Plasma Half Life and Urine Detection Window.

THC:Creatinine Ratio



- Can test levels over time to monitor abstinence
- Corrects for hydration status

Question 8

A teenage patient presents with altered mental status. Family witnessed him smoke from a pipe. Shortly after, he became agitated and began shouting to himself. His vital signs are HR 111 bpm, BP 142/88 mmHg; RR 22/min, and temperature 37.7 ° C. The drug screen result is pan-negative including for cannabinoids and stimulants.

Which of the following would be the most plausible explanation?

A. He submitted a false urine sample
B. He used synthetic cannabinoids
C. He used gamma hydroxybutyrate (GHB)
D. He has schizophrenia

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Synthetic Cannabinoids

- Over 180 known compounds manufactured in illicit drug labs
  - *Sprayed onto herbs and smoked, insufflated, orally ingested*
  - *K2, Spice, various names/brands*
  - *“Herbal incense” or “fragrant potpourri”*
- Potent full CB1 agonists (2-800x more potent than THC)
- Generally decreasing rates: adolescents (1.6% of high school students in 2021), forensic settings, military

NPR

Monitoring the Future 2021
Tait et al. 2015

Synthetic Cannabinoids

- Intoxication similar to cannabis, e.g., tachycardia, conjunctival injection, increased appetite, ataxia
- Higher risk of serious neuropsychiatric toxicity: agitation, delirium, hallucinations, psychosis, seizures, coma
- Diagnosis
  - *Not on standard UDS, typically not cross reactive with THC*
  - *Can get confirmatory testing*
- Treatment largely supportive: IV fluids (high risk of rhabdo) , quiet room
  - *Sedatives, antipsychotics for severe anxiety or agitation*

Tait et al. 2015

CSAM

Question 9

You are asked by your local community organizers to help disseminate information about the risks of cannabis use through a public health campaign. ***All of the following are true except:***

A. Cannabis use is not protected under the Americans with Disabilities Act (ADA)

B. Regular cannabis use increases the risk of being diagnosed with schizophrenia

C. Cannabis use, especially with alcohol, is linked with hepatic steatosis

D. Smoked cannabis causes chronic obstructive pulmonary disease (COPD)

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Adverse Effects of Cannabinoids

- Cardiovascular: increased heart rate, orthostatic hypotension
- Pulmonary: smoked cannabis associated with increased resp illness, upper airway inflammation/edema, NOT with small airway disease (e.g., COPD)
- Liver: contributes to steatosis=>cirrhosis risk
- Endocrine/reproductive effects: reduced pregnancy and IVF success, lower sperm count/motility, sex hormone effects
  - *ACOG: recommends abstinence, crosses placenta (endocannabinoids involved in normal development), enters breastmilk*
- Oncologic risks inconclusive

ACOG, Marijuana Use During Pregnancy and Lactation, 2017.
National Academies, 2017
ASAM Principles of Addiction Medicine, 6th ed.

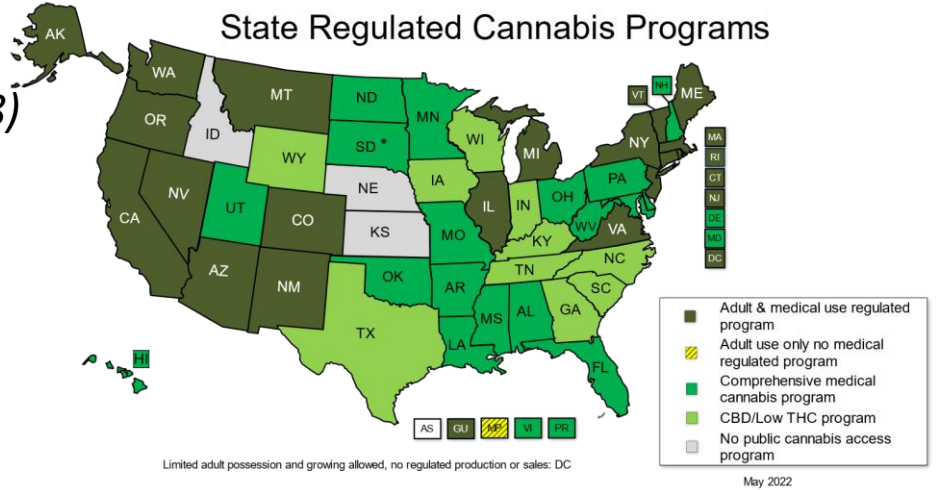
Neuropsychiatric Effects

- Risk worse with earlier onset use (before 16), higher THC potency, and frequent/daily use
- Neuropsychiatric
  - *APA: Position Statement in Opposition to Cannabis as Medicine*
  - *Psychosis, bipolar disorder, anxiety disorders, depressive disorders, PTSD*
  - *Impaired attention, working memory* *Crean, J Addict Med, 2012*
  - *Persistent cannabis use associated with IQ drop from childhood to adulthood* *Meier, Proc Natl Acad Sci, 2012*
    - Adolescent-onset use did not recompensate IQ after cessation; adult-onset did
  - *"Gateway drug" hypothesis simplistic but associations valid* *Jorgensen and Wells, 2021*

National Academies, 2017
ASAM Principles of Addiction Medicine, 6th ed.

Other considerations

- DEA Schedule I (federally illegal)
- Workplace testing
  - *Drug-Free Workplace Act (1988)*
  - *State-specific laws*
- Current use/impairment not protected under ADA
- Acute intoxication and DUI/DWI
  Brubacher et al., 2019; Rogeberg and Elvik, 2016
- Pediatric/accidental exposures
  Wang et al., 2016; Whitehill et al., 2019; Dilley et al., 2021



National Conference of State Legislatures

Question 10

A 65-year-old patient is currently prescribed an FDA-approved cannabinoid medication. ***For which condition is this medication prescribed?***

A. Fibromyalgia
B. Post operative nausea and vomiting
C. Chemotherapy-induced nausea and vomiting
D. Muscle spasticity related to multiple sclerosis

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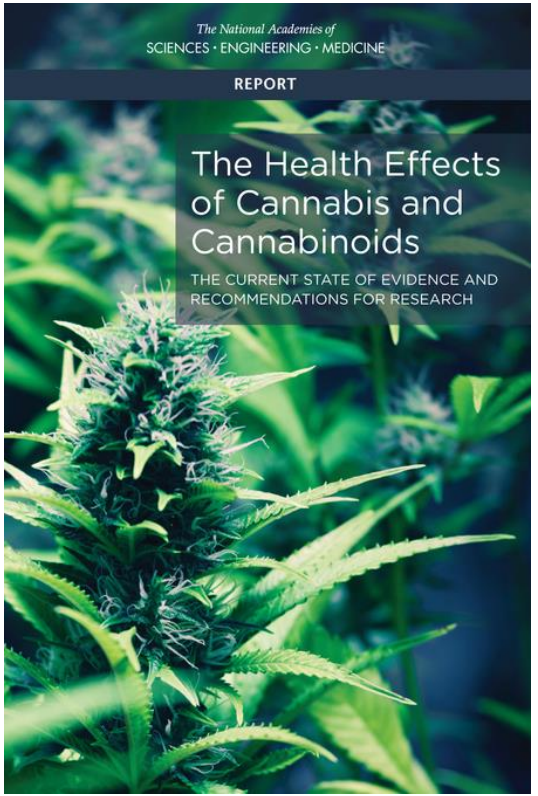
Only 3 FDA-Approved Cannabinoids as Medicine

- Dronabinol (THC)
  - *Anorexia/cachexia due to AIDS*
  - *Chemotherapy-induced nausea/vomiting*
- Nabilone (THC) [Discontinued]
  - *Chemotherapy induced nausea and vomiting*
- Cannabidiol (cannabis derived CBD)
  - *Seizures due to Lennox-Gastaut syndrome, Dravet Syndrome, tuberous sclerosis*



Uptodate
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END

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