

**QRS... TUV  
(MARIJUANA)**

Dan Quan, DO FAAEM FACEP FACMT  
Emergency Medicine/Medical Toxicology/Addiction Medicine  
Creighton University Emergency Medicine Residency  
Toxicology Consultants of Arizona  
Phoenix, Arizona

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**DISCLOSURES**

All relevant financial relationships(s) with any commercial interest to the provider's name of commercial interest(s) nature of the relationship with each

NONE

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**TECHNICAL TERMS**

- Cannabis
  - All products derived from the plant Cannabis sativa
- Marijuana
  - Parts of the plant that contains the most tetrahydrocannabinol (THC)
- Hemp
  - Contains little THC
- Cannabinoids
  - Chemicals found in the plant

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**CANNABINOIDS**

<ul style="list-style-type: none"> <li>• Psychoactive</li> <li>• Cannabinoid receptor 1 (CB1)</li> <li>• <math>\Delta^9</math>-tetrahydrocannabinol or <math>\Delta^9</math>-THC</li> <li>• <math>\Delta^8</math>-tetrahydrocannabinol or <math>\Delta^8</math>-THC</li> <li>• Cannabinol</li> <li>• 11-hydroxy- <math>\Delta^9</math>-THC</li> <li>• Anandamide</li> </ul>	<ul style="list-style-type: none"> <li>• Non-psychoactive</li> <li>• Cannabidiol (CBD)</li> <li>• Cannabichromene</li> <li>• (-) <math>\Delta^8</math>-THC-11-oic acid</li> </ul>
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R = H  $\Delta^8$ -Tetrahydrocannabinol (THC)  
R = OH 11-Hydroxy variant (11-OH-THC)

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**FDA APPROVED CANNABINOIDS**

- Epidiolex
  - Purified CBD
  - Indicated for the treatment of severe seizures
- Marinol - Dronabinol (Schedule III), Syndros (Schedule II)
  - Synthetic  $\Delta^9$  THC
- Cesamet (nabilone)
  - $\Delta^9$  THC synthetic analog
  - Used to treat nausea and vomiting caused by chemotherapy

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**CANNABINOID RECEPTORS**

- Cannabinoid receptor type 1 (CB1)
  - Brain – cognition, anxiety, addiction, sleep
  - CV – negative inotropy, vasodilation, cardiac function
  - GI – mobility, secretion of gastric acid, nausea and vomiting control
- Cannabinoid receptor type 2 (CB2)
  - Immune cells, peripheral tissues, cerebellum, brain stem

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**HEMP**

- Fibers and oil are used to make
  - Paper, rope, textiles, plastics, animal feed, building materials
- Higher concentration of CBD vs  $\Delta^9$  THC
- Legal to grow after the 2018 Farm Bill
  - May contain up to 0.3%  $\Delta^9$  THC

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**$\Delta^8$  THC**

- Derived from Cannabis sativa and mostly from hemp
- May be mixed with CBD products
- Less affinity at the CB1 receptor
- Similar "desired" effects as  $\Delta^9$  THC with less adverse effects
  - Decreases nausea and vomiting, stimulates appetite, less anxiety
  - Short-term memory problems, anxiety and paranoia, hallucinations, syncope
- Low amounts in cannabis
  - Converted from CBD using strong organic solvents
- DEA considers  $\Delta^8$  THC a Schedule I substance on 2/13/2023

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**CBD**

- Extracted from hemp
- Used for chronic pain and spasticity, nausea and vomiting due to chemotherapy, weight gain in HIV, sleep disorders, Tourette syndrome, seizures
- June 2018, Epidiolex was FDA approved
  - Purified CBD oral solution
- Rick Simpson's Oil (RSO)
  - [www.leafly.com/news/cannabis-101/what-is-rick-simpson-oil](http://www.leafly.com/news/cannabis-101/what-is-rick-simpson-oil)

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**NOT YOUR MAMA'S WEED**

- In the 1960s and 1970s marijuana contained less than 4% of THC along with nearly the same amount of CBD
- Today, the average amount is 16% THC and lower amounts of CBD
  - Result of cross breeding, preventing pollination (plant spends time making THC rather than seeds)



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**HASH OIL WITH 95% CANNABINOID, 75% Δ9-THC**



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**EDIBLES**

- Converts  $\Delta^9$ -THC to psychoactive 11-OH-THC by the liver
  - Stronger than THC
  - Generally, 10 mg THC is for recreational use products
- Eat low and go slow
  - May take 30 minutes to 3 hours before effects show up
  - Lasts longer, peaks in 3-4 hours



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**EDIBLE TOXICITY**

- Drowsiness, ataxia, hypo- or hypertonia, seizures, coma, altered mental status, agitation, euphoria, mydriasis, respiratory depression
- Pediatric
  - 3 mg/kg THC - observation
  - 7 mg/kg THC - admission and moderate intervention
  - 13 mg/kg THC - ICU admission and major interventions
- Keep out of reach from children

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**CANNABIS WITHDRAWAL**

- Occurs in 50% of regular THC users
- May be caused by decreased CB1 receptor stimulation
- Cessation or decrease use may cause symptoms
  - Onset is 1 to 2 days
  - Peaks in 2 to 6 days and lasts up to 3 weeks
- Symptoms
  - Anxiety, irritability, aggressive, angry behavior
  - Restlessness, shakiness, insomnia, depression, anorexia
  - Sweats, headaches, diaphoresis, abdominal pain, nausea, muscle cramps

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**CANNABIS WITHDRAWAL**

- Withdrawal scales
  - 16-item marijuana withdrawal checklist
  - 19-item cannabis withdrawal scale
  - Not well validated
- Treatment
  - Supportive
  - Dronabinol, edible THC
  - SSRI, antipsychotics, anticonvulsants, benzodiazepines

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**CANNABINOID HYPEREMESIS SYNDROME**

- No risk factors other than frequent THC users
  - Any age
  - Develops with no specific timeframe
- CB1 receptors are found in enteric nerves delaying gastric emptying
- Cannabinoids accumulate in fat stores
- Genetics
  - Polymorphism in P450 may affect metabolism rate of THC
    - CYP2C9, CYP2C19, CYP3A4

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**CANNABINOID HYPEREMESIS SYNDROME**

- Early phase
  - Nausea, anorexia
- Hyperemetic phase
  - Persistent and painful vomiting
  - May cause electrolyte abnormalities, dehydration, acute kidney injury
- Recovery phase
  - Abstinence and symptoms resolve

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**CANNABINOID HYPEREMESIS SYNDROME**

- IV fluids
- Electrolyte replacement
- antiemetics
  - Ondansetron
  - Droperidol
    - 0.625 to 2.5 mg IV may help
  - Haloperidol
    - 5 mg IV, may try 5 mg PO daily prescription

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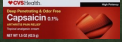
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**CANNABINOID HYPEREMESIS SYNDROME**

- Cessation from use
- Hot showers
  - Blood flow to skin away from the enteric system
- Topical capsaicin cream 0.075% to 0.1% over the abdomen
  - Inhibits substance P and disrupts TRPV1
  - Side effects – burning sensation, skin irritation, blistering



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**RAPID URINE DRUG SCREEN**

- Detects 11-nor- $\Delta^9$ -THC-9-carboxylic acid (THC-COOH)
- Positive
  - 3 to 10 days in occasional users
  - 30 to 45 days in habituated users
- Cannabidiol (CBD)
  - Does not generate THC-COOH metabolites
  - Products may contain THC (0.3% or more)
- $\Delta^8$ -THC
  - May test positive due to cross reactivity or contamination with  $\Delta^9$ -THC
- Does NOT indicate intoxication

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### METABOLISM OF CANNABIS

- Nonlinear
- Blood concentrations may drop as much as 90% in the first hour
- Cannot extrapolate backwards to determine levels
- Edibles can have a lower, gradual concentration compared to smoking

Plasma Concentration vs. Time  
Smoking 3.55% THC

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### ACCURACY OF TESTING

- Affected by body habitus and type of cannabis used
- THC rapidly redistributes to fat tissue from blood
  - Smoking marijuana has a maximum plasma concentration at a mean of 8.4 minutes after the start of smoking
- Effects of THC on cognitive function do not correlate with blood concentration
  - Peak impairment occurs during the 1st hour and may last 6 hours or more
  - Chronic users may have THC levels at the limit of detection (2 ng/mL – 5 ng/mL)

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### Time Course of Standardized THC Concentration in Plasma, Performance Deficit and Subjective High after Smoking Marijuana (Adapted from Berghaus et al. 1998, Sticht and Kiferstein 1998 and Robbe 1994)

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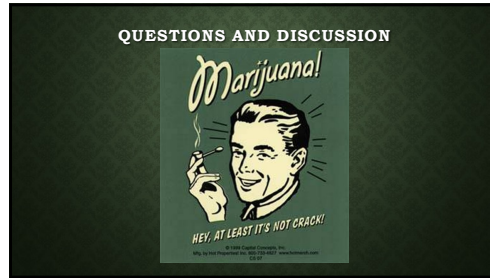
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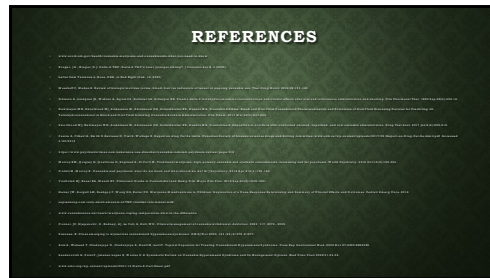
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