Medical Marijuana: Weeding Out the Myths

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Relevant Disclosure

Under the Oklahoma State Medical Association CME guidelines disclosure must be made regarding relevant financial relationships with commercial interests within the last 12 months.

Scott Schaeffer, RPh, DABAT
I have no relevant financial relationships or affiliations with commercial interests to disclose, Dude.
The use of cannabinoids in medicine isn’t new...
FDA Approval
1985

For the treatment of chemotherapy-induced nausea/vomiting (CINV) refractory to conventional antiemetic agents
FDA Approval 1985

For the treatment of chemotherapy-induced nausea/vomiting (CINV) refractory to conventional antiemetic agents.

FDA Approval 2016

- Anorexia associated with weight loss in patients with AIDS.
- Nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.
FDA Approval 2018

Treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age and older

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FDA Approval ???

Adjunctive treatment for symptomatic relief of spasticity in adult patients with multiple sclerosis (MS) who have not responded adequately to other therapy and who demonstrate meaningful improvement during an initial trial of therapy. (Canada)

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Marijuana: What is It?

- Dry, shredded mix of leaves, flowers, stems, and seeds, usually from *Cannabis sativa* or *Cannabis indica* plant
- Both are common subspecies of the hemp plant, which is common throughout the world
- Contains over 400 chemical compounds

SOURCE: SAMHSA, 2012
• Human body produces endocannabinoids, i.e., endogenous compounds that act at CB1 and CB2 receptors. Examples include anandamide, 2-arachidonoylglycerol
• Cannabinoids derived from plants are called phytocannabinoids. Examples include THC, cannabidiol, cannabinol

How is Marijuana Used?

<table>
<thead>
<tr>
<th>SMOKED</th>
<th>VAPORIZED</th>
<th>EATEN/DRUNK</th>
</tr>
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<tbody>
<tr>
<td>Smoked in a pipe, bowl, cigarette</td>
<td>Inhaled through machine that converts active compounds into inhalable form</td>
<td>Consumed as ingredient in baked goods, candies, sodas</td>
</tr>
<tr>
<td>Rapid effects</td>
<td>Rapid effects</td>
<td>Takes time to reach brain, so effects are delayed</td>
</tr>
<tr>
<td>Burning marijuana releases toxins that can cause pulmonary problems</td>
<td>Does not release toxins that cause pulmonary problems</td>
<td>Does not release toxins that cause pulmonary problems</td>
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### Immediate Effects

<table>
<thead>
<tr>
<th>Altered Mood</th>
<th>Reduced Anxiety</th>
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<tbody>
<tr>
<td>Cognitive Impairment</td>
<td>Sedation/Drowsiness</td>
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<tr>
<td>(Attention, Judgment)</td>
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<tr>
<td>Altered Perception</td>
<td>Sensory Intensification</td>
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<tr>
<td>Impaired coordination/balance</td>
<td>Increased heart rate</td>
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<tr>
<td>Hunger</td>
<td>Hallucinations (in large doses)</td>
</tr>
</tbody>
</table>

- Effects can vary by species / strain
  - *Sativa*: More euphoria, stress relief
  - *Indica*: Relaxation, physical (especially pain) relief
  - *Sativa* and *Indica* often combined
Adverse Effects

• Cannabis Hyperemesis Syndrome
  – Though cannabis is often thought of as being beneficial for nausea and vomiting, chronic use can cause cyclic n/v, abdominal pain, sweating, and weight loss
  – Serotonin antagonists (e.g., ondansetron) usually ineffective for treatment
  – Dopamine antagonists (e.g., phenothiazines, butyrophenones) somewhat more effective

Patients often self-treat by taking hot (>43°C) baths or showers, which provides both short- and long-term relief

• Relief can also be obtained by topical application of capsaicin (e.g., 0.075% cream) to torso
• Mechanism for both has been suggested to be increase in transient receptor potential vanilloid 1 (TRPV1), which acts at emesis center centrally

Effects on Driving

- Marijuana significantly impairs judgment, motor coordination, and reaction time, and studies have found a direct relationship between blood THC concentration and impaired driving ability.
- Role played by marijuana in crashes is often unclear because it can be detected in body fluids for days or even weeks after intoxication and because people frequently combine it with alcohol.

https://www.drugabuse.gov/publications/research-reports/marijuana/does-marijuana-use-affect-driving
• Implications for roadside testing?
  – The person who comes up with a reliable and cost-effective roadside test will strike it rich.
Mature plant ready for harvest

http://marijuana.heraldtribune.com/tag/marijuana-reform-illinois/

Trichomes

https://www.philosopherseeds.com/blog/en/cannabis-trichomes/
• Trichomes are where the biologically active cannabinoids and terpenes are located
• Extracted through a variety of means, including solvent extraction, supercritical CO₂ extraction, and extraction by physical processes (e.g., trimming)
• Hashish, hash oil, wax, budder, shatter
  – Concentrated extracts of cannabis plant
  – More potent than smoking the buds of the marijuana plant
  – Can be infused into edibles
“Moon Rocks”
Enter the “Budtender”

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Committee on the Health Effects of Marijuana consisted of 16 experts in the areas of marijuana, addiction, oncology, cardiology, neurodevelopment, respiratory disease, pediatric and adolescent health, immunology, toxicology, preclinical research, epidemiology, systematic review, and public health.

Conclusions of NAS Report

There is conclusive or substantial evidence that cannabis or cannabinoids are effective for:

- For the treatment of chronic pain in adults (cannabis)
- As antiemetics in the treatment of chemotherapy-induced nausea and vomiting (oral cannabinoids)
- For improving patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids)
There is moderate evidence that cannabis or cannabinoids are effective for:

- Improving short-term sleep outcomes in individuals with sleep disturbance associated with obstructive sleep apnea syndrome, fibromyalgia, chronic pain, and multiple sclerosis (cannabinoids, primarily nabiximols (Sativex®))

[Source](https://www.nap.edu/catalog/24625/the-health-effects-of-cannabis-and-cannabinoids-the-current-state)

There is limited evidence that cannabis or cannabinoids are effective for:

- Increasing appetite and decreasing weight loss associated with HIV/AIDS (cannabinoids)
- Improving clinician-measured multiple sclerosis spasticity symptoms (oral cannabinoids)

[Source](https://www.nap.edu/catalog/24625/the-health-effects-of-cannabis-and-cannabinoids-the-current-state)
• Improving symptoms of Tourette syndrome (THC capsules)
• Improving anxiety symptoms, as assessed by a public speaking test, in individuals with social anxiety disorders (cannabidiol)
• Improving symptoms of posttraumatic stress disorder (nabilone; a single, small fair-quality trial)

There is limited evidence of a statistical association between cannabinoids and:
• Better outcomes (i.e., mortality, disability) after a traumatic brain injury or intracranial hemorrhage
There is limited evidence that cannabis or cannabinoids are *ineffective* for:

- Improving symptoms associated with dementia (cannabinoids)
- Improving intraocular pressure associated with glaucoma (cannabinoids)
- Reducing depressive symptoms in individuals with chronic pain or multiple sclerosis (nabiximols, dronabinol, and nabilone)

There is no or insufficient evidence to support or refute the conclusion that cannabis or cannabinoids are an effective treatment for:

- Cancers, including glioma (cannabinoids)
- Cancer-associated anorexia cachexia syndrome and anorexia nervosa (cannabinoids)
• Spasticity in patients with paralysis due to spinal cord injury (cannabinoids)
• Symptoms associated with amyotrophic lateral sclerosis (cannabinoids)
• Chorea and certain neuropsychiatric symptoms associated with Huntington’s disease (oral cannabinoids)

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• Achieving abstinence in the use of addictive substances (cannabinoids)
• Mental health outcomes in individuals with schizophrenia or schizophreniform psychosis (cannabidiol)
• Epilepsy (cannabinoids)
• Motor system symptoms associated with Parkinson’s disease or the levodopa-induced dyskinesia (cannabinoids)
• Dystonia (nabilone and dronabinol)
• Symptoms of irritable bowel syndrome (dronabinol)

So, How Does This Work?

omma.ok.gov
What Gets Turned In?

- Form downloaded from OMMA website
- Patient supplies filled-out form to the physician
• Standard application fee for patient is $100
• SoonerCare or Medicare enrollees pay $20
  – If application is denied, payment is NOT refunded
• Applicant can designate one caregiver to receive a license. This person must fill out a similar application
What are the Physician Responsibilities?

• Is it necessary to register with the Oklahoma Medical Marijuana Authority (omma.ok.gov)?
  – Not necessary, but will help expedite the application process for the patient.
Phone Number:

- Telephone Number

Office Address:

- Street Address Line 1
- Street Address Line 2
- City
- State
- Zipcode

Professional Email Address:

- Email Address

Name of Practice or Affiliated Practice:

Licensing Entity:

- Oklahoma Board of Medical Licensure & Supervision
- Oklahoma State Board of Osteopathic Examiners
Physician Requirements

• A physician must be in good standing with his or her licensure board.
• The physician must establish a medical record for the patient and must have a bona fide physician-patient relationship.

• The physician must determine the presence of a medical condition(s) for which the patient is likely to receive therapeutic or palliative benefit from the use of medical marijuana.
• The physician must recommend a medical marijuana license according to the accepted standards a reasonable and prudent physician would follow for recommending or approving any medication.
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• The physician must verify the patient’s identity as provided in the Oklahoma Medical Marijuana Authority Rules (310:681-1-7).
• Once the recommendation has been made, there is nothing in the law requiring follow-up visits.
• Once the physician signs on the dotted line and the license is approved, there is no “taking it back.” The recommendation will stand for 2 years.

Is Special Training for the Physician Required?

• No
  – However, a physician must be board certified under rules established by either the Oklahoma Board of Medical Licensure or the Oklahoma State Board of Osteopathic Examiners, and his or her license must be in good standing.
Drug Interactions
(NOT all-inclusive)

• **Anything that causes drowsiness** - Effect can be additive or synergistic

• **Anticholinergics, cocaine, sympathomimetics**
  Cannabinoids can cause tachycardia, resulting in increased heart rate and/or hypertension

• **Disulfiram and fluoxetine** – can cause hypomania

• **Warfarin** – Concurrent use can result in increased INR, potentially leading to bleeding

• **Antiepileptics** – Increased levels of topiramate, zonisamide
### CYP1A2 Inducer – Increased Levels of:

<table>
<thead>
<tr>
<th>Drug</th>
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<tbody>
<tr>
<td>theophylline</td>
<td>flutamide</td>
<td>propranolol</td>
</tr>
<tr>
<td>aminophylline</td>
<td>fluvoxamine</td>
<td>ramelteon</td>
</tr>
<tr>
<td>caffeine</td>
<td>lidocaine</td>
<td>rasagiline</td>
</tr>
<tr>
<td>clozapine</td>
<td>melatonin</td>
<td>ropinirole</td>
</tr>
<tr>
<td>duloxetine</td>
<td>mexiletine</td>
<td>tizanidine</td>
</tr>
<tr>
<td>estradiol</td>
<td>mirtazapine</td>
<td>triamterene</td>
</tr>
<tr>
<td>estrogens</td>
<td>olanzapine</td>
<td>zolmitriptan</td>
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### Strong CYP3A4 Inhibitors – Increase Levels of THC and CBD

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<tr>
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<tbody>
<tr>
<td>clarithromycin</td>
<td>nefazodone</td>
<td>telaprevir</td>
</tr>
<tr>
<td>darunavir</td>
<td>nelfinavir</td>
<td>telithromycin</td>
</tr>
<tr>
<td>grapefruit juice</td>
<td>ombitasvir</td>
<td>verapamil</td>
</tr>
<tr>
<td>itraconazole</td>
<td>paritaprevir</td>
<td>voriconazole</td>
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<tr>
<td>ketoconazole</td>
<td>ritonavir</td>
<td></td>
</tr>
<tr>
<td>lopinavir</td>
<td>posaconazole</td>
<td></td>
</tr>
<tr>
<td>mifepristone</td>
<td>saquinavir</td>
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</tbody>
</table>
Strong CYP3A4 Inducers—Decrease Levels of THC and CBD

carbamazepine  rifampin
enzalutamide  rifapentine
fosphenytoin  St. John's wort
phenobarbital
phenytoin
primidone
rifabutin
Questions?