



**Ain't No Honky Tonk:  
Medical Cannabis for Pain Management**

Theresa Mallick-Searle, MS, PMGT-BC, ANP-BC

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**Title & Affiliation**

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Stanford, CA



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**Disclosure**

- Speakers Bureau: Salix, Avertas
- Any unlabeled/unapproved uses of drugs or products referenced will be disclosed.
- Covering a very LARGE topic in a short amount of time.



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**Learning Objectives**

<b>Cite</b>	potential drug interactions with cannabis
<b>Describe</b>	safety considerations for both patients and clinicians
<b>Summarize</b>	how to negotiate the dispensary

**Painweek**

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**Speaker's Expectations**

- You have heard about cannabis.
- You know a little about the differences between THC & CBD.
- You have a vague grasp of the endocannabinoid system.
- Your patient wants to try/has questions about/likes to joke about/is using cannabis.
- You are "a busy clinician and have 15 (maybe 20) minutes to learn all that I need to know about cannabis."

**Painweek**

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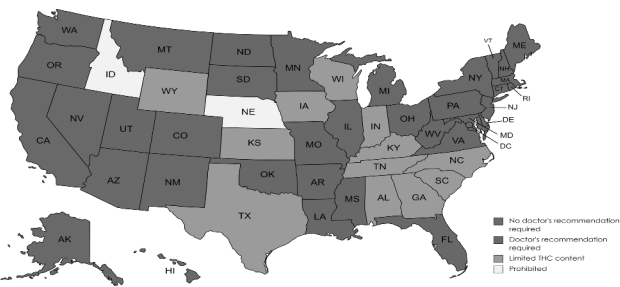
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**Where Does the Country Stand – as of March 2022**

<https://www.mpp.org/states/>



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### Agriculture Improvement Act/Hemp Farming Act 2018

- Removed hemp for the U.S. list of scheduled substances.
- Did not remove hemp derived cannabinoids from the list of scheduled I substances.
- Amended the definition of marijuana → included an exemption for hemp → defined as "any part" of the Cannabis sativa L. plant → containing no more than 0.3% THC.
- Ongoing legislation → federal & regulatory agency guidance.
- States setting their own rules for the hemp industry.
- USDA has broad regulatory "authority" over hemp industry.



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### Cannabis Administration & Opportunity Act 2021

- Senate Majority Leader Chuck Schumer (D-NY), Senate Finance Committee Chairman Ron Wyden (D-OR) & Sen. Cory Booker (D-NJ)
  - federally deschedule cannabis
  - expunge prior convictions
  - maintain the authority of states to set their own marijuana policies
  - impose a federal tax on marijuana products
  - social equity components
- The Marijuana Opportunity, Reinvestment & Expungement (MORE) Act passed the House but did not advance in the Senate under GOP control.
- Separately, a proposal to federally deschedule marijuana that does not include social equity components was recently filed by a pair of Republican congressmen.



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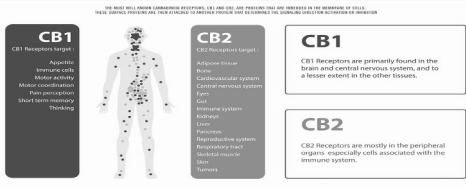
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### Endocannabinoid System: Endogenous-Homeostatic regulatory system-Inherited by all mammals

#### HUMAN ENDOCANNABINOID SYSTEM



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**Clinical Endocannabinoid Deficiency**  
**Ethan Russo, MD (2004/2016)**

- The eCS theory of disease.
- Lack of sufficient endocannabinoids/dysregulation of the eCS.
- Result in higher susceptibility (fibromyalgia, irritable bowel syndrome, depression, anxiety, migraine).
- Phytocannabinoids (THC, CBD) can bind to the cannabinoid receptor sites (CB1, CB2), and mimic the physiological processes seen with binding of the endocannabinoids.



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**Genetic & Epigenetic Influences on eCS**

- Seizures, nerve pain, sleep deprivation - ↑ CB1R in brain (Karlocai et al, 2011; Navarro et al, 2003; Siegling et al, 2001).
- Crohn's - ↑ CB1R in intestines (Izzo et al, 2001).
- Autistic children - ↑ CB2R on white blood cells (Siniscalco et al, 2013).
- Depression/suicidality - ↑ CB1R (Hungund et al, 2004).
- Studies have looked at association between ADHD and a specific polymorphism of the cannabinoid CB1 receptor gene. (Lu et al, 2008).

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**What fraction of cannabis users develop a use disorder?**

- A 2016 study conducted by the National Institute on Alcohol Abuse and Alcoholism, → 2.5% percent of American adults experienced cannabis use disorder in the 12 months prior to the study → 6.3% had met the diagnostic criteria for the disorder at some point in their lives.
- The genome-wide association study (GWAS), a "meta-analysis" of 20 existing population samples - analyzed genome data of 20,196 individuals with cannabis use disorder & 363,116 controls.  
 –cannabis use disorder is positively correlated, at the level of genetic variation, with other psychiatric disorders, including ADHD, major depression, & schizophrenia.

(Johnson, et al., 2020)

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### Entourage Effect: Sum of the Parts

- The entourage effect is a proposed mechanism by which cannabis compounds act synergistically to modulate the overall physiological effects of the plant.
- Example: CBD + THC = possibly mitigating some of the psychosis-like effects of THC.
- Cannabis is a multimodal treatment. It can be used to treat multiple symptoms & conditions concurrently, which can therefore help to reduce polypharmacy burden.



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### What is Cannabis Sativa (aka marijuana)?

- It is a Plant w/over 400 different chemicals:
- >60 types of cannabinoids
    - delta-9-tetrahydrocannabinol (THC)
    - Cannabidiol (CBD)
    - Cannabinol (CBN)
    - Cannabichromene (CBC)
    - Cannabigerol (CBG)
    - Tetrahydrocannabivarin (THCV)
  - Flavonoids, Terpenes, Terpenoids
  - Fungus? Bacteria? Pesticides?
  - Byproducts of manufacturing (solvents, heavy metals)



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### Current Reviews/Meta-analysis



Cannabis-based medicines for chronic neuropathic pain in adults (Review) 2018

Mücke M, Phillips T, Radbruch L, Petzke F, Häuser W

III META-ANALYSIS

Anesth Analg 2017;125:1638-52

#### Selective Cannabinoids for Chronic Neuropathic Pain: A Systematic Review and Meta-analysis

Howard Mong, MD,\* Bradley Johnston, PhD,†§§ Marina Englesakis, MLIS,¶ Dwight E. Moulin, MD,¶ and Anuj Bhatia, MBBS, MD, FRCPC, FRCA, FFPMRCA, FIPR EDRA, CIP§\*

JAMA. 2015;313(24):2456-2473. doi:10.1001/jama.2015.6358

The National Academies of SCIENCES • ENGINEERING • MEDICINE

Original Investigation

#### Cannabinoids for Medical Use A Systematic Review and Meta-analysis

Penny F. Whiting, PhD; Robert F. Wolff, MD; Sohan Deshpande, MSc; Marcello Di Nisio, PhD; Steven Duffy, PgD; Adrian V. Hernandez, MD, PhD; J. Christiaan Keurentjes, MD, PhD; Shona Lang, PhD; Kate Misso, MSc; Steve Ryder, MSc; Simone Schmidlkofer, MSc; Marie Westwood, PhD; Jos Kleijnen, MD, PhD



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## Can I Get My Patient Into a Clinical Trial?

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NLM U.S. National Library of Medicine  
**ClinicalTrials.gov** Find Studies About Studies Submit Studies Resources About Site PRS Login

ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

Explore 367,204 research studies in all 50 states and in 219 countries.

See listed clinical studies related to the coronavirus disease (COVID-19)

ClinicalTrials.gov is a resource provided by the U.S. National Library of Medicine

Find a study (or both options)

Status

Recruiting and not yet recruiting studies  All studies \*

Condition or disease  (For example: breast cancer)

<https://clinicaltrials.gov/>

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**Tell me EVERYTHING I need to know in  
 ≈20 minutes!**

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### Important Talking Points

- Encourage open/non-judgmental dialogue.
- Driving "under the influence".
- Recommend obtaining medical marijuana card issued by state.
- Traveling considerations.
- Provide website resources.
- Share the extend of the research that is known .
- Discuss drug to plant interactions, side effects, risk of addiction.
- Know what to look for in products.
- How to recognize who is behind the counter in the dispensary.



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### Is Medical Cannabis Safe for My Patients?

Review Article  
 "Is medical cannabis safe for my patients?" A practical review of cannabis safety considerations.  
 Caroline A. MacCallum<sup>1,2,3,4</sup>, Lindsay A. Lee<sup>1</sup>, Michael Bains<sup>1</sup>

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### Is Medical Cannabis Safe for My Patients?

Table 1. Precautions and Contraindications.

Considerations <sup>a</sup>	Precautions <sup>b</sup>	Relative Contraindications <sup>c</sup>	Contraindications <sup>d</sup>
Immunocompromised	Concurrent mood or anxiety disorder	Under 25 years of age	Unstable cardiovascular disease
Chronic Kidney Disease	Have risk factors for cardiovascular disease	Current or past cannabis use disorder	Respiratory disease (if smoking cannabis)
Older adults	Tobacco use	Current or past substance use disorder	Personal or strong family history of psychosis/ bipolar
Patients with concurrent medical conditions	E-cigarette use		Pregnant, planning on becoming pregnant, or breastfeeding
Polypharmacy	Severe liver dysfunction/disease		
Potential drug interactions	Medications associated with sedation or cognitive impairment		
	Driving or safety sensitive occupations		

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### Traveling

Interstate transportation of these products is federally illegal.



- TSA security does not search for marijuana or other illegal drugs, but if any illegal substance is discovered during security screening, TSA will refer the matter to a law enforcement officer.
- Marijuana is illegal under federal law, & federal law governs airplane travel in this country.
- Recently, the TSA updated its rules for flying with medical marijuana, allowing travelers to now carry products like Cannabidiol (CBD) oil that contain < 0.3% THC. Passengers can bring products that are approved by the FDA in their checked or carry-on luggage.

**Amtrak** "The use or transportation of marijuana in any form for any purpose is prohibited, even in states or countries where recreational use is legal or permitted medically."

**Greyhound** bans alcohol/drugs "anywhere on the bus (including in your checked baggage)."

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### Driving under the influence/Driving impaired

- Decreases reaction time.
- Feelings of drowsiness or inattention.
- Poor coordination affecting the mechanics of driving (steering, working, braking, etc.).
- Alters rational decision making.
- Alters the ability to judge car's position on the road, road signs, location of other vehicles/object/pedestrians.

**Tip:** If documenting the discussion of cannabis use either recreationally or medicinally with a patient

DOCUMENT the advisement of risks with automobile usage.

▪ ANYTHING THAT A POLICE OFFICER DEEMS APPROPRIATE!

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### Drug Testing for Cannabis

**Many factors:**

- Route of administration (inhaled, oral, topical)
- Duration of use (acute v/s chronic usage)
- Blood, sweat, tears (hair, saliva)
- Sensitivity of the test (immunoassay – screening; v/s GC-MS – confirmatory)
- Genetics – CYP450 variations, adipose tissue



➤ In general, the detection time is longest in hair → urine, sweat, oral fluid & blood.  
 ➤ The average limit or cut-off level for testing positive on a drug test for marijuana (THC) is 50 ng/ml (15 ng/ml for GC-MS).



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### Drug Testing for Cannabis

**Cannabinoid Test Results** 12/01/2018

Cannabinoid analysis utilizing High Performance Liquid Chromatography (HPLC, QSP 5-4-4-4)

	mg/g	%	LOD mg/g	LOQ mg/g
THC	ND	ND	0.000034	0.001
THCa	ND	ND	0.000066	0.001
CBD	10.797	1.0797	0.000057	0.001
CBDa	ND	ND	0.000038	0.001
CBN	ND	ND	0.000029	0.001
CBDV	0.049	0.0049	0.000065	0.001
CBDVa	ND	ND	0.00003	0.001
CBG	ND	ND	0.000086	0.001
CBGa	ND	ND	0.000072	0.001
THCV	ND	ND	0.000035	0.001
Δ8 - THC	ND	ND	0.000083	0.001
CBC	ND	ND	0.000095	0.001
<b>Sum of Cannabinoids:</b>	<b>10.846</b>	<b>1.0846</b>		<b>845.988 mg/Unit</b>
Total THC (Δ9THC+0.877*THCa)	ND	ND		ND
Total CBD (CBD+0.877*CBDa)	10.797	1.0797		842.166 mg/Unit



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### Tolerance & Adverse Effects (AEs)

**Tolerance**

- Mood, sleep
- Psychomotor performance
- Arterial pressure
- Antiemetic properties

**Common AEs**

- > **Anticholinergic effects** (dry mouth, blurry vision, urinary retention, tachycardia, constipation, hypertension).
- > **CNS effects** (ataxia, cognitive dysfunction, hallucination).

Cannabis Hyperemesis Syndrome




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### Cannabis Hyperemesis Syndrome (CHS)

**The risk of developing CHS depends on multiple factors:**

- How much cannabis is used
- Method of administration.
- Confounding medical, psychiatric, ethnic & socioeconomic conditions.

**What is it?**

- Characterized by chronic cannabis use, cyclic episodes vomiting, frequent hot bathing
- Without other organic etiology
- Hypothesized to be a dysregulation of the CB1 receptor (delay in gastric emptying)
- Chronic stimulation of (CB1 receptor, with THC?) may produce a paradoxical emetic response in susceptible individuals

(Perisetti, et al., 2020)




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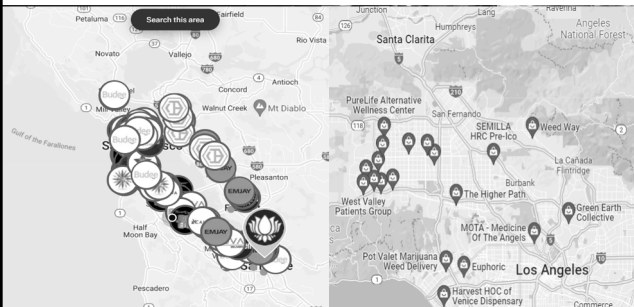
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### At The Dispensary: virtual/in-person/www




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### The “Budtenders” aka “Who’s Behind the Counter”

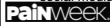
158 budtenders, 56% had received formal training to become a budtender

For workplace characteristics, trained budtenders were

- More likely to report budtender as their primary job (74% vs 53%)
- Practice more than 5 years (34% vs 11%)
- Receive sales commission (57% vs 16%)
- Less likely to perceive medical decision-making as very important (47% vs 68%) & have a patient-centered philosophy (77% vs 89%)

Budtenders who are formally trained exhibit significantly different patterns of interaction with medical cannabis patients

- Were significantly more likely to exchange information with patients through e-mail (58% vs 39%), text message (46% vs 30%), mobile app (33% vs 11%), video call (26% vs 3%) & social media (51% vs 23%).



(Peiper, et al., 2017)

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### The “Budtenders” or “Who’s behind the counter”

55 dispensary staff, 55% reported some formal training → 20% reporting medical/scientific training. 94% indicated that they provide specific cannabis advice.

- Indica for anxiety, chronic pain, insomnia, nightmares & Tourette’s syndrome.
- Indica/hybrid plants for post-traumatic stress disorder (PTSD)/trauma and muscle spasms.
- Recommend a 1:1 ratio (THC):(CBD) for patients suffering from anxiety, Crohn’s disease, hepatitis C, PTSD/trauma
- Patients seeking appetite stimulation were most likely to be recommended THC.
- High CBD for arthritis & Alzheimer’s disease.
- High CBD or 1:1 ratio for ALS, epilepsy, & muscle spasms.

Conclusions:

Although many dispensary staff are making recommendations consistent with current evidence

→ some are recommending cannabis that has either not been shown effective for, or could exacerbate, a patient’s condition.

Findings underscore the importance of consistent, evidence-based, training of dispensary staff who provide specific recommendations for patient medical conditions.

(Haug, et al., 2016)

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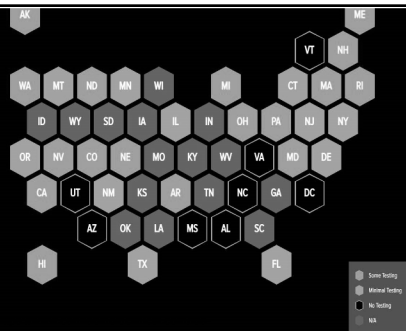
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### The State of Cannabinoid Testing

Of the thousands of cannabinoid products being sold in the market, only a handful undergo testing for quality, safety, and effectiveness. This map shows how cannabinoid products are regulated by each state, in comparison to FDA-approved medications.

FDA APPROVAL PROCESS

Valid as of August 25, 2019. Check a state’s website for the most up-to-date information.



regulation-cannabinoids

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### Recommend Only Products that Are Properly Labeled

- Label information should include the ingredients and the milligrams of each cannabinoid per dose.
- Recommend only products from companies that test for potency, pesticides, mold, and bacteria.
- Mindful of byproducts of production (e.g., solvents).

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### Chemical Varieties/"chemovars"

Though cannabis is biologically classified as a single species: *Cannabis Sativa*, there are at least three distinct plant varieties:

- Cannabis Sativa
- Cannabis Indica
- Cannabis Ruderalis (Pennisi, 2017)

**Indica**

**Morphology:** Short and bushy; suitable for indoor gardens.

**Geographical Origins:** Areas between 30 to 50 degrees latitude.

**Effects:** Tend to be sedating and relaxing with full-body effects.

**Symptom Relief:** Anxiety, insomnia, pain, muscle spasms.

**Sativa**

**Morphology:** Tall and thin; suitable for outdoor gardens.

**Geographical Origins:** Areas between 0 and 30 degrees latitude.

**Effects:** Tend to be uplifting and creative with cerebrally-focused effects.

**Symptom Relief:** Depression, ADD, fatigue, mood disorders.

↓THC ↑CBD      ↑THC ↓CBD

[www.leafly.com](http://www.leafly.com)  
[www.safeaccessnow.org/using\\_medical\\_cannabis](http://www.safeaccessnow.org/using_medical_cannabis)

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### Practical Dosing

Regardless of the specific physiological system, the effects of cannabis are dependent on many factors:

- Dose, variety
- Route (Inhalation, oral, transmucosal, transdermal, topical)
- Timing
- General health (medical co-morbidities), Age
- Use of other substances/medications
- Chronic user of cannabis versus naive

[https://www.colorado.gov/pacific/sites/default/files/MED%20Equivalency\\_Final%2008102015.pdf](https://www.colorado.gov/pacific/sites/default/files/MED%20Equivalency_Final%2008102015.pdf)

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**Lack of Standardization Makes Dosing a Challenge for Patients & Practitioners**

**Overconsumption:**

- > Re-dosing too soon
- > Delayed on-set with oral dosing (>120 minutes)
- > Hostile behavior/erratic speech/mild psychosis

**The L.E.S.S. Method:** A measured approach to oral cannabis dosing

**Start Low**

- > Establish potency
- > Go slow
- > Supplement as needed

(Erowid & Erowid, 2011)



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**Oral vs Inhaled**

	INHALED	ORALLY INGESTED
Peak Blood Levels (min)	3-10	60-120
Bioavailability (%)	10-40	<15
Time to peak psychoactive activity (min)	20	120-240

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**Practical Dosing**

**Average adult dosing of THC:**

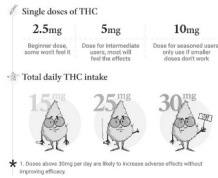
- > Cannabis-naïve individuals 2.5-5 mg
- > Daily - weekly users 10-20 mg
- > Daily+ 25 mg+

**Average adult dosing of CBD:**

300-1500 mg/day  
<https://www.webmd.com/vitamins/ai/ingredientmono-1430/cannabidiol>  
 (MacCallum & Russo, 2018)

> Doses exceeding 20–30 mg/day may increase adverse events or induce tolerance without improving efficacy.

<https://www.leafly.com/news/cannabis-101/cannabis-edibles-dosage-guide-101>  
 (MacCallum & Russo, 2018)



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## Practical Dosing

- Sativex® (1:1 THC/CBD): Spasticity due to multiple sclerosis.  
 > 2.7mg/2.5mg BID  
 (max 32.4mg/30mg/day)  
<https://www.medicines.org.uk/emc/product/602>

- Epidiolex® (CBD): Seizures (Dravet/Lennox-Gastaut)  
 > 5 mg/kg oral BID  
 (max 20 mg/kg/day)  
[https://www.epidiolex.com/sites/default/files/EPIDIOLEX\\_Full\\_Prescribing\\_Information.pdf](https://www.epidiolex.com/sites/default/files/EPIDIOLEX_Full_Prescribing_Information.pdf)



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## Cannabidiol (CBD)

### Defining Terms:

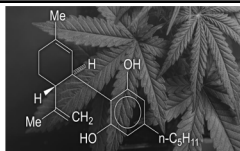
- > CBD from Hemp (↑contaminants, ↓THC)
- > CBD from cannabis sativa (↑THC, ↑purity)
- > Hemp Oil (seeds of hemp plant, little/no CBD, no THC, +essential fatty acids, +omega three)

### Research:

- Epidiolex®
- Other - preliminary research included studies of anxiety, cognition, movement disorders, and pain (anti-inflammatory).
- Efficacy most antidotal (discuss current animal studies).

**Safety:** Dosing toxicity? Anti-inflammatory effects? CYP450 metabolism.

**Side Effects:** Fatigue, diarrhea, changes of appetite/weight, dry mouth. Transaminase elevations (reported in Epidiolex studies).



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## Practical Discussion in the Office

- Patient provider treatment agreement (if for medicinal use).  
<https://adai.uw.edu/mcaco/docs/treatmentagreement.pdf>
- Requirement of patient obtaining a state issued medical cannabis card.
- Documentation of counseling if recreational use discussion.
- It is not illegal to have a discussion and provide counseling.
- Having the discussion, does not mean your endorsement or condoning of behavior.
- Provide resources

[The Medicinal Cannabis Treatment Agreement: Providing Information to Chronic Pain Patients via a Written Document](#) (Wiseya, et al., 2015)

- Obligation to understand and inform patients on key issues of the evidence base on cannabinoid therapeutics.
- One way to fulfill this obligation might be to use of a written agreement to describe & minimize risks.
- Method of educating patients in a manner analogous to other treatment agreements.



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### Final Takeaways

- Familiarize yourself with
  - THC, CBD dosing
  - drug : drug (plant) interactions, side effects, withdrawal
  - local dispensaries & counsel patient to accordingly
- Consider The Treatment Agreement
  - Continue to remember “marijuana” is Federally illegal
  - Informed about state laws
  - Mindful of addiction, abuse, mental health issues




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### Thank You



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### Resources

#### Dispensary Information: Patient Focused Certification

<http://patientfocusedcertification.org/certification/>

- Addresses product & distribution safety.
- Based on quality standards for medical cannabis products and businesses issued by the American Herbal Products Association (AHPA) and the American Herbal Pharmacopoeia (AHP) Cannabis monograph.

<http://camcd-acdcm.ca/>

- More and more states are mandating certification and regulated licensures from dispensaries (e.g. FL).




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### Resources

Canadian Consortium for the Investigation of Cannabinoids (CCIC): [www.ccic.net](http://www.ccic.net)  
> Accredited cannabinoid education (ACE) programs  
> Informed by needs assessments, expert faculty

- International Cannabinoid Research Society (ICRS): <https://icrs.co/>
- International Association for Cannabinoid Medicine (IACM): [www.cannabis-med.org](http://www.cannabis-med.org)
- University of Washington & Alcohol and Drug Abuse Institute (ADA) <http://ada.uw.edu/mcaco/index.htm>
- Society of Cannabis Clinicians: [www.cannabisclinicians.org](http://www.cannabisclinicians.org)
- <https://www.cannabinoidclinical.com/cannabinoid-resource> (site sponsored by Greenwich Biosciences, Inc.)



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### Resources

<https://www.ukmccs.org/wp-content/uploads/2020/06/A-Clinicians-Guide-to-CBD-v1-June-2020.pdf>



TABLE OF CONTENTS		
01	Introduction	11 Discussing CBD with patients
02	The Endocannabinoid System	12 Drug interactions
03	What is CBD?	14 Side effects
06	Key differences between medical CBD and cannabis oil	16 Legality of CBD products in the UK
07	Individual cases of CBD	18 What should clinicians be looking for?
08	Oral CBD: the patient's experience	19 Consider the CBD product
10	Smoking CBD	20 References



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### Resources

#### Cannabis & CBD Guide - Consumer Reports

Your Guide to CBD



A Guide to CBD and Cannabis for Older Adults



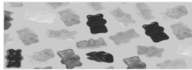
Is It Safe to Vape CBD?



CBD Goes Mainstream



How to Shop for CBD



How to Safely Use CBD: Should You Inhale, Spray, Apply, or Eat It?



CBD May Be Legal, But Is It Safe?



<https://www.consumerreports.org/cbd/cannabis-and-cbd-guide/>

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