Consideration of Medical Marijuana Inclusion in Life Care Planning: Implications and Challenges

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Learning Objectives

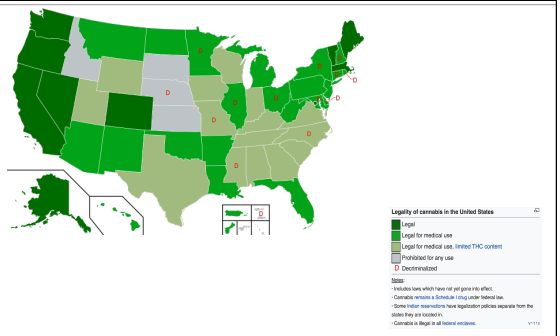
- Identify terms related to medical marijuana, cannabinoids and cannabis
- Define cannabis specific recommendations/ prescriptions based on medical diagnosis
- Understand challenges and implications related to inclusion of cannabis in life care plans
- Define solutions related to inclusion of cannabis in life care plans

The Legality of Medical Cannabis

Here in the US, there are now 46 states + the District of Columbia that have legalized medical cannabis to some degree

That is about 90% of this country whose politicians and voters have decided they are on board with seeing the medical benefits of cannabis

Legality of Cannabis in the US

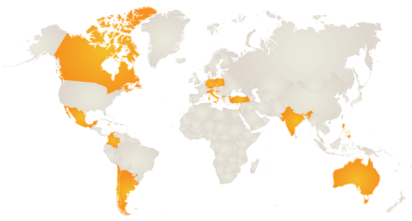


Legality of Cannabis in Canada

- Canada has been crafting regulations to have a system for the legal cultivation, sale, and consumption of cannabis for adults, which was to be put in place by July 2018 so adults over the age of 18 can legally possess up to 30 grams of dried flower (currently on track for implementation 10-15-18)
- Individual provinces can decide to raise the legal minimum age
- A medical cannabis program run by Health Canada called the Access to Cannabis for Medical Purposes regulations outlines specific conditions that allow medical patients access to cannabis medicine

Nickus, L. 11-1-17 (updated 3-15-18) Marijuana.com
https://www.marijuana.com/news/2017/11/where-in-the-world-is-marijuana-legal/

Worldwide Legality of Cannabis



MacIver B. 6-29-17 Cannabis Legalization World Map
http://www.cannabisbusinesstimes.com/article/cannabis-legalization-world-map/

Politics & Cannabis

- Trying to stay up to date on the latest comments from our US politicians has been a moving target
- On 04/11/18, Former House Speaker, John Boehner (R-Ohio) announced that he had joined the board of a top cannabis corporation (Acreage Holdings) to promote the use of medical marijuana, which was a shift from his once-adamant opposition to legalization of the substance. He and Massachusetts Gov. Bill Weld (Libertarian), in a joint statement, stated, that "They are hoping to de-schedule cannabis from a Class 1 drug at the federal level so it can be used for medical purposes."

The Hill http://thehill.com/blogs/blog-briefing-room/news/382614-boehner-joins-board-of-cannabis-company-for-push-for-medical

Politics & Cannabis

- June of 2018: Time Magazine Special Edition: "Marijuana The Medical Movement". Within this publication, there is discussion on how the Obama administration sent out memos that gave people in the industry some assurance that if they abided by their state laws, when it came to marketing and selling marijuana, then there would be only a small risk of federal prosecution. However, in January 2018, Attorney General Jeff Sessions rescinded those memos, allowing federal prosecutors to enforce federal marijuana laws.
- On 08/22/18, Senator Warren (D-MA) stated to Jen Rogers on the Final Round, that the federal government should "back off" while an increasing number of US states legalize marijuana for various reasons. She went on to say, paraphrased, just let the states do their job and enforce their own laws.
- Senator Elizabeth Warren (D-MA) and Cory Gardner (R-CO) are attempting to pass bipartisan legislation to amend the Controlled Substances Act (CSA) to prevent prosecution of individuals and businesses that comply with state and tribal laws

https://www.yahoo.com/news/senator-warren-weed-legalization-federal-government-just-back-off-191426405.html?.tsrc=1jc_news_index

VA Policy for Military Veterans

- December 2017: VA Issued a Medical Marijuana Policy for Military Veteran
- Doctors with the VA were told that they could not recommend medical marijuana, but they were encouraged to talk more about it with military veterans
- The directive urged government doctors to "discuss with the Veteran marijuana use, due to its clinical relevance to patient care, and discuss marijuana use with any Veterans requesting information about marijuana."
- However, the policy reiterated the department's long-held position that "to comply with Federal laws such as the Controlled Substances Act…providers are prohibited from completing forms or registering Veterans for participation in a State-approved marijuana program."

https://www.forbes.com/sites/tomangell/2017/12/19/v-a-issues-new-medical-marijuana-policy-for-military-veterans/#1588454d5b90

Definitions

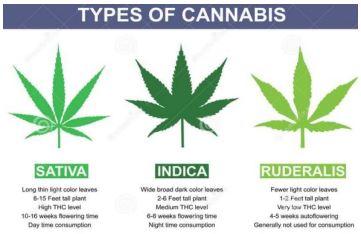
- Cannabis
- Marijuana
- Medical Marijuana / Medical Cannabis
- Cannabinoids

- For purposes of clarity, presentation will use cannabis and medical marijuana interchangeably

Definitions: Cannabis

- Cannabis: Botanical Genus name for the plant known as hemp, pot, marijuana, ganja, weed, dope, Mary Jane, etc.
- Cannabis is classified into three distinct species
  - Sativa
  - Indica
  - Rideralis

Definitions: Cannabis



https://www.google.com/search?q=cannabis+3+species&source=lnms&tbm=isch&sa=X&ved=0ahUKEwj_ibT2mqDdAhWZJDQIHQ8VA6sQ_AUICigB&biw=1920&bih=974#imgrc=DRx57D1etJ_8MM

Definitions: Cannabis


C. Sativa


C. Indica


C. Ruderalis

https://www.google.com/search?q=Cannabis+sativa&source=lnms&tbm=isch&sa=X&ved=0ahUKEwjmytXKnKDdAhWDJDQIHXpvCHEQ_AUICigB&biw=1920&bih=974#imgrc=j7e4ceCql9xBsM

https://www.google.com/search?q=cannabis+indica&source=lnms&tbm=isch&sa=X&ved=0ahUKEwjYmMGAnaDdAhWLIjQIHdYcCmMQ_AUICigB&biw=1920&bih=974#imgrc=H-QqOeEmts1jNM

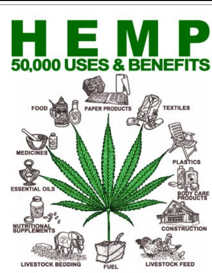
https://www.google.com/search?q=cannabis+ruderalis&source=lnms&tbm=isch&sa=X&ved=0ahUKEwjq26PanaDdAhVCHTQIHdTBA58Q_AUICigB&biw=1920&bih=974#imgrc=fQ83zUsudQ514M

Definitions: Cannabis Sativa

- Cannabis sativa :
  - Cannabis sativa can be grown for industrial (non-drug purposes)
    - When cannabis sativa is grown for medicinal uses, it has higher concentrations of THC, but generally has a poor fiber quality and is not typically used industrially
  - Uses of hemp (cannabis plant) include textiles, paper, fuel, food and oil
    - Grows quickly with few chemicals
    - The seeds of hemp contain high quantity protein, 11 grams protein per 3 tablespoons, i.e.: 30 g/serving*

* https://www.livestrong.com/article/486854-are-hemp-seeds-a-good-source-of-protein/

Definitions: Cannabis Sativa



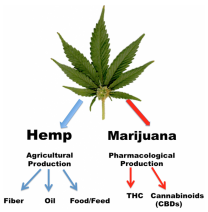
https://www.google.com/search?q=cannabis+3+species&source=lnms&tbm=isch&sa=X&ved=0ahUKEwj_ibT2mqDdAhWZJDQIHQ8VA6sQ_AUICigB&biw=1920&bih=974#imgdii=OdugLxlZk4ESLM:&imgrc=ZCI3SaGMukxJqM

Definitions: Marijuana

- Marijuana: Name for cannabis plant or specifically the drug preparation from it
  - Definition varies by jurisdiction
    - Whole cannabis plant
    - Any part of cannabis plant
    - Distinctive strain of cannabis
    - Or portion of cannabis plant that contains high levels of THC
- Term originated in Mexican Spanish
  - Term 'marijuana' was promoted by opponents of the drug
    - Stigmatize cannabis as foreign
    - Racist meme to characterize social deviancy in minorities*

* Halperin A. 1-29-18 The Guardian https://www.theguardian.com/society/2018/jan/29/marijuana-name-cannabis-racism

Definitions: Marijuana



Definitions: Medical Marijuana

- Medical Marijuana: Refers to cannabis available by prescription and used to treat a variety of medical conditions

Definitions: Cannabinoids

- Cannabinoids: The natural chemical compounds the cannabis plant produces
  - There are 113 known cannabinoids, which are produced from the resin of cannabis plant
    - The most substantial body of research has been completed on THC, CBD and CBN
    - The major difference between cannabinoids is the extent that they are psychologically active

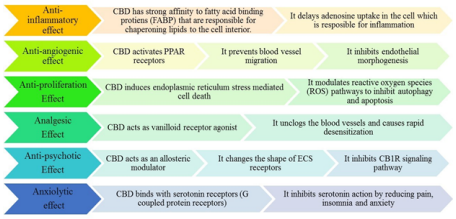
Cannabinoid Subclasses

- Non-Psychoactive Cannabinoids
  - Cannabidiol (CBD)
  - Cannabigerol (CBG)
  - Cannabichromene (CBC)
  - Cannabicyclol (CBL)
  - Cannabielsoin (CBE)
- Psychoactive Cannabinoids
  - Tetrahydrocannabinol (THC)
  - Cannabinol (CBN)
  - Delta-8-Tetrahydrocannabinol (Δ-8-THC)
- Psychoactive Function Unknown
  - Cannabitriol (CBT)

Non-Psychoactive Cannabinoids

- Cannabidiol (CBD)
  - 40% of cannabis extracts from *Cannabis sativa* plant
  - Ongoing research on efficacy of CBD for treatment of multiple sclerosis, Alzheimer's, Parkinson's Disease, PTSD, anxiety, bipolar disorder, dystonia, seizures, schizophrenia, pain and insomnia

Non-Psychoactive Cannabinoids



http://www.whybiotech.com/how-does-cbd-work-in-the-body

Non-Psychoactive Cannabinoids

- Cannabigerol (CBG)
  - Ongoing research on efficacy of CBDs for use as sedative, antibiotic and analgesia
  - During growth, most CBG is converted to other cannabinoids, primarily tetrahydrocannabinol (THC) or cannabidiol (CBD)
    - "Stem cell" cannabinoid, 'mother cannabinoid'
- Cannabichromene (CBC)
  - Binds to pain receptors
  - Works synergistically with other cannabinoids: 'entourage effect'
- Cannabicyclol (CBL)
  - Little is known about CBL or its potential in medicine
  - Formed from degraded CBC
- Cannabielsoin (CBE)
  - Metabolite of cannabidiol (CBD)

Psychoactive Cannabinoids

- Tetrahydrocannabinol (Δ-9-THC)
  - Major active ingredient of cannabis plant extracts
  - Delta-9-tetrahydrocannabinol (Δ 9-THC) primarily responsible for psychoactive effects of cannabis
  - Alterations in memory, movement, mood, perception and cognition
    - Increase dopamine release
    - Produces euphoric sensation: 'high'
- Delta-8-Tetrahydrocannabinol (Δ-8-THC)
  - Antiemetic, anxiolytic, appetite-stimulating, analgesic and neuroprotective properties
- Cannabinol (CBN)
  - THC degradation occurs when exposed to light and air, oxidizing THC into CBN and becomes weakly psychoactive
  - CBN interacts with THC to reduce its effects and potency

Psycho-activity Unknown

- Cannabitriol (CBT)
  - Identified 2014
  - Until clinical trials have been conducted, it is unknown if CBT has a medical or psychoactive effect

Definitions: THC Vs. CBD

- CBD and THC both found in seeds, stalks and flowers of both hemp and marijuana
  - Marijuana primarily contains THC
    - Marijuana has been manipulated and cloned to increase THC concentration, which can be as low as 3%, but on average, strains contain ~12% THC
  - Hemp (fiber of cannabis plant) primarily contains CBD
    - Chemical makeup of hemp is primarily CBD with THC content of less than 0.3%
    - Nearly 10 times less potent than the least potent strain of marijuana

Definitions: THC Vs. CBD

- Side effects and safety
  - THC's psychoactive properties can cause temporary side effects including:
    - Memory impairments
    - Lower reaction times
    - Increased heart rate
    - Coordination problems
    - Dry mouth
    - Red eyes
  - CBD's reported side effects:
    - Dry mouth
    - Low blood pressure
    - Light headedness
    - Drowsiness
- National Cancer Institute indicates it is not possible to have a fatal overdose of THC or CBD*

*NIH, National Cancer Institute. Cannabis and Cannabinoids-Health Professional Version
https://www.cancer.gov/about-cancer/treatment/cam/hp/cannabis-pdq

Historical Use of Cannabis

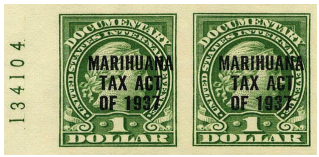
- Medicinal use of cannabis was described in Chinese texts in third millennium BC for relief of pain
- Ancient India recorded use of ingested marijuana for anxiety relieving affect more than 3000 years ago
- Cannabis was introduced into Western medicine in 1839 by W.B. O'Shaughnessy, a surgeon who learned its analgesic, sedative, anti-inflammatory, antispasmodic and anticonvulsant effects while working in India
- Cannabis extracts gained widespread use for medicinal purposes in America until 1937, when dangers of abuse prevailed

US History of Cannabis Legislation

- 1937: US Treasury Department: Marihuana Tax Act (original spelling):
  - Federal legislation 'Marihuana'…all parts of *Cannabis sativa,* with exception of mature stalks, oil and & cake made from cannabis seeds or other products of the plant utilized by the hemp industry in America
  - Imposed $1.00 per ounce tax for medicinal use and $100.00 per ounce for nonmedicinal use
  - The American Medical Association (AMA) was opposed to the act because
    - Physicians were taxed for prescribing cannabis
    - Physicians were forced to use special order forms to procure cannabis and keep specialized records for professional use
    - Physicians argued for cannabis to be added to the Harrison Narcotics Tax Act*
      - Harrison Narcotics Tax Act regulated and taxed production, importation and distribution of opiates and coca products

US History of Cannabis Legislation

- Stamp farmers could acquire to cultivate fiber hemp



Rough, L. 5 Facts About the Marihuana Tax Act of 1937. *Leafly.* 8-2-17

US History of Cannabis Legislation

- 1942: Cannabis removed from the US Pharmacopoeia due to concerns about its 'potential' to cause harm
- 1951: Congress passed the Boggs Act
  - For the first time cannabis was listed as a narcotic drug
- 1970: Controlled Substances Act (CSA)
  - Congress officially outlawed cannabis for any use, including medical usage
- 1978: Compassionate Use Investigational New Drug Program
  - US government allowed distribution of cannabis on a case-by-case basis, outside clinical trials, for people with a life threatening condition or failure to meet clinical trial enrollment criteria
- 1992: The Compassionate Use Investigational New Drug Program was closed to new patients

US History of Cannabis Legislation

- Currently, the legality of cannabinoid products in the US is dependent on its concentration and source
  - Marijuana and THC are listed in the US Controlled Substances Act
  - Classified as Schedule I agents and prohibited under federal law
    - High potential of abuse
    - No accepted medical use
    - The US Food and Drug Administration (FDA) has not approved cannabinoid products **as treatment for** any medical condition, including cancer

US History of Cannabis Legislation

- Commercially available and made available in 1985: Cannabinoids were approved **drugs for treatment of cancer-related side effects***
  - Dronabinol (Marinol)**
  - Nabilone (Cesamet) ***

* NIH National Cancer Institute https://www.cancer.gov/about-cancer/treatment/cam/hp/cannabis-pdq#section/all

** Dronabinol/Marinol: synthetic THC used to treat nausea and vomiting associated with cancer chemotherapy

*** Nabilone/Cesamet: synthetic THC to treat nausea and vomiting due to chemotherapy

US History of Cannabis Legislation

- 46 states allow cannabidiol for medical purposes although laws vary
  - States may legalize only one ingredient such as cannabidiol (CBD)
  - States may limit the medical conditions for which treatment with cannabis is allowed
  - Technically TCH is illicit, therefore, if medical marijuana is illegal in a state, the concentration of TCH determines if a CBD product is illicit
    - If THC < 1% (0.3% in some states) CBD is considered hemp-derived

US History of Cannabis Legislation

- Under US Federal law, hemp-derived CBD products are illegal
  - Title 21 United States Code (USC) Controlled Substances Act (CSA) (21 U.S.C. § 811)*
  - Federal Government and DEA guidance is clear: Cannabidiol is illegal and "always has been"**

*US Department of Justice, Drug Enforcement Administration, Diversion Control Division https://www.deadiversion.usdoj.gov/21cfr/21usc/811.htm

**Hudak J., Stenglein C. 2-6-17 DEA guidance is clear: Cannabidiol is illegal and always has been. FIXGOV https://www.brookings.edu/blog/fixgov/2017/02/06/cannabidiol-illegal-and-always-has-been/

US History of Cannabis Legislation

- Under federal law, possession of cannabinoid products are illegal, except within approved research settings
- To complete clinical research, researchers are required to:
  - File an Investigational New Drug (IND) application with the FDA
  - Obtain a Schedule I license from the US Drug Enforcement Administration
  - Obtain approval from the National Institute on Drug Abuse

US History of Cannabis Legislation

- Federal law regulating cultivation of industrial hemp for academic research
  - U.S. Code § 5940 (U.S. Code, Title 7, Chapter 88, Subchapter VII, §5940) - Legitimacy of industrial hemp research (Pub. L. 113–79, title VII, §7606, Feb. 7, 2014, 128 Stat. 912; Pub. L. 114–95, title IX, §9215(f), Dec. 10, 2015, 129 Stat. 2166.)

https://www.law.cornell.edu/uscode/text/7/5940

Industrial Hemp derived CBD

- CBD extracted from industrial hemp (C. Sativa species of Cannabis) produce "nearly no" THC and "high-CBD" products
  - The process in which CBD is extracted, manufactured, concentrated, formulated, delivered or administered can vary
  - Distributors that sell product that contain < 0.3% THC assert they are allowed to ship products across state borders
  - The FDA regulates Hemp CBD as a dietary supplement*
    - FDA is not authorized to review dietary supplements for safety and effectiveness
    - Medical and recreational CBD markets are becoming known for strict testing standards
    - Medical marijuana CBD products contain higher concentrations of CBD than hemp-derived CBD
    - Many producers utilize stringent production, manufacturing and testing guidelines

* Wilder, Z. How Is Hemp CBD Oil Different From Marijuana CBD Oil? *Merry Jane* 7-2-18
https://merryjane.com/health/british-scientists-discover-how-cbd-can-fight-symptoms-of-psychosis

**US Food and Drug Administration: Warning Letters and Test Results for Cannabidiol-related Products.
https://www.fda.gov/NewsEvents/PublicHealthFocus/ucm484109.htm

Hemp Seed Oil CBDs

- Hemp Seed Oil CBD
  - Extraction is a very expensive process using state-of-the-art technology
  - If CBD is extracted with a low quality extraction process, the product will contain very little, if any, CBD
    - Low cost hemp seed oil is likely to have little, if any, CBD
    - Hemp seed oil is a good source of protein, vitamin E, phosphorus, potassium, sodium, magnesium, sulfur, calcium, iron and zinc

https://www.marijuanabreak.com/amazon-hemp-oil-vs-real-cannabis-cbd-oil
https://groncbd.com/cbd-revolution/

CBDs From Other Plants

- CBD is created through process that combines evergreen plant material with citrus, under heat and pressure: chocolate bars & capsules are common

CBDs From Other Plants

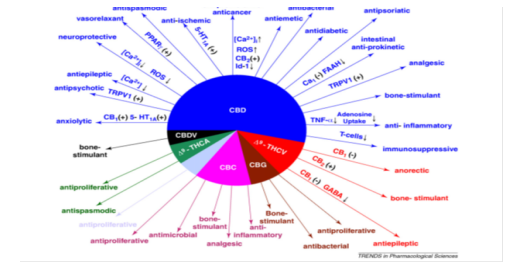
- Echinacea (Coneflower)
  - Cannabimimetcs instead of cannabinoids in the endocannabinoid system (CB_2 receptor)
    - Regulating immune system, pain and inflammation

CBDs From Other Plants

- Acmella oleracea (Electric Daisy)
  - Inflammation, pain killing gel by blocking pain receptors
- Italian Strawflower (Helichrysum umbraculigerum)
  - Mood-stabilizing, anti-depressant affect due to CBG (cannabigerol)
- Liverwort (Radula marginata)
  - Perrottetinenic acid-similar to THC, binds to CB_1 receptors to treat bronchitis and alleviate gallbladder, liver and bladder problems
  - Not known to have psychoactive effects
- Black Pepper - (Piper nigrum)
  - Common aroma molecule (terpene), beta-caryophyllene (BCP) binds to CB_2 receptors to reduce inflammation
  - Research suggests may be useful for arthritis, osteoporosis and potentially increase effectiveness of certain anti-cancer drugs




Pharmacology of Cannabinoids



D9-THC, D9-tetrahydrocannabinol; D8-THC, D8-tetrahydrocannabinol; CBN, cannabinol; CBD, cannabidiol; D9-THCV, D9-tetrahydrocannabivarin; CBC, cannabichromene; CBG, cannabigerol; D9-THCA, D9-tetrahydrocannabinolic acid; CBDA, cannabidiolic acid; TRPV1, transient receptor potential vanilloid type 1; $PPAR_\delta$, peroxisome proliferator-activated receptor δ; ROS, reactive oxygen species; 5-HT1A, 5-hydroxytryptamine receptor subtype 1A; FAAH, fatty acid amide hydrolase. (+), direct or indirect activation; ↑, increase; ↓, decrease

http://biochanvre.ch/info/en/IMG/pdf/Non-psychoactive-Cannabinoids.pdf

Pharmacology of Cannabinoids

- Phytocannabinoids such as THC, CBD, and CBN were identified first and isolated from the plant
- Then, in 1988, while scientists were investigating how THC exerted its effects, the ENDOCANNABINOID SYSTEM was discovered within our bodies

Pharmacology of Cannabinoids

- The discovery of this endogenous system has led to exploration of how cannabinoids, including both the plant molecules and synthetic versions developed in laboratories, might be used for therapeutic purposes
- Researchers are continuing to investigate the therapeutic potential of phytocannabinoids, while also exploring the development of synthetic cannabinoids that mimic their effects
- Compounds that are researched and developed may focus on a single type of cannabinoid or may combine more than one type of cannabinoid

Pharmacology of Cannabinoids

- Dronabinol (Delta 9-tetrahydocannabinol, THC), the main source of the pharmacological effects caused by the use of cannabis, is an agonist to both the CB1 and the CB2 subtype of cannabinoid receptors
- The non-psychotropic cannabidiol (CBD), some analogues of natural cannabinoids and their metabolites, antagonists at the cannabinoid receptors and modulators of the endogenous cannabinoid system are also promising candidates for clinical research and therapeutic uses
- Cannabinoid receptors are distributed in the central nervous system and many peripheral tissues, including spleen; leukocytes; reproductive, urinary and gastrointestinal tracts; endocrine glands; arteries; and heart

Endocannabinoid System

A Beginner's Guide to the Endocannabinoid System

- Cannabis medications work so efficiently because of the endocannabinoid (EC) system, present in all humans and many animals as well. This system consists of a series of receptors that are configured to accept cannabinoids, especially THC and CBD. Not enough research has been done on CBN and CBG plus others, to know much about their mechanisms of effect.
- This system, an integral part of our physiologies, was discovered in the mid-1990s by Israeli researcher Dr. Ralph Mechoulam, who also identified THC as the main active ingredient in cannabis in the early 1960s. Israel has been one of the most progressive nations for cannabis research and currently has one of the most advanced medical marijuana programs in the world. They are international leaders in advanced greenhouse technology, routinely producing flowers with 20 percent or greater THC.
- Dr. Mechoulam's world-changing research discovered two main receptors, cannabinoid 1 (CB1) and cannabinoid 2 (CB2), that are keyed to both the endocannabinoids that our body naturally produces and phytocannabinoids (plant-based) like THC and CBD. Our bodies actually produce the ECs similar to how our body produces narcotic-like endorphins. Synthetic cannabinoids, like the ones found in Marinol, also fit the receptor sites, but don't work as efficiently as the natural ones.

http://reset.me/story/beginners-guide-to-the-endocannabinoid-system/

Endocannabinoid System

- The endocannabinoid system can impact a person's physiological processes, including:
  - Pain and inflammation
  - Feeding and energy regulation
  - Learning and memory
  - Emotion regulation

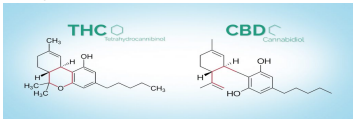
Endocannabinoid System

- Endocannabinoids identified so far include:
  - Anandamide (AEA)
  - 2-arachidonoylglycerol (2-AG)
  - Virodhamine
  - N-arachidonoyl dopamine (NADA)
  - Noladin ether (2-arachidonyl glyceryl ether)
    - These neuroregulatory molecules bind to cannabinoid receptors (such as CB_1 and CB_2) that have been found within the central nervous system, reproductive organs, skin, and digestive tract

https://www.cannabinoidclinical.com/science-cannabinoids

Endocannabinoid System

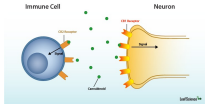
- CBD and THC share the same chemical composition, molecular formula and molecular weight, but the anatomic arrangements of the two cannabinoids differ slightly. CBD has an open ring with a hydroxyl and alkene group while THC has a closed ring with an esther group. It is this slight difference in atom arrangement that dramatically affects CBD and THC's interactions with endocannabinoid receptors.



https://news.medicalmarijuanainc.com/differences-cbd-thc/

Endocannabinoid System

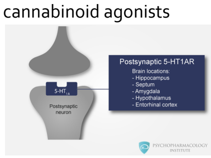
- THC binds directly with CB_1 and CB_2 receptors with higher affinity for CB_1 receptors
  - CB_1 primarily in brain, spinal cord and nerve endings
  - CB_2 receptors primarily in peripheral nervous system , especially concentrated in immune cells



https://www.leafscience.com/2017/03/17/the-endocannabinoid-system-a-beginners-guide/

Endocannabinoid System

- CBD's suppress CB_1 and CB_2 activation
  - CBD's interact with non-cannabinoid receptors ($5\text{-}HT_1A$ receptors* and vannilloid receptor $TRPV\text{-}_1$ **)
  - CBD is an indirect antagonist of cannabinoid agonists



https://www.google.com/search?q=5-ht1a+receptors&source=lnms&tbm=isch&sa=X&ved=0ahUKEwj41LCOvaDdAhU1KX0KHcgEBVIQ_AUICigB&biw=1920&bih=974#imgrc=_6yqlzBhnoX63M:

* 5-HT-1 A receptor: subfamily of 5-HT serotonin receptors

** Vannilloid receptor (TRPV-1): peripheral nociceptors-transduction of noxious chemical and thermal stimuli, evidence receptor involved in cancer and inflammatory pain

Cannabinoids: Indications For Use

- Multiple sclerosis
- Spasticity
- Crohn's disease / Ulcerative colitis
- ADHD
- Seizure disorders / Epilepsy
- PTSD
- Depression / Anxiety
- Insomnia
- Nausea / Vomiting
- Glaucoma
- Headaches / Migraines
- Cancer
- HIV / AIDS
- Parkinson's disease
- Chronic pain
  - Fibromyalgia
  - Arthritis
  - Neuropathy
  - Phantom pain

Cannabinoids: Contraindications

Contraindications:

- Low Blood Pressure
- High Heart Rate
- Driving / Operating machinery
- Immunosuppression (specific to smoking due to risk of Aspergillus that may affect lungs or sinuses)

Cannabinoids: Contraindications

Potential interactions with other prescription medications

- Warfarin: CBD reduces the enzymatic degradation of Warfarin, thereby increasing its duration of action and effect
- Anti-seizure medications: Some epileptic patients have encountered issues with how CBD interacts with their medications, such as clobazam
- Opioids: May amplify the side effects of drowsiness, depression and decreased respirations
- Sedatives: May increase the potency of the sedatives
- Antihistamines: May increase the side effect of drowsiness
- Metformin: Cannabis has been shown to decrease the effectiveness of this blood sugar controlling medication
- Theophyllines are a group of drugs often used in the treatment of asthma and COPD (chronic obstructive pulmonary disease): These drugs are related to caffeine and Cannabis has been shown to increase the metabolism of these drugs; therefore, the dose or frequency of these medications may require adjustment when combined with Cannabis

Special Precautions and Warnings

Other Precautions and Warnings

- **Pregnancy**: Marijuana is **UNSAFE** when taken by mouth or smoked during pregnancy. Marijuana passes through the placenta and can slow the growth of the fetus. Marijuana use during pregnancy is also associated with childhood leukemia and abnormalities in the fetus.
- **Breast-feeding**: Using marijuana, either by mouth or by inhalation is **LIKELY UNSAFE** during breast-feeding. The dronabinol (THC) in marijuana passes into breast milk and extensive marijuana use during breast-feeding may result in slowed development in the baby.
- **Heart disease**: Marijuana might cause rapid heartbeat, short-term high blood pressure. It might also increase the risk of a having heart attack.
- **A weakened immune system**: Cannabinoids in marijuana can weaken the immune system, which might make it more difficult for the body to fight infections.
- **Lung diseases**: Long-term use of marijuana can make lung problems worse. Regular, long-term marijuana use has been associated with lung cancer and also with several cases of an unusual type of emphysema, a lung disease.
- **Seizure disorders**: Marijuana might make seizure disorders worse in some people; in other people it might help to control seizures.
- **Surgery**: Marijuana affects the central nervous system. It might slow the central nervous system too much when combined with anesthesia and other medications during and after surgery. Stop using marijuana at least 2 weeks before a scheduled surgery.

Mainstream RX Vs Dispensary

Mainstream RX

Marinol (dronabinol)

- **FDA approved in 1985**
- Man-made THC, in capsule form
- Made by AbbVie Inc.
- It is approved for use in two patient groups: HIV/AIDS patients, who use it to improve appetite and fight weight loss, and cancer patients, who use it to relieve nausea and vomiting caused by chemotherapy
- With the addition of some many other products out there, that are natural and from the plant extract itself, Marinol is losing popularity, however, interestingly, it has finally come to be accepted by insurance / payor sources, such as the VA, Kaiser and others
- Cost = $200 to $1000.00/month (2.5 mg to 10 mg once to three times per day: GoodRx.com]

Mainstream RX

Mainstream RX

Sativex®

- **FDA approval pending**
- Oral spray is meant to relieve muscle spasticity (stiffness and lack of control) related to multiple sclerosis (MS)
- Sativex is a whole plant-based peppermint flavored mouth spray, using formulated extract of the *Cannabis sativa* plant that contains the principal cannabinoids THC and CBD, as well as specific minor cannabinoids and other non-cannabinoid components
- It is made by British pharma manufacturer GW Pharma
- It is currently available in 28 countries
- Cost = $745.00 for 6 to 8 week supply (emergehealth.com.au)
  - Conversion = $1.00 au to $0.71 us

Mainstream RX

Mainstream RX

Cesamet

- **FDA approved in 1985**
- Synthetic cannabinoid, which is an older medication that was introduced to the consumer market during the 1980s
- Cesamet's active ingredient is nabilone, a synthetic cannabinoid or man-made imitation THC
- Meda Pharmaceuticals, the company that currently owns Cesamet, describes it as "a prescription medicine that may help relieve nausea or vomiting caused by chemotherapy," adding, "It's for people who continue to feel nauseous or are vomiting, even though they've already taken medicine to treat these symptoms"
- Cost = $2,300 to $2,500.00/month (1 mg twice per day: GoodRx.com)

Mainstream RX

Mainstream RX

Epidiolex

- **FDA approved June 2018 / Not available in pharmacies until the end of 2018**
- Epidiolex isolates CBD from the dozens of other cannabinoids, which are also present in marijuana
- Epidiolex is made by GW Pharmaceuticals, which describes this medication as "a liquid formulation of pure plant-derived Cannabidiol (CBD) as a treatment for various orphan pediatric epilepsy syndromes"
- These syndromes are listed as, Dravet syndrome, Lennox-Gastaut syndrome (LGS), Tuberous Sclerosis Complex (TSC) and Infantile Spasms (IS)
- Advertised: Epidiolex started in EU as a mouth spray for children with very rare genetic causes of epilepsy – not common types of epilepsy
- Now offered by GW Pharmaceuticals as a strawberry-flavored syrup
- Cost = $2,500 to $5,000.00/month (Dosage not specified: New York Times 03/15/16)

Mainstream RX

Mainstream RX

Cannador®

- Registered in Germany, this an oral capsule containing a whole plant extract, with standardized THC content and a CBD amount controlled to lie within a fixed narrow range with a THC:CBD ratio of about 2:1
- It has been used in several clinical trials and is a registered trademark in many countries
- It has been clinically tested for reduction of muscle stiffness, spasms and associated pain in Multiple Sclerosis, for anorexia, in cancer patients, and for post-operative pain management

Mainstream RX

An interesting side note, Cannador® in the US is actually a company that provides "premium storage for the connoisseur"

Dispensaries

Examples of How to Find a Dispensary

- Wheresweed.com
- Weedmap.com
- Leafly.com/finder

Every state with legalized cannabis has their own websites for finding dispensaries

Dispensaries

Dispensaries

What Are the Most Popular Marijuana Products Being Purchased at the Dispensaries?

According to the data, Flower, which is a "traditional" marijuana bud, is still the most popular product, with 49% of the transactions, as compared to only 13% for edibles, the next highest

Edibles, pre-rolled blunts, and THC in pill form are the most profitable product types

Dispensaries

Dispensaries

Dispensaries

Dispensaries

Dispensaries

- Many non-traditional products like Live Resin, a special type of concentrate, and Carbonated Beverages are on the rise
- Live resin is a concentrate, like wax or shatter, that is higher in terpenes than other cannabis material
- Terpenes are oils secreted by the cannabis plant that give each strain its unique taste and smell

Dispensaries

Cost (costhelperhealth.com) =

- Marijuana buds can vary based on quality and the location of the purchase. Typically, a gram of buds can cost **$5-$20**; an eighth (3.5 grams) costs **$20-$60**; and an ounce can cost **$200-$400**.
- Concentrated forms, including hash products, oils and waxes made with higher levels of THC. Concentrates are typically more potent than buds. Concentrates are typically sold in half-gram and gram quantities and generally cost **$20-$60** per gram.
- Edible products usually are based on dosages, which should be labeled on the package. Expect to pay about **$2-$5** per dose for edible medical marijuana items.
- Tinctures-- concentrated liquid medical marijuana -- are typically sold in one-ounce bottles, capped with a dropper. Tinctures are often used in cooking and benefit patients who prefer to not smoke. Tincture bottles sell for **$15-$50**, depending on strength.

Presenter's experience, based on life care planning in CA and AZ: Users spending $100.00 to $300.00/ month for variety of product options based on obtaining dispensary receipts / history of purchase logs

Dispensaries

Taxes vary state by state and city by city and can add a very large expense to the cost of product

- The California Dept of Tax & Fee Admin recently determined the cannabis excise tax mark-up rate will continue to be 60 percent for the next six months beginning July 1, 2018. The CDTFA is responsible for determining a mark-up rate on a biannual basis in six-month intervals. The mark-up rate must be used by distributors to compute the average market price of cannabis or cannabis products sold or transferred to a retailer in an arm's length transaction

http://www.cdtfa.ca.gov/industry/cannabis.htm

Mail Order Products

Mail Order Products

Mail Order Products

Montel Williams is In the Game

- **Alert** Formulated with terpenes known to: aide anxiety, depression; pain management; act as an anti-inflammatory and soothe stress; promote alertness and memory retention
- **Relax** Formulated with terpenes known to enhance mood, promote relaxation and restful sleep, quell anxiety, depression and insomnia; act as an antioxidant and anti-inflammatory
- Cost = $80.00 for #50 (selectcdb.com)

Cannabis Research Efforts

A Yahoo Headline on 08/30/18: A Single Dose of CBD Reset the Brains of People at High Risk of Psychosis

- Psychosis, a severe mental disorder characterized by a loss of grip on reality, can include unsettling hallucinations and delusions. As no one's been able to pin down a single cause of psychosis, it's been even harder to pin down a treatment. But researchers behind a new *JAMA Psychiatry* study seem to be on the right track. In the study, they report that they've found a way to "reset" the psychosis-afflicted brain using an unlikely plant: marijuana.
- Researchers are increasingly finding evidence that the active components of marijuana can help ease symptoms in people with epileptic seizures, chronic pain, and PTSD, but there's much to be learned about its relationship to psychosis. The most well-known cannabinoid-- THC --has previously been linked to the development of psychosis in some people. But in the new study, the authors report that another cannabinoid called cannabidiol (CBD) can actually help treat it.
- Cannabidiol (CBD), another compound found in cannabis, appears to "reset" the brains of people at high risk of psychosis, at high doses.
- In the paper, a team of UK researchers show that a single dose of CBD can normalize brain activity associated with psychosis. Psychosis is associated with distinctive patterns of brain activation as detected by MRI in the striatum, medial temporal lobe, and midbrain. In a double-blind study of 33 people at high risk of psychosis and 19 healthy controls, the study's authors found that patients at high risk of psychosis had abnormally elevated activity in these regions compared to the control subjects. But one large dose of CBD — 600 milligrams — quickly and significantly reduced the brain activity in those brain regions down to normal levels.

https://www.yahoo.com/news/single-dose-cbd-reset-brains-100000080.html?.tsrc=fauxdal

Cannabis Research Efforts

- Ongoing cannabinoid research by diagnosis
  - Table format defining primary findings and link to study synopsis
  - Open studies included

  Database on Clinical Studies and Case Reports. (2018) Studies and Case Reports. http://www.cannabis-med.org/english/studies.htm#_Toc514775510 & http://www.cannabis-med.org/studies/study.php
- ABDC Study (Adolescent Brain Cognitive Development)
  - Collaboration between National Institute on Drug Abuse (NIDA), National Institutes of Health (NIH), National Cancer Institute (NCI) in partnership with Centers for Disease Control and Prevention (CDC), etc.
  - Annual release of curated, anonymized data to facilitate ability of scientists across the world to conduct research on adolescent brain development and factors that impact it
  - One focus is to study exposure to substances, including marijuana and the impact on developmental outcomes

  Volkow N., Koob G., Croyle R., Bianchi D., Gordon J., et al. The conception of the ABCD study: From substance use to broad NIH collaboration. *Developmental Cognitive Neuroscience.* 2018; 32: 4-7. https://d14rmgtrwzf5a.cloudfront.net/sites/default/files/nida_abcdflyer_2.pdf

LCP Implications

- State laws changing, requiring research & monitoring of legal status of medical cannabis
- Federal law prohibits patient from possessing cannabis if crossing state border or flying
  - Cannabis management when LCP evaluee travels for work, vacation, etc.

LCP Implications

- Ability to drive and/or operate machinery while on prescribed cannabis
  - Driving under influence of intoxicants- DUII
- Employer mandated drug testing
- Product availability varies between dispensaries

LCP Implications

- Security Clearances or Background Checks can be at risk
- Those who have gun permits / concealed weapon permits may be in jeopardy
- Lack of support by prescribing physicians
  - Lack of support by payor source, such as VA

LCP Implications

- Bias of life care planner authoring plan
- Bias of retaining attorney
- Concern that judge/jury may have bias that could impact credibility of Life Care Planners testimony
  - Federal Court venues

Solutions

- LCPer must take each implication / challenge and apply it to the individual whom the LCP is being created
- Risk / Benefit Ratios should be considered
  - Has an injured or chronically ill individual successfully reduced or discontinued opioids due to successful treatment with cannabis
- LCPer must have a consistent methodology for inclusion of - or lack of inclusion of - cannabis in their plans

Solutions

- LCPer should assure that the other collaborating professionals are comfortable with inclusion, including if collaboration is with treating providers
- LCPer should check for potential medication interactions and medical contraindications with cannabis use, even if the injured person is already using cannabis, if it is being included in the plan
- LCPer may need to discuss the issue with retaining attorney to consider their input from legal strategy perspective

LCP Example Inclusion of Cannabinoids

Treatment Modality	Year Initiated	Year Suspended	Frequency	Cost	Comments
CBD hemp based extract	5/2018	8/2018	25 mg 2/day	$200.00 per month	Pain and spasm management secondary to spinal cord injury.[1,2,3,4,6]
CBD non-hemp based extract	9/2018	LE	10 mg/ serving 7-10 servings per day (70-100 mg per day)	$410.00 to $485.00 per month	Updated prescription upon transition to non-hemp based extract.[7] Current utilization 70-100 mg/ day. Utilization of CBD extract may change over time as dose-response titration is adjusted.

LCP Example Inclusion of Cannabinoids

- 1. 5-5-18 _____ MD, progress note: Approve participation in CBD research protocol for pain management and spasms.
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- 6. Carter G. (2014). The Use of Medical Marijuana to Manage Symptom Burden in Spinal Cord Injury. *2014 Spinal Cord Injury Wellness Summit.* Lecture conducted from Seattle Washington.
- 8. 9-7-18 ____ MD: patient cleared to take CBD oil on as needed bases with no upper limit.

Case Studies

- Presenters to briefly share case studies
  - Life Care Planning
  - Case Management

Conclusions

- Identified terms related to medical marijuana, cannabinoids and cannabis
- Defined cannabis specific recommendations/ prescriptions based on medical diagnosis
- Discussed the challenges and implications related to inclusion of cannabis in life care plans
- Defined solutions related to inclusion of cannabis in life care plan

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