

A Prelude to Medical Cannabis

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- Cleveland Area Hospital
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- Member: Society of Cannabis Clinicians
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Objectives

- Become familiar with some of the history behind the use of cannabis as a medicine.
- Become familiar with why cannabis was criminalized.
- Receive an introduction to the Endocannabinoid System and its relation to disease processes and pain.
- Become familiar with some of the phytocannabinoids and their function in the body.
- Review some of the different disease processes that medical cannabis can treat.
- Explain how medical cannabis is a viable option for chronic pain over, or in conjunction with, opioid pain medications.
- Review the various ways to use medical cannabis and their pros and cons.
- Review some of the side effects of medical cannabis.
- Be able to understand and treat your patients better that are utilizing medical cannabis.

Medical Cannabis - History

- The use of cannabis for purposes of healing predates recorded history.
- The earliest written reference is found in the 15th century BC Chinese Pharmacopeia, the Rh-Ya.
- Ancient Chinese Pharmacopia called it the most important medicinal herb with properties of Yen & Yang.
- Historic references regarding the use of therapeutic cannabis for a variety of female medical conditions, including difficult childbirth, date back to the 7th century BC.

Medical Cannabis - History

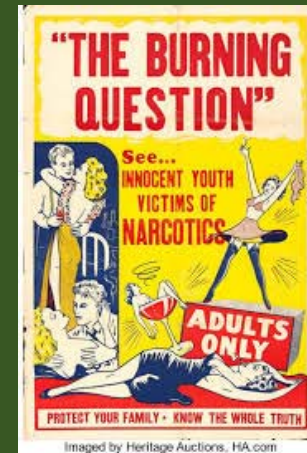
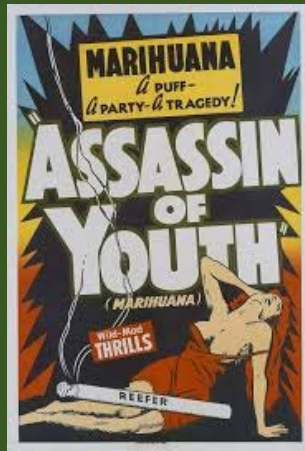
- Holy anointing oil, as described in the original Hebrew version of the recipe in Exodus (30:22-23), contained over six pounds of kaneh-bosem, a substance identified by respected etymologists, linguists, anthropologists, botanists and other researchers as cannabis, extracted into about six quarts of olive oil, along with a variety of other fragrant herbs. The ancient anointed ones were literally drenched in this potent mixture.“
- The King James version of the Bible translated it to calamus.
- Jesus = The Anointed One

Medical Cannabis - History

- Described in the United States Pharmacopoeia for the first time in 1850.
- Prior to 1900 was one of the most widespread ingredient in medicines used for pain.
- Cannabis was dropped from the United States Pharmacopoeia in 1942

Medical Cannabis - History

MARIJUANA



Medical Cannabis - History

- William Randolph Hurst
- LaMont Dupont vs Henry Ford
- Harry Anslinger
- AMA
- Marijuana Papers
- Marijuana was used to demonize Hemp as well.
- Marijuana Tax Act of 1937
- The LaGuardia Report
 - The report was prepared by the New York Academy of Medicine. Released in 1944,

Medical Cannabis - History

- Prohibition under federal law occurring with the Controlled Substances Act of 1970.
 - Made Marijuana (Cannabis) a Schedule 1 drug.
 - Defined by the federal government as a drug with no currently accepted medical use and a high potential for abuse.
 - Schedule 1 drugs are the most dangerous drugs of all the drug schedules with potentially severe psychological or physical dependence
- Richard Nixon
 - War on Drugs
 - Shafer Commission
 - 1972 report stated that cannabis should be decriminalized, and that prosecuting cannabis was a distraction from the fight against heroin.

Medical Cannabis - History

- In 1996, California became the first state to permit legal access to and use of cannabis for medicinal purposes under physician supervision with the enactment of the Compassionate Use Act.
- As of January 1st, 2020, 34 states as well as Washington, D.C., Guam, and Puerto Rico have enacted legislation governing medicinal cannabis sale and distribution
- 12 states, including Alaska, California, Colorado, Illinois, Maine, Massachusetts, Michigan, Nevada, Oregon, Vermont and Washington, as well as the District of Columbia, the Northern Mariana Islands, and Guam, have legalized use of cannabis for adult use.
- Another 15 states and the U.S. Virgin Islands have decriminalized cannabis.

Medical Cannabis in Oklahoma

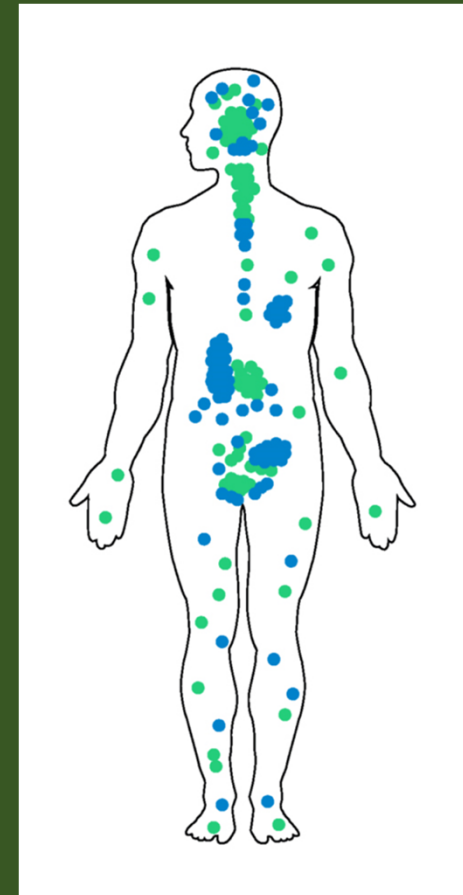
- On June 26th 2018, Oklahoma became the 30th State to vote and pass legislation for cannabis as medicine.
- State Question 788 became the most liberal medical cannabis law passed in the country to date.
- Oklahoma is the fastest state to go from the vote to having product on the shelves (less than 6 months).
- Oklahoma's Patient numbers have surpassed all other medical states in much less time.

Medical Cannabis - Canna-bits

- No where is Recreational use of Cannabis in Children or Adolescents legal.
- There are limited studies on the use of Cannabis in children. Those studies often contradict each other.
- Randomized, double blind, placebo controlled studies in cannabis are very hard to perform at this time.
- Low quality inconsistent product yields low quality inconsistent study results.
- The dangers stated from the smoking of Cannabis and regards to second-hand smoke continues to be inferred from the smoking of cigarettes.

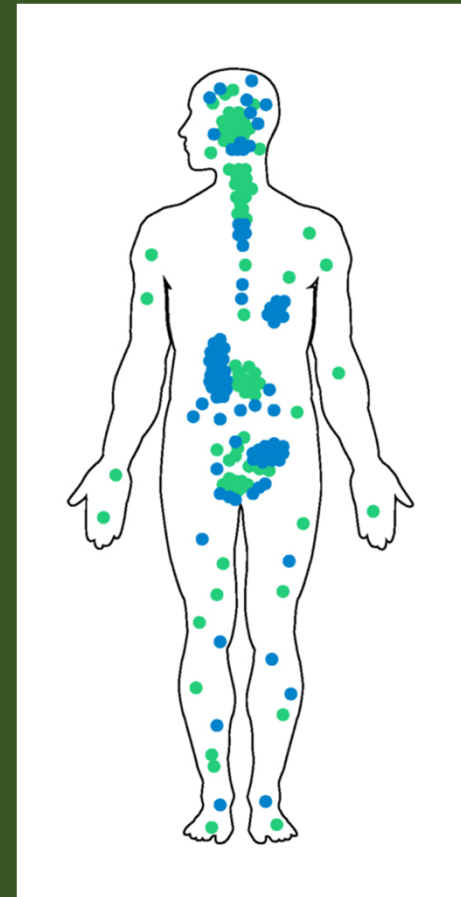
The Endocannabinoid System (ECS)

- Largest receptor system in the body.
- The ECS consists of receptors, endogenous ligands, and ligand metabolic enzymes.
- Endocannabinoids and their receptors are found throughout the human body
 - Nervous system, internal organs, connective tissues, glands, and immune cells.
- Since the ECS is so large and consists of so many different parts, it has a role in the pathology of many disorders as well as also serving a protective function in certain medical conditions.
- Not taught in Medical School



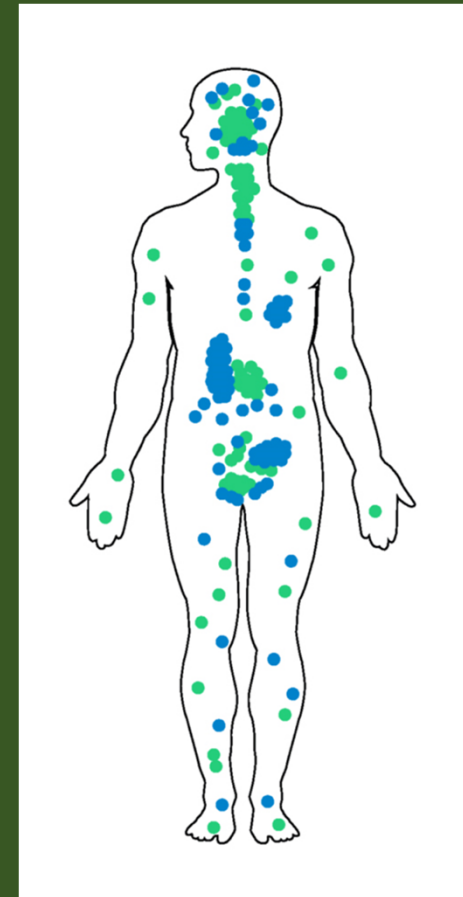
The Endocannabinoid System (ECS)

- The ECS has a homeostatic role, characterized as “eat, sleep, relax, forget, and protect.”
- The ECS plays a role in the pathology of many disorders while also serving a protective function in certain medical conditions.
 - Clinical ECS deficiency syndromes include:
 - migraine, fibromyalgia, irritable bowel syndrome, depression, schizophrenia, multiple sclerosis (MS), Huntington’s disease, Parkinson’s disease, anorexia, chronic motion sickness, and failure to thrive in infants.
- The ECS helps bring the body back into balance so it can heal itself. Sound Familiar?



The Endocannabinoid System (ECS)

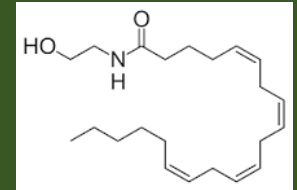
- Cannabinoid receptor type 1 (CB1●) is the most abundant G-protein–coupled receptor.
 - expressed in the central nervous system, non-neuronal cells, such as adipocytes and hepatocytes, connective and musculoskeletal tissues, and the gonads.
- Cannabinoid receptor type 2 (CB2●)
 - principally associated with cells governing immune function, in the central nervous system and the peripheral nervous system.



Endocannabinoids

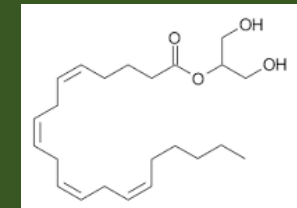
- Anandamide

- N-arachidonylethanolamine (AEA)
- Fatty acid neurotransmitter derived from the non-oxidative metabolism of eicosatetraenoic acid, an essential omega-6 fatty acid.
- Sanskrit word ananda, which means "joy, bliss, delight", and amide.



- 2-Arachidonoylglycerol (2-AG)

- An endogenous agonist of the CB₁ receptor and the primary endogenous ligand for the CB₂ receptor.
- An ester formed from the omega-6 fatty acid arachidonic acid and glycerol.



The Phytocannabinoids

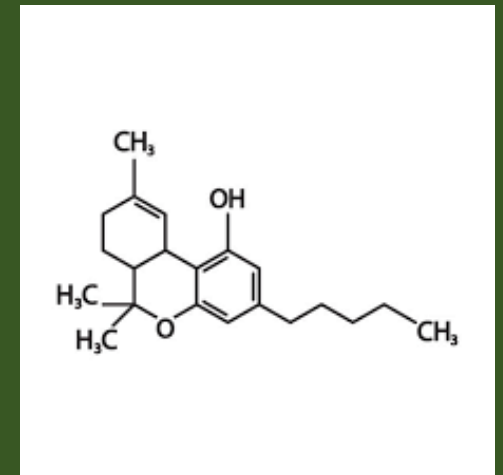
- THC
 - major psychoactive component of cannabis
 - mediated by activation of the CB1 receptors in the central nervous system
 - Mimics Anandamide
- CBD
 - elicits its pharmacological effects without exerting any significant intrinsic activity on CB1 and CB2 receptors.
 - Modulates the binding of THC to Cannabinoid Receptors.
 - Prevents the breakdown of our own endocannabinoids.
 - Keeps THC in check.
- THC : CBD must balance

The Phytocannabinoids

- Some Phytocannabinoids found in Cannabis. (~100+)
 - THC (Δ^9 -tetrahydrocannabinol)
 - CBD (Cannabidiol)
 - CBC (Cannabichromene)
 - CBGV (Cannabigerivarin)
 - THCV (Tetrahydrocannabivarin)
 - CBDV (Cannabidivarin)
 - CBCV (Cannabichromevarin)
 - CBG (Cannabigerol)
- Terpenes (~200+)
 - Give Cannabis its aroma and taste.
 - Essential oils of cannabis
- Entourage Effect

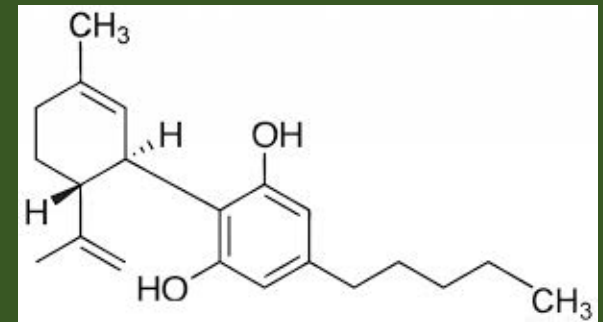
The Phytocannabinoids – What do They Do?

- THC – Tetrahydrocannabinol
 - Psychoactive
 - Reduces chronic pain
 - Reduces inflammation
 - Reduces nausea and vomiting
 - Decreases muscle spasms
 - Increases appetite
 - Helps to treat withdrawal symptoms
 - Reduces digestive problems as an anti-spasmodic
 - Has Anti-tumor/cancer properties



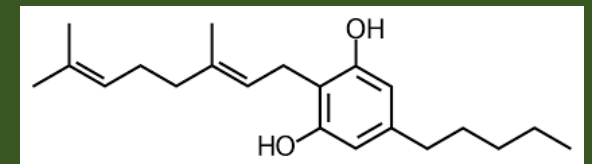
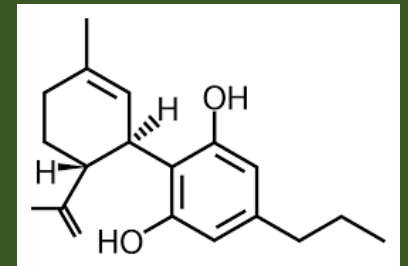
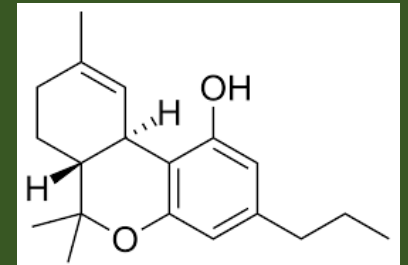
The Phytocannabinoids – What do They Do?

- CBD – Cannabidiol
 - Non-psychoactive
 - Reduces chronic pain
 - Reduce seizures
 - Reduces anxiety and depression
 - Reduces inflammation
 - Has anti-psychotic effects
 - Reduces nausea
 - Improves efficiency of the cardiovascular system
 - Neuroprotective



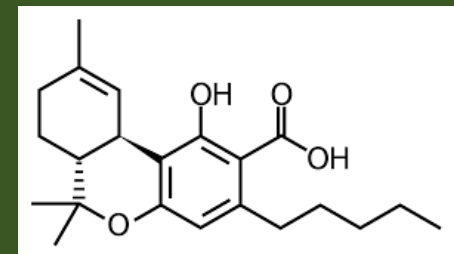
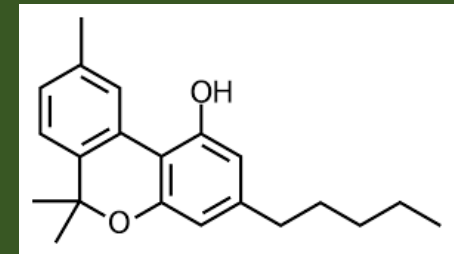
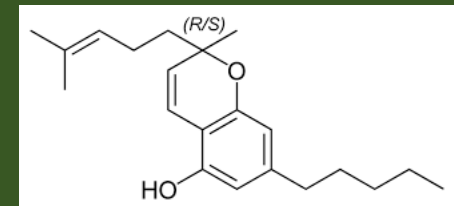
The Phytocannabinoids – What do They Do?

- **THCV – Tetrahydrocannabivarin**
 - Psychoactive
 - Reduces Appetite and may assist in weight-loss
 - May help with symptoms from diabetes
 - May be helpful for those with anxiety disorders or PTSD
 - Reduces inflammation
- **CBDV – Cannabidivarin**
 - Similar effects as CBD
- **CBG – Cannabigerol**
 - Non-psychoactive
 - Helps to treat neurological disorders
 - Helps to treat skin disorders like psoriasis and acne
 - Has antifungal and antibiotic properties



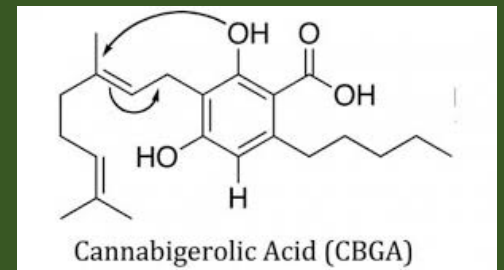
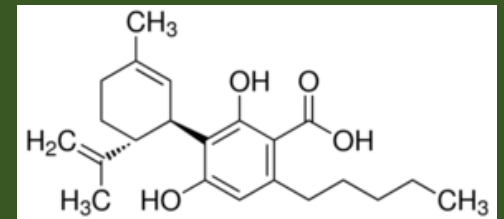
The Phytocannabinoids – What do They Do?

- CBC – Cannabichromene
 - Non-psychoactive
 - Reduces pain
 - Reduces inflammation
 - Has been shown to help in treatment of cancer and tumors
- CBN – Cannabinol
 - Mildly psychoactive
 - Increases appetite
 - Promotes sleep
 - Reduces anxiety
 - Reduces pain
 - Reduces inflammation
- THCA – Tetrahydrocannabinolic Acid
 - Non-psychoactive
 - Reduces inflammation
 - Reduces nausea



The Phytocannabinoids – What do They Do?

- CBDA – Cannabidiolic Acid
 - Same benefits as CBD
- CBGa – Cannabigerolic Acid
 - Non-psychoactive
 - A building block for other cannabinoids
 - Has been shown to help in treatment of cancer and tumors
 - Encourages apoptosis (esp in cancer cells)
- There are many more cannabinoids that are still being studied and it is important to know that their therapeutic effects could change based on further research.



Basic Botany of Cannabis

- Cannabis Sativa
 - Known for its Energizing effects
- Cannabis Indica
 - Known for its sedative effects.
- Hybrids
 - Mixture of both Indica and Sativa
- Hemp
 - Variety of the Cannabis sativa plant species that is grown specifically for the industrial uses of its derived products. It is one of the fastest growing plants, and was one of the first plants to be spun into usable fiber over 26,000 years ago. It can be refined into a variety of commercial items including paper, textiles, clothing, biodegradable plastics, paint, insulation, biofuel, food, and animal feed.
 - Hemp has lower concentrations of THC and higher concentrations of cannabidiol (CBD), which decreases or eliminates its psychoactive effects
 - Recent Passage of the Farm Bill
- Strains/Cultivars
 - Individual names for various hybrid cannabis plants

What Does Medical Cannabis Treat?

- **Anti-inflammatory Effect**
 - Chronic Pain, Arthritis, Rheumatoid Arthritis, Lupus, Scleroderma, Sarcoidosis, Raynaud's, Glaucoma, Gout, Ulcerative Colitis, Crohn's Disease, Headaches, Asthma, COPD
- **Peripheral Nervous System**
 - Neuropathies (Idiopathic, Diabetic, Other), Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Fibromyalgia, ALS, Incontinence
- **Central Nervous System**
 - MS, Autism, Alzheimer's disease, Parkinson's disease, Huntington's, epilepsy, stroke, Migraines
- **Psychiatric Disease**
 - PTSD, Anxiety, Depression, Panic Attacks, Bipolar, Schizophrenia, ADD/ADHD, Insomnia, Anorexia, IBS, Substance Abuse, Alcohol Abuse, Withdrawal symptoms
- **Sympathetic Tone**
 - Essential hypertension, postural tachycardia, obesity, polycystic ovary syndrome, heart failure, myocardial infarction, sexual dysfunctions, BPH.
- **Cancer**
 - Has been shown to stimulate apoptosis in cancerous cells.
 - Decreases Angiogenesis.

Cannabis and Chronic Pain

- Cannabis was cited for rheumatic pain relief over 4000 years ago.¹⁵
- Chronic Pain is the most common ailment for which people use medical cannabis.¹⁶
- There are over 300 studies - including 36 double blind randomized controlled clinical trials that have shown cannabinoids can help patients with chronic pain.^{17,18}
- Over three dozen pre-clinical and clinical trials have shown that low dose cannabis also relieves neuropathic pain.¹⁹

Cannabis and Chronic Pain

- Chronic Pain affects over 100,000,000 Americans, more than diabetes, heart disease, and cancer combined.²⁰
- Opioids and NSAIDs are the most commonly prescribed medications for both acute and chronic pain.
- The total annual cost of health care due to pain ranges from \$560 billion to \$635 billion, which equals about \$2,000 per year for everyone living in the U.S.²¹
- In 2018 Deaths from opioid overdoses exceeded the number of people killed that year in automobile accidents.
- In 2018 – An average of 130 Americans died every day from an opioid overdose.²²
- The United States consumes more than 80% of the worlds opioids while only accounting for 5% of the overall world population.

Cannabis and Chronic Pain

- Medicare data from 2010 to 2013 show that once a state institutes medical cannabis the overall use of prescription drugs falls significantly.²³
- Patients on Medicare filled 14 percent fewer prescriptions for opioids after medical marijuana laws were passed in their respective states.
- Medicaid enrollees filled nearly 40 fewer opioid prescriptions per 1,000 people each year after their state passed any law making cannabis accessible.
 - Greater drops were seen in states that legalized both medical and recreational cannabis.
- U.S. states with medical cannabis laws report 25% lower opioid overdose mortality rates.²⁴
- Surveys of medical cannabis patients indicate that about half of all patients have been able to reduce their use of opiate medication.^{25,26}

Cannabis and Chronic Pain

- Opioid Addiction and Misuse
 - More than 11 million people in the US abuse prescription opioids.
 - A short term prescription for opioid-naïve patient significantly increases the chances that patients will be using the opioids for the long term.
 - According to a March 2017 report from the CDC, opiate-naive patients with a 6-day prescription have a 12% chance of being on opioids one year later.
 - If the prescription is for two weeks, the patient's chances of being on opioids for a year doubles to 24%.
 - Those with a month-long prescription face a 30% likelihood that they'll still be using opiates a year later.
 - Approximately 7% of initial opiate prescriptions exceed a 1-month supply.²⁷
 - Oklahoma has used this to decrease opioid prescriptions for acute conditions.

Cannabis and Chronic Pain

- Cannabinoid receptors are located throughout the nervous system and regulate pain perception.²⁸
- Cannabis has both Analgesic and Anti-Inflammatory properties.
- Phytocannabinoids in cannabis relieve pain through a variety of mechanisms.²⁹
 - Decreases the release of inflammatory cytokines.
 - Modulates the release of neurotransmitters sending/creating pain signals.
 - Increases the release of the body's own endocannabinoids.
 - Decreased transmission of pain signals through retrograde transmission.
 - Alters chondrocyte signaling, thereby preventing destruction of cartilage and collagen breakdown.³⁰

Cannabis and Chronic Pain

- Synergistic and additive interactions exist between cannabis and opiates.^{31,32,33}
 - CB1 receptors and opioid receptors, specifically the μ -opioid receptors that modulate pain, are found expressed together in the spinal cord, the periaqueductal gray, and the brain's reward centers, places that are important in the perception of pain.
 - When combined with opiates, medical cannabis helps patients find better relief.³⁴
- CB1 and μ -opioid receptors physically interact.
 - Activation of one receptor affects how the other one responds.
 - The consequence of this interaction depends on where in the brain they're found.
 - Their co-activation by low amounts of drug leads to a stronger effect than what would be predicted by activating either CB1 or opioid receptors on their own.

Cannabis and Chronic Pain

- When Cannabis and Opioids are taken together, cannabis can increase opioid's pain-relieving effects by modulating opioid-receptor signaling directly through physical interaction between CB1 and opioid receptors, and by increasing the body's own opioid levels.
 - This effect is reciprocal; THC can increase opioid levels to help relieve pain, and using drugs to boost the body's own opioid levels enhances THC's pain-relieving effects.
- Cannabis can be used when opiates are ineffective or not tolerated.⁴⁴
- Cannabinoids can prevent the development of tolerance to opiates.⁴⁵
- Cannabis can also be used to effectively reduce drug cravings and the chance of relapse.

Cannabis and Chronic Pain

- Anti-inflammatory Properties of Cannabis
 - Eight times the anti-inflammatory effect of ibuprofen.
 - Two times the anti-inflammatory effect of hydrocortisone.
 - Twenty times the anti-inflammatory effect of aspirin.³⁵
- The 15th leading cause of death in the United States is bleeding and other adverse effects of NSAIDs.
- Approximately 107,000 patients are hospitalized annually for NSAID related GI complications. – AJM July 1998
- 16,500 NSAID-related deaths occur each year among arthritis patients alone.
- One of the most common causes of kidney failure and kidney disease in the United States is the use/overuse of NSAIDs.

Cannabis and Chronic Pain

- Human and animal studies show that cannabis protects the stomach from alcohol, NSAIDs and stress,³⁶ as well as gastric inflammation.³⁷
- COX-2 inhibitors (such as NSAIDs) preserve the anti-inflammatory effects of cannabis
- NSAIDs also reduce cognitive effects and lethargy associated with high THC doses.³⁸
- Cannabis acts as an organ protectant
 - CB2 activation by exogenous and endogenous cannabinoids protects the body's organs.³⁹

Medical Cannabis Modalities

Routes of administration (Modalities) for Medical Cannabis are:

- Inhalation
- Sublingual
- Mucosal
- Oral (aka Edibles)
- Topical

Medical Cannabis Modalities

- Inhalation:
 - Includes smoking, oil vaping, dry vaping, and dabbing.
 - Is a fast-acting method of administration with a short duration.
 - Smoking
 - Involves the ignition of the cannabis flower or leaf.
 - Popular methods include joints, blunts, bongs, pipes, pinch hitters, etc.
 - Oil Vaping
 - Involves the heating of concentrated cannabis oil to form a vapor which is inhaled.
 - Comes in prefilled cartridges, pens, or refill syringes or bottles.
 - Dry vaping
 - Involves the heating of the cannabis flower to produce a vapor using a dry herb vaporizer which is inhaled.
 - Dabbing
 - Involves superheating highly concentrated cannabis, also known as wax, shatter, or crumble.
 - Is usually very high in THC.

Medical Cannabis Modalities

- Sublingual
 - Modality that involves using concentrated cannabis oil, or Tincture, placed under the tongue and absorbed.
 - Is an intermediate-acting method of administration with a medium duration.
- Oral or Edibles
 - Modality that involves ingesting food products, capsules, drinks, etc., that have been infused with cannabis.
 - Edibles must go through digestion.
 - During digestion the THC molecule is changed in the liver to a more psychoactive, longer lasting substance.
 - Is a slow-acting method of administration with a long duration.
 - Can have Drug-Drug interactions.
 - Respect the Edible!

Medical Cannabis Modalities

- Transmucosal
 - Modality that involves the mucosal administration of concentrated cannabis.
 - Typically used nasally via a spray, or rectally via a suppository.
 - Is a fast-acting method of administration with a moderate duration.
- Topical
 - Involves use of a lotion, salve, ointment, or cream applied directly to the skin over an area of irritation.
 - Unless a lot is used is not psychoactive.
 - Is a fast-acting method of administration with a short duration.
 - Bath bombs, bath salts, and lip balms also fall into this category.

Medical Cannabis Side Effects

- Side Effects are usually dose dependent or related to their cultivar
 - Anxiety or Uneasiness
 - Paranoia
 - Thirst and Dry Mouth
 - Hunger
 - Insomnia
 - Red Eyes
 - Short Term Memory loss
 - Heightened Sensory Perception
 - Drowsiness, Dizziness, and Impaired Judgment
 - Respiratory Issues

Medical Cannabis Side Effects

- Side Effects are usually dose dependent or related to their cultivar
 - Giddiness
 - Tolerance
 - Fatigue
 - Slower Reaction Time
 - Diarrhea and Constipation
 - Increased Heart Rate – Short term
 - Impaired Balance
 - Urinary Retention
 - Slurred Speech
 - Dependency – Non-Addictive
 - Addiction Scale
 - Overdose
 - LD50

Medical Cannabis What I Recommend

- Low Doses, Small Amounts, “One Puff”
- Start Low and Go Slow.
- Strains/Cultivars high in CBD 1:1 Or greater.
- Patients must find what works best for them and their most comfortable way of using this medicine.
- Respect the Edible.

Summary

- Cannabis as medicine has been used for thousands of years.
- The Endocannabinoid System is the largest receptor system in the body. It interacts with almost every bodily function and almost every disease state.
- Phytocannabinoids can bind to endogenous cannabinoid receptors and modulate functions in the body.
- Cannabis has been shown to be an effective treatment in over 250 different disease states.
- Medical cannabis has been shown to be a viable treatment option for patients with chronic pain and many other ailments.
- Cannabis can be used by itself or in conjunction with opioid pain medication or NSAIDs for even greater effects.
- There are multiple modalities in which to treat patients with medical cannabis. Not just smoking.

Summary

- Even though side effects are usually minimal with the medicinal use of cannabis, there are some side effects that are important to know about.
- The use of medical cannabis is not at all about getting “High,” its about increasing function and improving quality of life.
- Substituting safer drugs for harmful ones is intelligent medicine, especially if they deliver the same relief.
- Medical Cannabis is not a cure all, but a treatment option.
- Perhaps cannabinoid therapy will someday be considered first line therapy for patients suffering from chronic pain and other illnesses.

Quote

- “There were never so many able, active minds at work on the problems of disease as now, and all their discoveries are trending toward the simple truth that you can't improve on nature.”

--Thomas Edison (1902)

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QUESTIONS?



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