



Deciphering Smoke Signals: An Update on Marijuana Use in Hospice and Palliative Care

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Objectives

- ▶ Discuss the history of cannabis use and regulations in the United States
- ▶ Examine the endocannabinoid system
- ▶ Review the clinical advantages and concerns with cannabis use
- ▶ Describe the current laws and regulations related to cannabis use



Patient Case (HA)

- ▶ HA is 42 year old male admitted for poor intake
- ▶ Pulse 125 bpm, skin cold and clammy
- ▶ “unable to swallow liquid or quench thirst—every attempt to swallow water or trickle drips on tongue lead to severe spasm.”
- ▶ Significant history: Untreated dog bite from 3 weeks prior
- ▶ Initial treatment: 129mg of cannabis extract Q1h

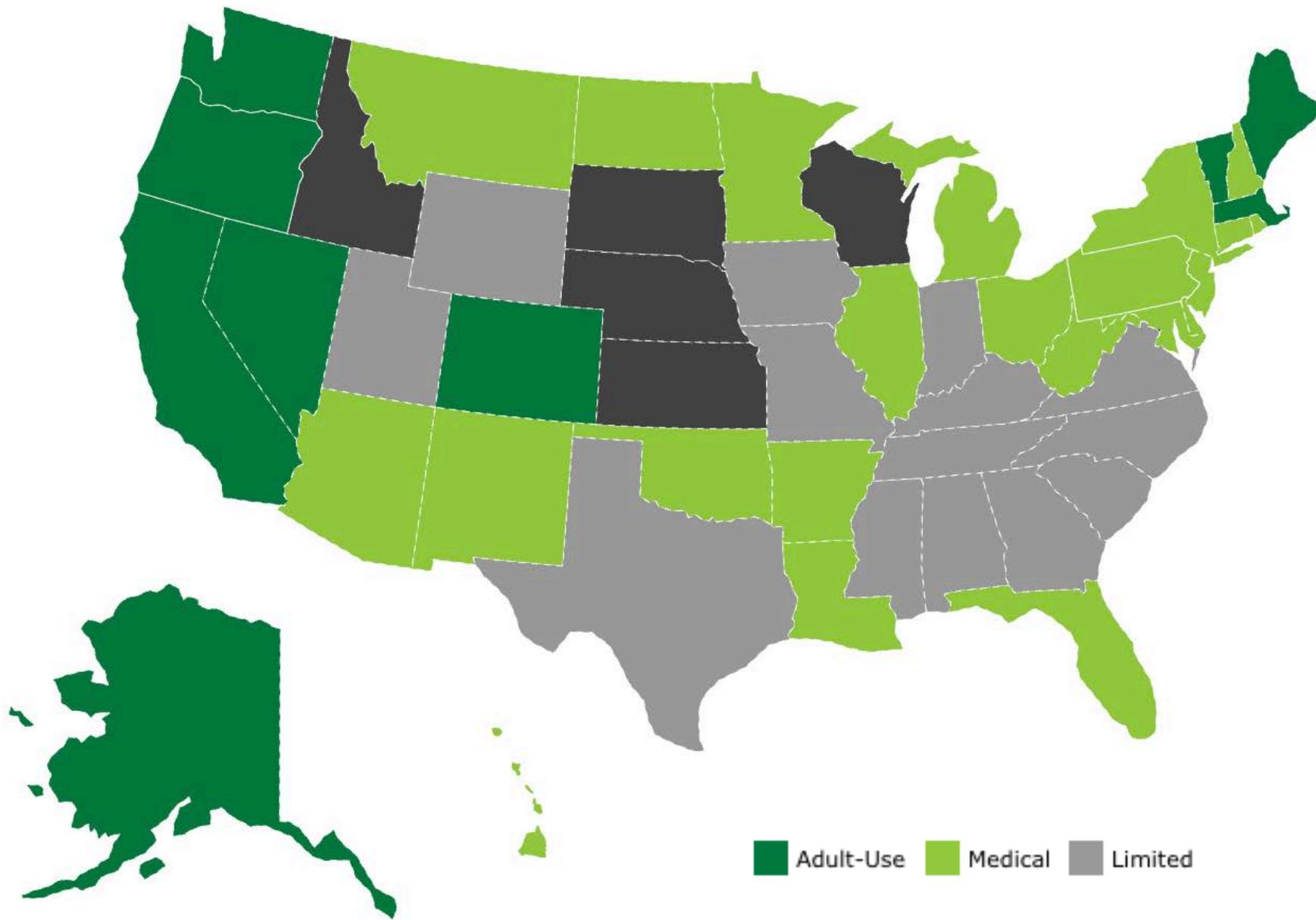


Historical Use in America

- ▶ Early American colonists cultivated hemp for rope and textiles
- ▶ In the early 1600s, farmers in Virginia, Massachusetts, and Connecticut were required to grow hemp
- ▶ Early 1800's saw Sir William Brooke O'Shaughnessy studying cannabis to treat stomach pain and vomiting in cholera
- ▶ By the late 1800's cannabis was sold by pharmacists and doctors
- ▶ Recreational use brought to America during the Mexican Revolution

Historical Use in America

- ▶ Marijuana Tax Act of 1937
- ▶ Controlled Substance Act of 1970
- ▶ California Compassionate Use Act of 1996
- ▶ 29 States have legalized medical use of cannabis
- ▶ Remains a Schedule-I federally illegal drug



Ask the Audience

How often do patients request information on medical cannabis?

How often is your organization asked to provide medical cannabis?

How many of you have patients who actively use cannabis now?

Does your organization provide medical cannabis for any patients?

Endocannabinoid System

- ▶ Regulates synaptic neurotransmission and modulates the immune system
- ▶ Comprised of two identified cannabinoid receptors
 - ▶ CB1
 - ▶ CB2
- ▶ Receptors are bound by internal and external ligands

Endogenous "Endocannabinoids"	Exogenous "Cannabinoids"
Anandamide	Δ9 - Tetrahydrocannabinol (THC)
2-arachidonoylglycerol	Cannabidiol (CBD)
-	Cannabinol (CBN)



Tetrahydrocannabinol



Cannabidiol



Cannabinol

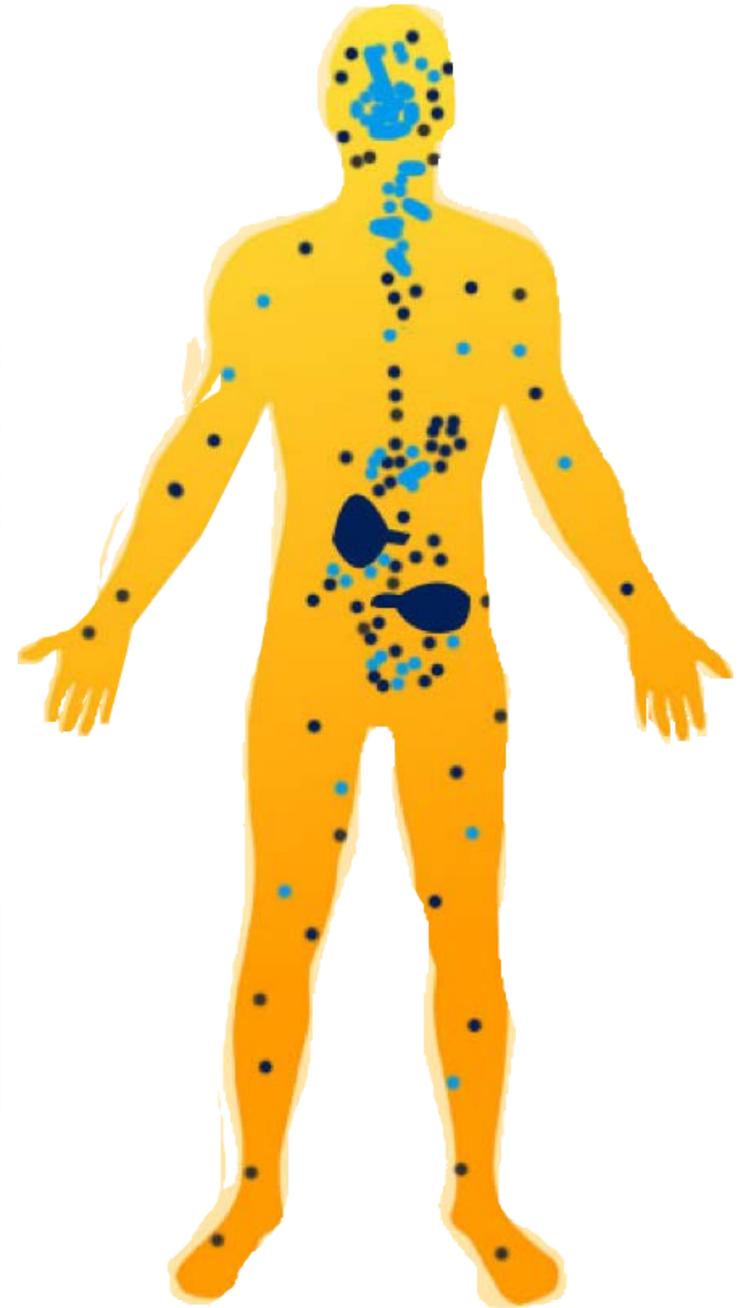
CB1 receptors are primarily found in the brain and central nervous system, and to a lesser extent in other tissues.



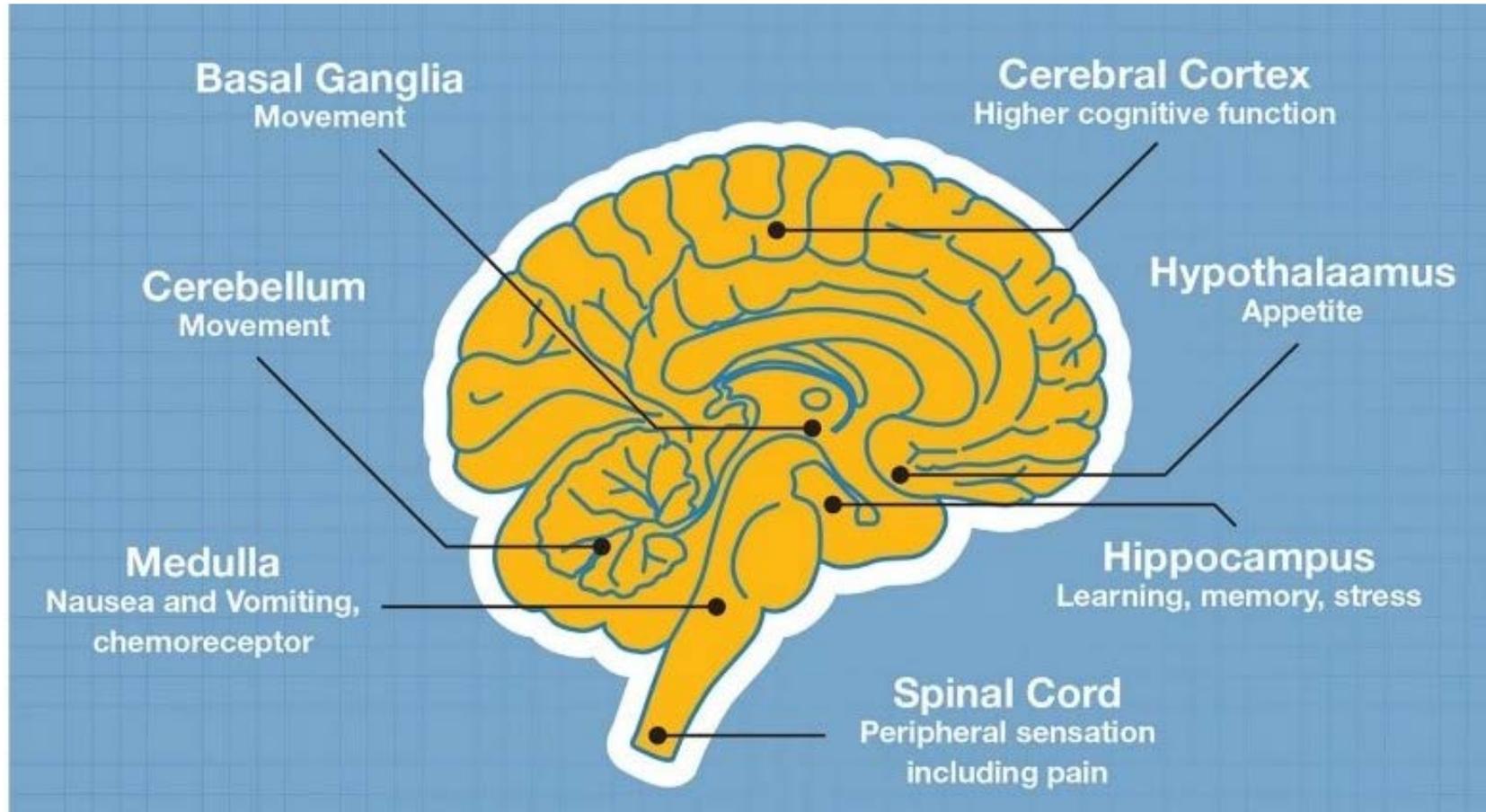
CBD does not directly fit CB1 or CB2 receptors but has powerful indirect effects still being studied.



CB2 receptors are mostly in the peripheral organs especially cells associated with the immune system.



CB1 Receptors



CB2 Receptors

- ▶ Mainly concentrated in the periphery
 - ▶ Immune cells, especially in the spleen and tonsils
 - ▶ Inflammatory cells of gastrointestinal system
 - ▶ Peripheral nervous system

Cannabis By Species

Indica



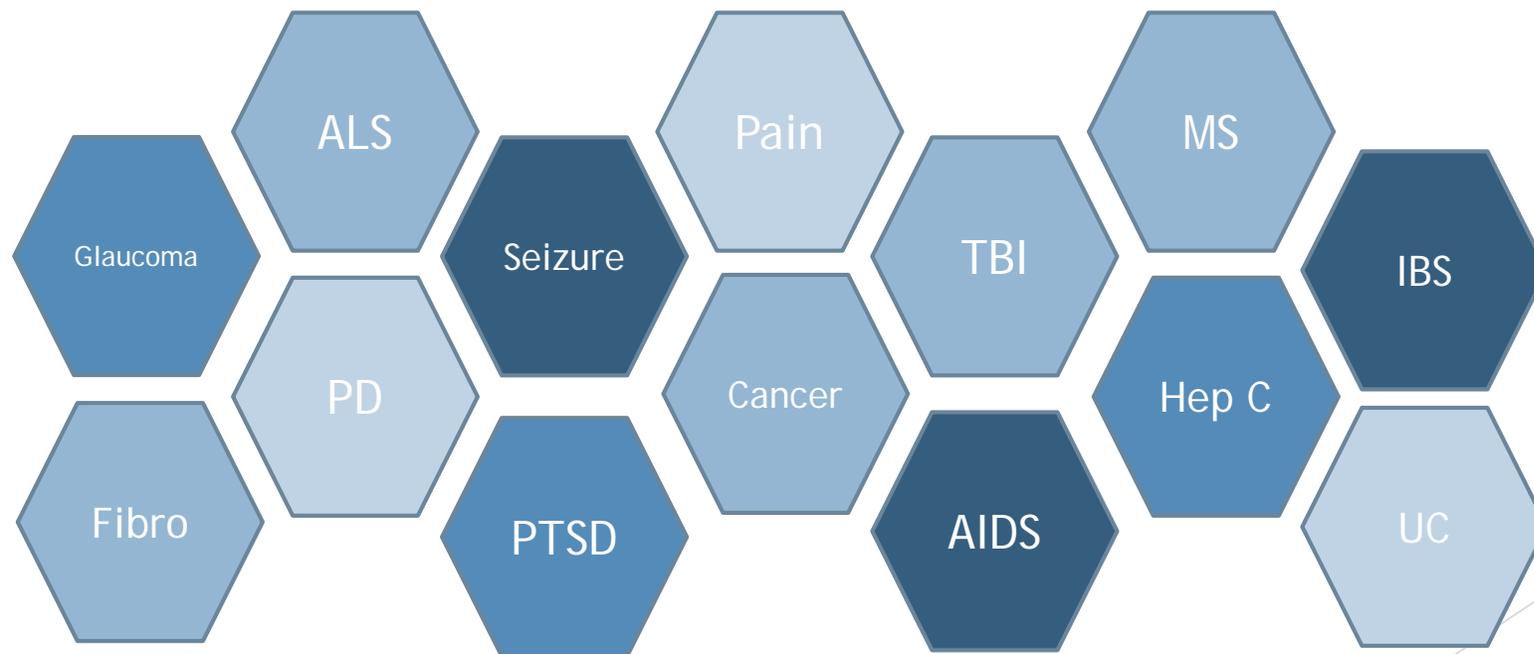
Sativa



CBD Dominant	THC Dominant
Produces euphoric "high"	Produces relaxed "high"
Analgesic, anti-emetic, anti-inflammatory, & anti-spasmodic effects	Appetite stimulant, anti-emetic, and neuropathic pain relief properties
More common in medical use	Often used recreationally

Qualifying Conditions

- ▶ Cannabis has been used for countless medical conditions
- ▶ Each state defines its own qualifying conditions for use
- ▶ Ohio, for example, has approved the following:



Neurodegenerative Disease

- ▶ Cannabis may play a role in various neurological disorders
 - ▶ Stroke, Parkinson's Disease, Multiple Sclerosis, Huntington's Disease, and Epilepsy
- ▶ Studies have demonstrated protective effects of cannabinoids on the glutamate induced excito-toxicity of neurons
 - ▶ Suggests they may slow progression of neurodegeneration
 - ▶ Not enough clinical evidence to support a strong recommendation



Multiple Sclerosis (MS)

- ▶ Cannabis may have benefit for symptoms of MS
 - ▶ Spasticity, tremor, pain, urinary frequency, and mood
- ▶ American Academy of Neurology supports the following:
 - ▶ Oral cannabis extract and synthetic THC are probably effective for reducing patient-reported symptoms of spasticity and pain
- ▶ Limited conclusive evidence and conflicting studies
 - ▶ Subjective improvements only and significant side effects



Parkinson's Disease (PD)

- ▶ Cannabinoids inhibit glutamate release and counteract oxidative damage to dopaminergic neurons
- ▶ High levels of CB1 receptors located in the basal ganglia
 - ▶ Potential benefit for dyskinesia and tremor
- ▶ Studies show patient-reported improvement in pain and spasticity
- ▶ Smoked marijuana found to worsen most patients due to increased hallucinations and memory disturbances

Nausea and Vomiting

- ▶ Cannabinoids are thought to exert their anti-emetic effects in Dorsal Vagal Complex (DVC)
 - ▶ Impact dopamine and 5HT-mediated receptors
- ▶ Higher risk of cannabis related adverse effects
 - ▶ Dizziness, dysphoria, hallucinations, and paranoia
- ▶ Minimal studies comparing cannabis to first line agents limits its clinical use

Chemotherapy-Induced Nausea and Vomiting (CINV)

- ▶ Several studies targeting cannabinoids following chemo
- ▶ Synthetic THC (Dronabinol)
 - ▶ superior anti-emetic activity to neuroleptics
 - ▶ Non-inferiority to ondansetron
 - ▶ Synergistic effect for dronabinol and prochlorperazine
- ▶ Prolonged use of smoked marijuana has been known to cause THC cyclic vomiting disorder

Appetite Stimulation and Weight Gain

- ▶ Cannabis only moderately effective in cancer patients for this indication
- ▶ No statistical significance in improvement in weight with Dronabinol, either alone or in combination
- ▶ Oral Dronabinol vs. Megace
 - ▶ Megace, superior in increasing appetite, weight gain > 10% baseline and improving health related quality of life
- ▶ THC vs THC + CBD vs Placebo
 - ▶ No significant improvements in survival, weight gain or other nutritional variables

Pain Management

- ▶ Analgesic effects may be mediated at the spinal cord
 - ▶ CB1 receptors: Similar neurochemical and pharmacological characteristics to opioid receptors
- ▶ Beneficial in refractory neuropathic pain and pain associated with MS and cancer
- ▶ Consistently better than placebo but comparable to codeine
- ▶ Greatest benefits seen in neuropathic pain and as adjunct to other pain regimens

Seizures

- ▶ Moderate evidence to support cannabidiol (CBD) use for treatment of epilepsy and other seizure activity
- ▶ Best evidence for treatment refractory children and adolescents with rare and serious types of epilepsy
 - ▶ Lennox-Gastaut syndrome
 - ▶ Dravet syndrome
- ▶ June 25th - Epidiolex approved in the US

Ask the Audience

What forms of marijuana or cannabis are you familiar with?



Dronabinol (Marinol[®], Syndros[®])

- ▶ Commercially available synthetic Δ^9 - THC
- ▶ Anorexia in patients with AIDS
 - ▶ 2.5mg - 20mg PO daily
- ▶ Chemotherapy-induced nausea and vomiting
 - ▶ 5 mg/m² before and after chemotherapy
- ▶ Available in capsules and oral solution
 - ▶ Onset: 30-60 minutes
 - ▶ Duration: 4-6 hours



Nabiximols (Sativex®)

- ▶ Oral Mucosal Spray with Combination THC and CBD
- ▶ Spasticity or neuropathic pain associated with MS
- ▶ Intractable Cancer Pain
- ▶ Dosage is self-titrated by the patient. Usual 4-8 per day
 - ▶ Max dose: 12 sprays per day
 - ▶ Onset: 15-40 min
 - ▶ Duration: 2-4 hours



Cannabidiol (Epidiolex®)

- ▶ First pharmaceutical formulation of highly-purified, plant-based cannabidiol (CBD)
- ▶ Indicated for Seizure disorders in patients > 2 years of age
 - ▶ 2.5-5 mg/kg twice daily
 - ▶ Can take up to 4 weeks to reach steady state
 - ▶ Duration: Prolonged, Half-life elimination up to 60 hours



Adverse Effects

Euphoria	Sedation	Psychosis	Memory Loss/ Disturbance
CNS Depression	Agitation	Aggression	Sleep Disturbances
Dry Mouth	Hallucinations	Appetite changes	Fatigue / Malaise
Increased risk of infection*	Bronchitis / Lung Disease*	Dizziness / mental clouding	Stroke, MI, Cardiovascular risk

*Inhaled form only

Drug Interactions

Medication / Drug Class	Interaction
Alcohol	CNS Depression
Barbiturates	CNS Depression
Benzodiazepines	CNS Depression
Opioids	Potential of effects
Corticosteroids	Increased Immunosuppression
Lithium	Increased serum lithium concentrations
Anticholinergics	Tachycardia and exacerbate hypertension
Theophylline	Increases clearance of Theophylline

Routes of Administration

Smoking	Vaporization	Oral	Topical
<ul style="list-style-type: none">• Most common• Fast acting• Irritating to bronchial mucosa• Chronic use associated with respiratory damage• Dosing very inconsistent and produces toxic byproducts	<ul style="list-style-type: none">• Fast acting• Less concern for lung damage• Still may be irritating to bronchial mucosa• Easier to obtain more standard dosing	<ul style="list-style-type: none">• Oil and capsules provide most consistent dosing• Slower onset but longer duration• Edibles have varying absorption and dosing is very difficult• Delayed onset possible with edible products	<ul style="list-style-type: none">• Poor absorption and high concentration required• Better for local use, less systemic effects• May have benefit for localized neuropathic pain

Dosing Strategies

- ▶ Must be individualized per patient “ Start Low and Go Slow”
 - ▶ Promotes tolerance to psychoactive side effects
- ▶ Encourage consistency and avoid rapid titrations up or down
- ▶ Recommend patients keep a “Cannabis” journal

Legal Concerns

- ▶ Marijuana in all forms remains classified as a federal Schedule-I, illegal, dangerous substance
 - ▶ “No accepted medical use and high potential for abuse”
- ▶ Hospice organizations obtain a majority of their funding from CMS via Medicare (a federal agency)
- ▶ Prevents hospice from legally furnishing patients with cannabis in any form

Legal Concerns

- ▶ Marijuana, CBD Oil, Cannabis Edibles
 - ▶ NOT an herbal or dietary supplement
- ▶ Remember that Cannabis can cause significant side effects
 - ▶ Especially varieties that are high in THC
- ▶ Encourage patients to follow state law and to avoid public use
- ▶ Hospice physicians should refrain from recommending or adjusting current or future doses
 - ▶ Should not be a part of hospice benefit

What you *can* do!

- ▶ Document that the patient intends to use cannabis
- ▶ Provide the patient with evidenced-based counseling and resources
- ▶ If the patient is going to use cannabis anyway, encourage safe and consistent use, document recommendation to D/C
- ▶ Have the patient or caregiver keep a cannabis journal

Patient Case (LS)

- ▶ LS is 68 year old male admitted for pancreatic cancer
- ▶ Pain is his chief complaint
 - ▶ Methadone 10mg PO TID
 - ▶ Oxycodone 10mg 1-2 tabs PO q2h prn pain (6-7 doses per day)
- ▶ Today, LS asks if he can try marijuana to better control his pain.
- ▶ **How should you respond?**



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