



Radicle Health Presents:

Using Cannabis to Help Alleviate Symptoms Associated with Cancer Treatment

Radicle Health Team



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- Has treated over 5000 patients
- The average age of patient is 76
- 90% have previously never used cannabis
- 85% are female
- 45% want to use cannabis to treat pain
- 45% want to use cannabis to treat sleep issues
- Most new patients don't want psychoactivity
- Most new patients don't want to smoke

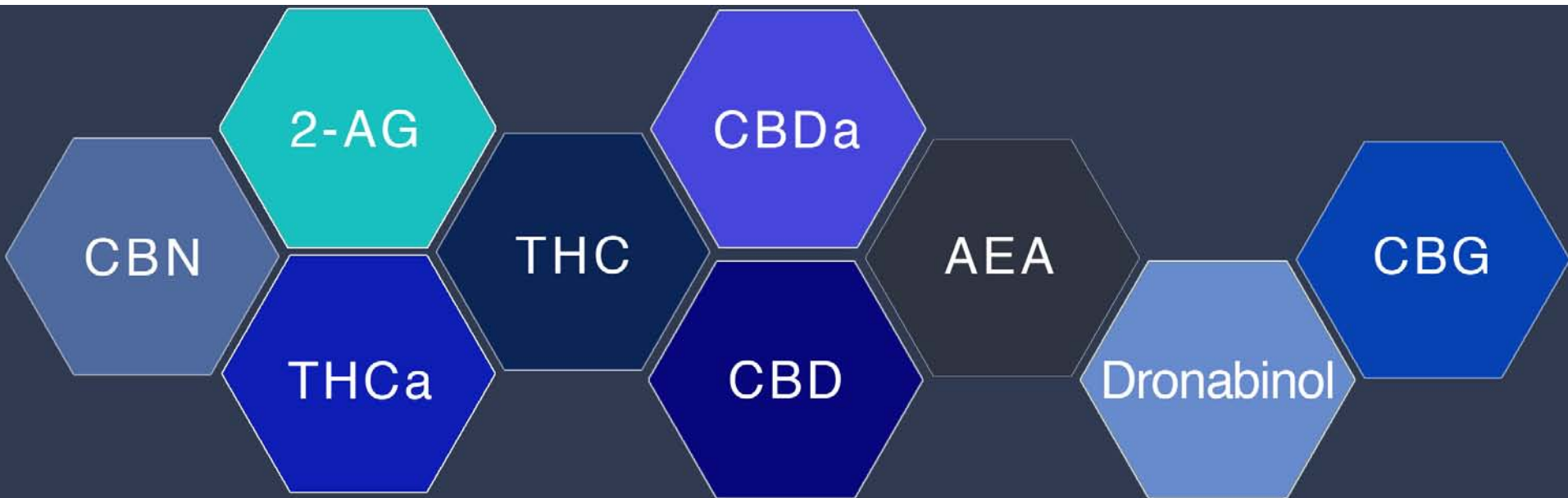


ECS: A group of neuromodulatory lipids, their receptors, enzymes, and neurons.

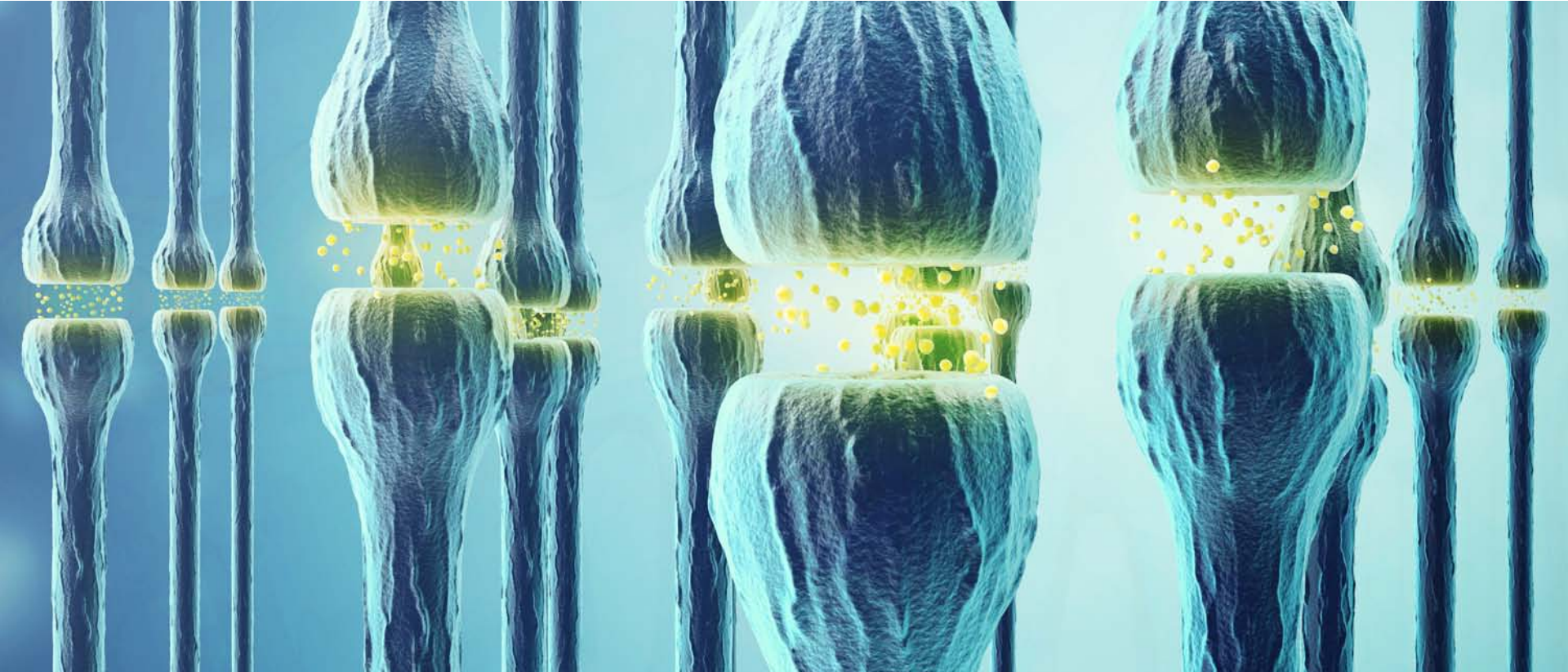
ECS

Responsible for maintaining homeostasis; for regulating mood, appetite, pain-sensation, memory, and sleep. The ECS is found in all vertebrate animals and some invertebrate animals.

Cannabinoids include naturally occurring chemicals, compounds that occur naturally, and synthetic cannabinoids.



Your endocannabinoids are anandamide (AEA) and 2-arachidonoylglycerol (2-AG).



Dronabinol and Nabilone are synthetically-made cannabinoids.

Marinol (Dronabinol) was approved for N/V and for appetite stimulation.
The average dose is between 2.5-20mg per day.

Cesamet (Nabilone) was approved for N/V. The average dose is between
1-2mg BID.

The primary cannabinoid receptors are CB1 and CB2.

CB1 and CB2

- Brain
- Organs
- Connective tissues
- Glands
- Immune cells

C1 and CB2 receptors are G-protein-coupled receptors.

Endocannabinoid receptors are the most common type of cell receptor in the body. In fact, there are more endocannabinoid receptors than all other types of cell receptors combined. Additional cannabinoid receptors include GPR55 and TRPV1.

CB1: predominately in the nervous system, CB2 receptors are primarily found in the immune system.

The homeostatic effects produced by CB1 stimulation include an increased drive to sleep and eat, a reduction in perceived pain, a reduction in the release of inflammatory mediators, and a reduction of immune cells migration into the brain.

There are very few CB1 receptors in the brainstem or in the cardiorespiratory centers, which accounts for the absence of a lethal dose with cannabis.

Clinical Endocannabinoid Deficiency: diseases that arise from deficiencies in the ECS.

CED may be the cause of FBM, migraines, IBS, cancer, depression, anxiety, heart disease, stress, Cystic Fibrosis, phantom limb pain, PTSD, and dysmenorrhea. CED is a condition characterized by a deficit in endocannabinoid system signaling. Dr. Ethan Russo suggests that all humans have a base level of endocannabinoids, and when this level is deficient, it manifests in diseases marked by chronic pain, dysfunctional immune systems, fatigue, and mood imbalances.

Stress seems to play a major role in CED.

Research in animal models has demonstrated that stress-induced anxiety is directly related to anandamide deficiency in mice, and that increasing anandamide levels reduces stress-induced anxiety.

CED can also arise from genetic or congenital issues or from intercurrent injury or disease.



Cannabinoids can be endogenous, plant-based, or synthetic compounds.

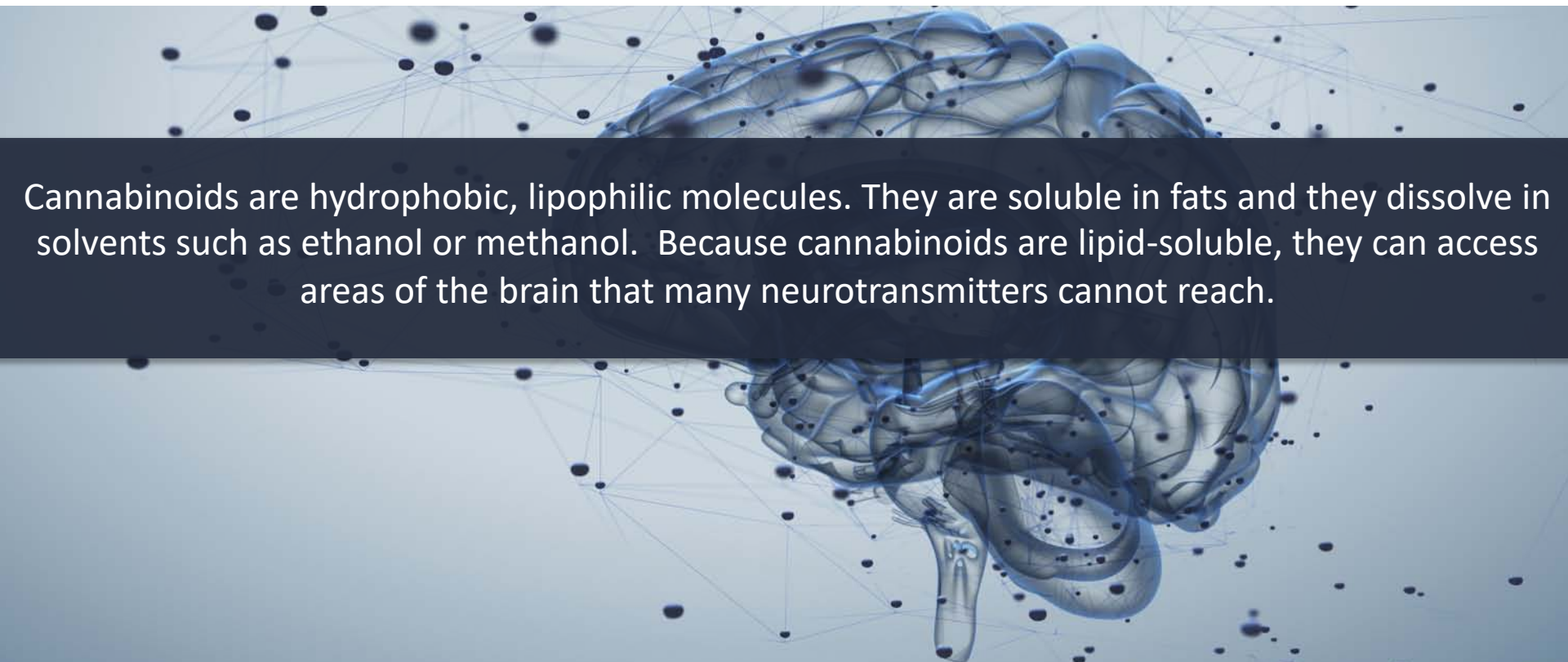
CANNABINOIDS

Phytocannabinoids are cannabinoids found in plants.

The resin secreted by
cannabis flowers is
stored in trichomes.



Many cannabinoids are psychoactive to varying degrees.



Cannabinoids are hydrophobic, lipophilic molecules. They are soluble in fats and they dissolve in solvents such as ethanol or methanol. Because cannabinoids are lipid-soluble, they can access areas of the brain that many neurotransmitters cannot reach.

THC binds to CB1 receptors and causes a change to the function of that cell.

THC

Can produce euphoric effects, and can alter behavior, consciousness, mood, and perception.

THC is a potent anti-inflammatory and analgesic.



THC can treat:

- Nausea
- Pain
- Appetite loss
- Insomnia
- Sleep apnea
- Anxiety
- Inflammation
- PTSD
- Tourette's Syndrome
- Cancers

THC is not a COX-1 or COX-2 inhibitor.



THC side effects:

- Increased heart rate
- Increased appetite
- Fatigue
- Dizziness
- Low blood pressure
- Low body temperature
- Dry mouth and eyes
- Decreased urination
- Hallucination
- Paranoia
- Forgetfulness
- Anxiety

CBD has neuroprotective effects that are more potent than Vitamins C and E.

CBD

*Antipsychotic, anxiolytic, antidepressant;
relieves anxiety, depression, and psychosis.
CBD is a mood-altering substance.*

CBD is cytotoxic in breast cells while preserving normal cells.



CBD can treat:

- Nausea
- Seizures
- Psychosis
- Inflammation
- Neurodegeneration
- Cancer
- Anxiety
- Depression
- Diabetes
- Bacterial infections
- Bone fractures
- Insomnia
- Pain
- Spasms

CBD is well-tolerated and safe, even at high doses.



CBD side effects:

- Dizziness
- Lightheadedness
- Anxiety
- Increased heart rate
- Decreased appetite
- Drug interactions
- Jitteriness
- Drowsiness
- Diarrhea

CBD is not psychoactive in same manner as THC.

CBD can be used as an antipsychotic, an anxiolytic, and an antidepressant, and a substance that can relieve anxiety, depression, and psychosis is, in fact, a mood-altering substance, even if it doesn't necessarily produce euphoria.

CBN may be an immunomodulator because of its affinity with the CB2 receptor.

CBN

CBN can induce sedative-like effects and is often recommended for sleep.

As an analgesic, CBN is 3 times stronger than aspirin.



CBN can treat:

- Pain
- Inflammation
- Appetite issues
- Cancers
- Insomnia
- Bacterial infection
- Auto-immune disease
- Seizures
- Spasms
- Bone fractures

THCa can be a good option for patients wanting to avoid impairment.

THCa

THCa is the most abundant cannabinoid in raw cannabis.

THCa is a potent anti-inflammatory.



THCa can treat:

- Neurodegeneration
- Nausea
- Inflammation
- Cancer
- Pain
- Spasms

CBDa might inhibit the migration of human breast cancer cells.

CBDa

CBDa is the biological precursor to the cannabinoid CBD.

CBDa is effective at treating anticipatory nausea and vomiting.



CBDa can treat:

Bacterial infection

Nausea

Cancer

Inflammation*

Pain*

Fatigue*

ADHD*

Improved Cognition*

*Radicle Health
observational data

THCv is psychoactive and is an antagonist of both the CB1 and CB2 receptors.

THCv

THCv can suppress appetite, lower blood sugar, reduce panic attacks, and stimulate bone growth.

CBG can inhibit the uptake of GABA, which can decrease anxiety and muscle tension.

CBG

CBG has anti-inflammatory properties and has been used for clinical experimentation in IBD patients.

Terpenes produce plant aromas and protect from bacteria and fungus.



TERPENES

Caryophyllene: anti-inflammatory, anti-proliferative, and antioxidant. Strains high in caryophyllene have a pepper or clove scent.

Linalool: analgesic, sedative, anxiolytic, and anesthetic. Strains high in linalool have a lavender scent.



TERPENES

Myrcene: analgesic, anti-insomnia, anti-proliferative, and anti-inflammatory. Strains high in myrcene have a musky, spicy scent.

Limonene: anxiolytic, antifungal, anti-proliferative, and immuno-stimulant. Promotes an overall uplifted, positive mood.



Pinene: anti-inflammatory, bronchodilator, antibiotic, and memory aid. Strains high in pinene have a pine or woody scent.

Strains high in limonene have a citrus scent.

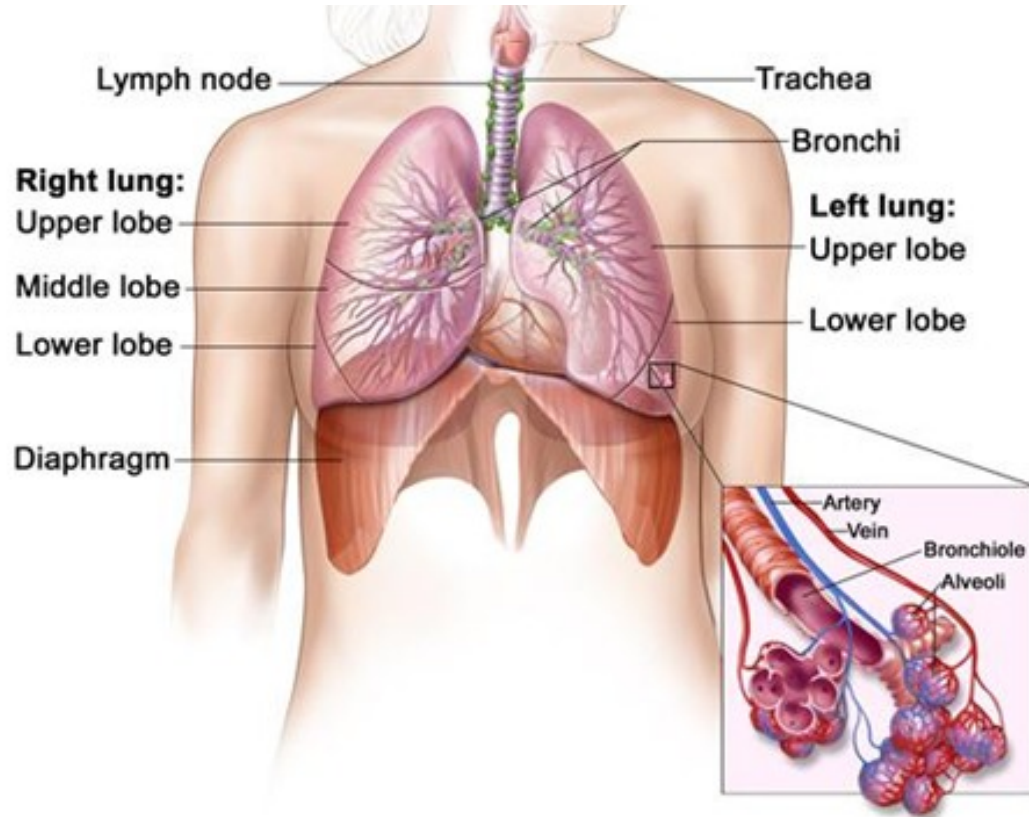
The route of administration can influence how patients benefit from cannabis.

ROUTES OF ADMINISTRATION

Smoking raw cannabis flowers can produce rich and nuanced therapeutic effects.



Inhaled cannabis enters the body through passive diffusion into the capillaries.



Long-term, heavy cannabis smoking can lead to chronic bronchitis and airway inflammation.



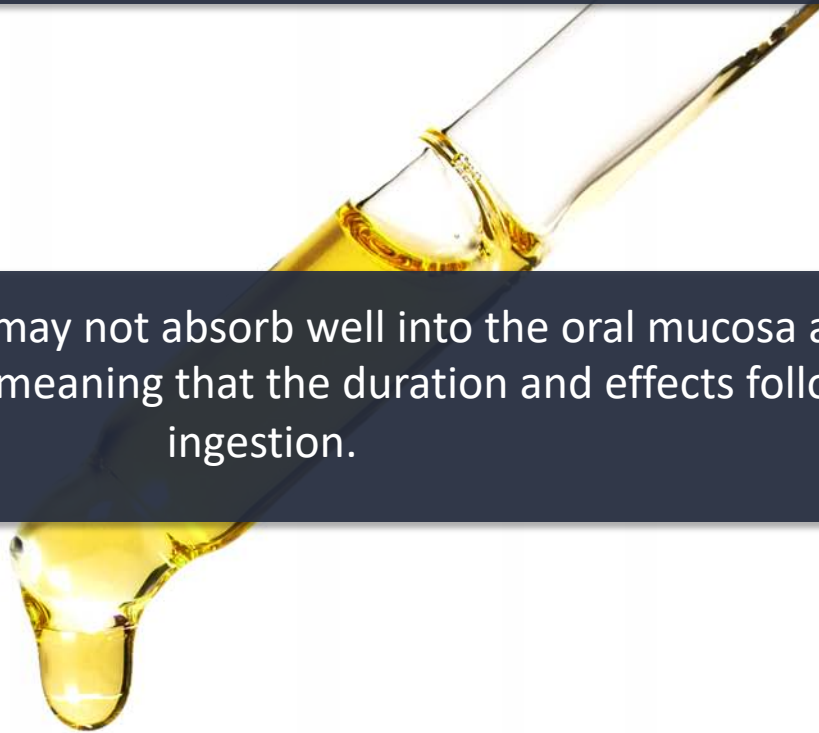
When would you recommend vaporizing vs. smoking?



Multiple studies have shown that propylene glycol and polyethylene glycol break down the carcinogens formaldehyde and acetaldehyde — especially when vaped at high temperatures.

Liquid cannabis extracts offer patients dosage control and fast-acting effects.

Cannabis-infused medications may not absorb well into the oral mucosa and much of the preparation is likely swallowed, meaning that the duration and effects follow the pattern of ingestion.



Edibles are associated with an onset that is both variable and lengthy.



Because the time of onset is variable and lengthy, edibles are difficult to dose and difficult to titrate. Many patients, and unfortunately, many first-time patients, can over-medicate using edibles and experience very unpleasant side effects.



A cannabis-infused tea (with fat) can be effective for treating body pain and sleep issues.



Topicals can treat itchy, painful areas of the skin.

Patients new to cannabis or anxious about using cannabis might be willing to try less invasive external applications. Generally, topicals have no systemic side effects.



Transdermal products enter the bloodstream, avoiding first-pass metabolism.

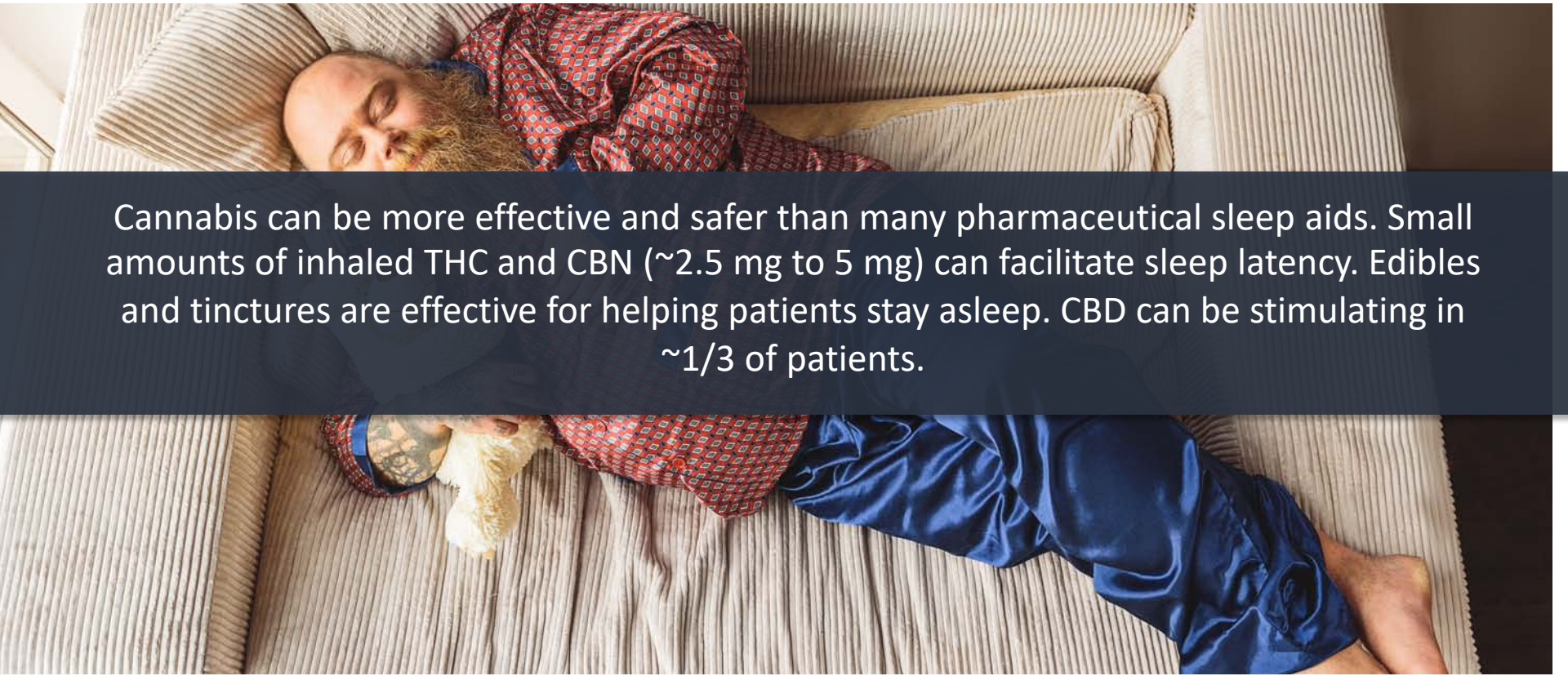


What can we treat effectively using cannabis?

A detailed 3D rendering of a virus, likely HIV, with a green, textured surface and numerous yellow, conical spikes. The virus is surrounded by several red blood cells, which are depicted as smooth, biconcave discs in shades of red. The background is dark, making the virus and cells stand out.

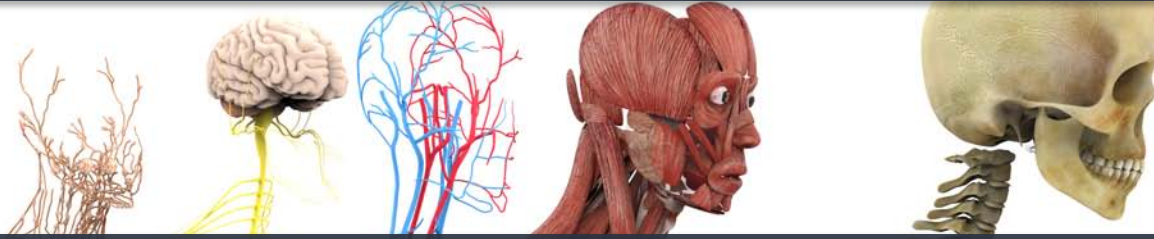
CLINICAL IMPLICATIONS

Clinical Implications: Insomnia

A photograph of a man with a long, full beard and mustache, wearing a red patterned shirt and blue pajama pants, sleeping peacefully on a light-colored corduroy sofa. He is lying on his side, and his eyes are closed. The background is a plain, light-colored wall.

Cannabis can be more effective and safer than many pharmaceutical sleep aids. Small amounts of inhaled THC and CBN (~2.5 mg to 5 mg) can facilitate sleep latency. Edibles and tinctures are effective for helping patients stay asleep. CBD can be stimulating in ~1/3 of patients.

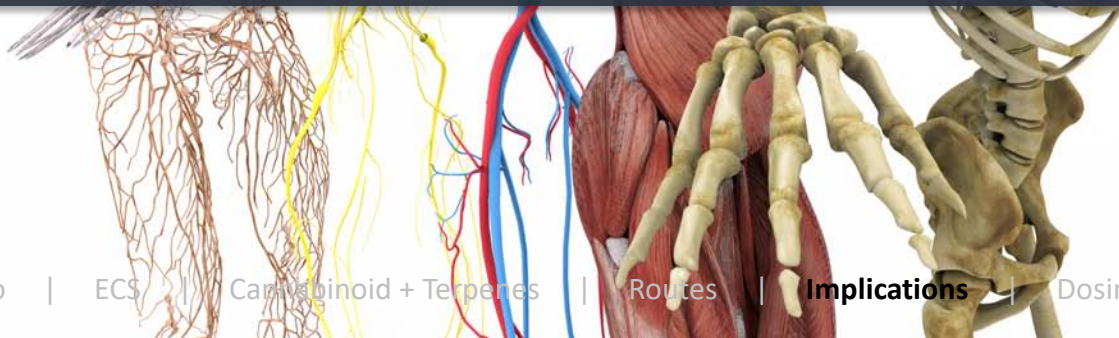
Clinical Implications: Chronic Pain



Research supports a synergistic interaction between cannabinoids and NSAIDs. For example, Indomethacin was shown to increase 2-AG and Anandamide levels in mice and Acetaminophen was shown to increase Anandamide levels.

Also, NSAIDs can reduce the memory impairing effects of chronic THC use.

THCa, CBDa, CBG, and CBGa can inhibit COX-2 activity by as much 30%.





Clinical Implications: Chronic Pain


Cannabis is not toxic like opioids and other non-narcotic pain medications. Unlike opioids, cannabis does not cause constipation (though it can exacerbate it), does not cause any physical dependence, and has fewer side effects. Also, there is no lethal dose of cannabis.

Clinical studies have demonstrated that patients use fewer opioids when medicating with cannabis.

A cannabis treatment depends on the type of pain.



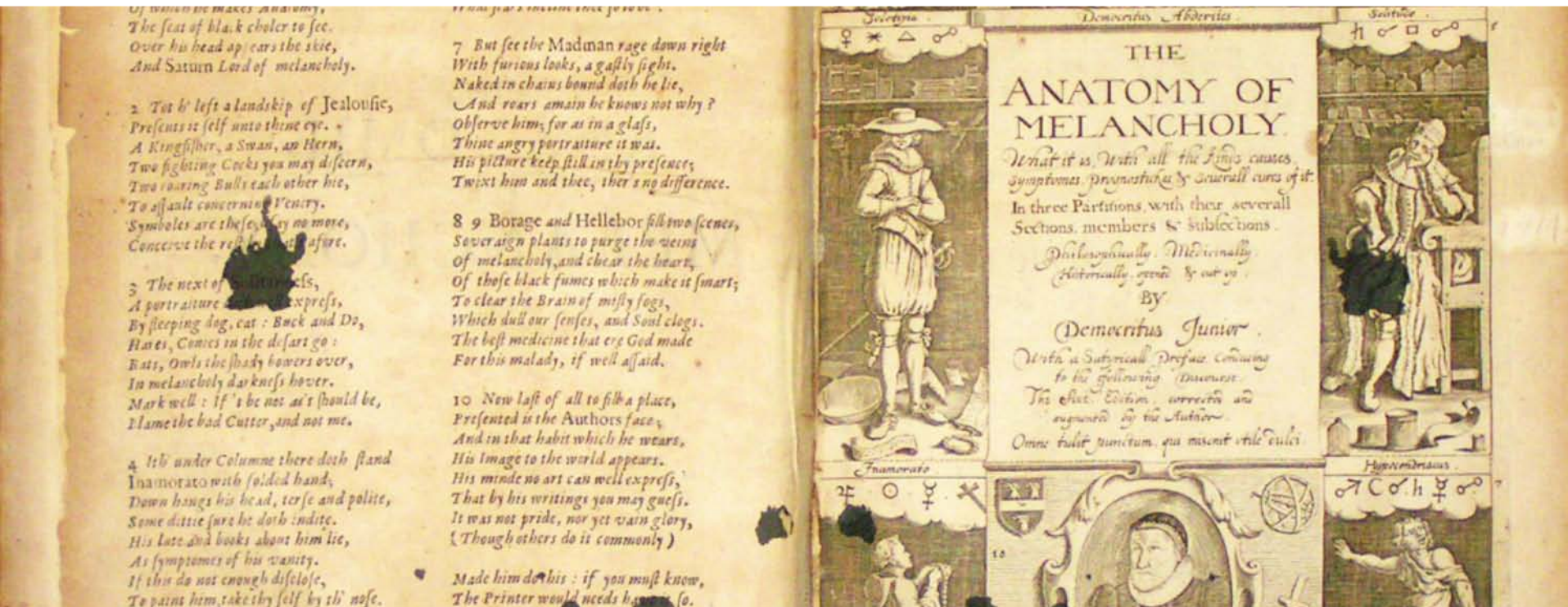
Clinical Implications: Anxiety and Depression



Anxiety and depression may be caused as a result of other underlying issues: pain, insomnia, other health issues, fear of aging and dying, or the loss of a spouse.

Medications prescribed for anxiety and depression are associated with severe side effects—they can be addicting and nearly impossible to wean from completely (ie, Benzodiazepines). Females typically need 30% less THC than males. Too much THC and CBD can cause anxiety.

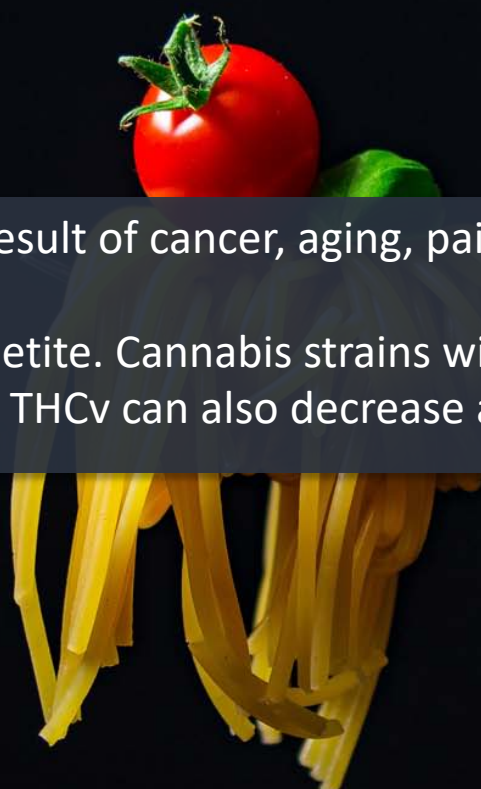
In 1621, Robert Burton recommended cannabis for depression in *The Anatomy of Melancholy*.



Terpenes contribute to efficacy of cannabis when treating anxiety and depression.



Clinical Implications: Appetite and Weight Loss



Appetite issues can be a result of cancer, aging, pain, tremors, or due to a side effect.

CBD can suppress appetite. Cannabis strains with higher than normal levels of THCv can also decrease appetite.

CBD and THCV can decrease appetite.



Clinical Implications: Dementia, Alzheimer's, and Neurological Disorders

Patients can exhibit aggressive behaviors, wandering, and lack of appetite. Medications commonly prescribed to treat these issues often include a Black Box Warning.

Parkinson's tremors and rigidity affect quality of life and Carbidopa and Levodopa become less effective over time.

CBD can reduce stiffness and rigidity; THC and THCa can improve tremors.

Clinical Implications: Cancer

Cannabis can reduce side effects associated with chemotherapy, biotherapy, and radiation. And, side effects from cancer treatment can delay treatment, lead to reduced dosing, or even termination of treatment.

The National Cancer Institute acknowledged that cannabis may help treat cancer.



ABOUT CANCER | CANCER TYPES | RESEARCH | GRANTS & TRAINING | NEWS & EVENTS | ABOUT NCI | search

6. Have any preclinical (laboratory or animal) studies been conducted using *Cannabis* or cannabinoids?

Preclinical studies of cannabinoids have investigated the following:

Antitumor activity

- A laboratory study of delta-9-THC in hepatocellular carcinoma (liver cancer) cells showed that it damaged or killed the cancer cells. The same study of delta-9-THC in mouse models of liver cancer showed that it had antitumor effects. Delta-9-THC has been shown to cause these effects by acting on molecules that may also be found in non-small cell lung cancer cells and breast cancer cells.
- A laboratory study of cannabidiol (CBD) in estrogen receptor positive and estrogen receptor negative breast cancer cells showed that it caused cancer cell death while having little effect on normal breast cells. Studies in mouse models of metastatic breast cancer showed that cannabinoids may lessen the growth, number, and spread of tumors.
- A laboratory study of cannabidiol (CBD) in human glioma cells showed that when given along with chemotherapy, CBD may make chemotherapy more effective and increase cancer cell death without harming normal cells. Studies in mouse models of cancer showed that CBD together with delta-9-THC may make chemotherapy such as temozolomide more effective.

As far back as 1975, the National Cancer Institute reported that THC inhibits growth of lung cancer tumors and that bone marrow treated with cannabinoids demonstrated dose-dependent resistance to cancer.

Research: Chemotherapy-Induced Nausea

Despite the advent of anti-emetic drugs, chemotherapy-induced nausea remains problematic.

If nausea and vomiting are not properly controlled, anticipatory nausea (a conditioned response of psychological nausea and vomiting that is believed to be a learned response to chemotherapy) can develop. Anticipatory nausea is refractive to current anti-emetics.

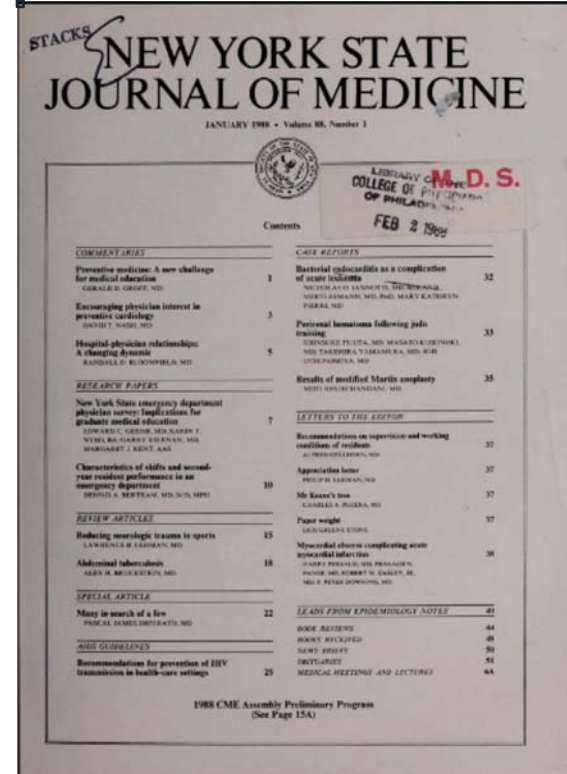


Research: Chemotherapy-Induced Nausea

Inhaled cannabis attenuates chemotherapy-induced nausea and vomiting (CINV) [1], though there exists no clinical trials comparing inhaled cannabis to current first-line antiemetic therapies (5-HT3 receptor antagonists). [2]

Multiple clinical studies demonstrate that partial agonists at CB1 and CB2 receptors (Δ^9 -THC and synthetic Δ^9 -THC) are more effective than dopamine 2 receptor antagonists (anti-emetics which predated the 5-HT3 receptor antagonists).

[3]



Research: Chemotherapy-Induced Nausea

Multiple studies in animal models demonstrate that $\Delta 9$ -THC, THCa, CBD, and CBDa have anti-emetic and anti-nausea properties.[1]

CBD and CBDa are effective in a dose-dependent manner, where suppression was effective at low doses (10mg/kg) but not at high doses (20-40mg/kg).



Research: Chemotherapy-Induced Nausea

Rats cannot vomit, but they display conditioned gaping reactions that are reliable models of acute nausea in rats.

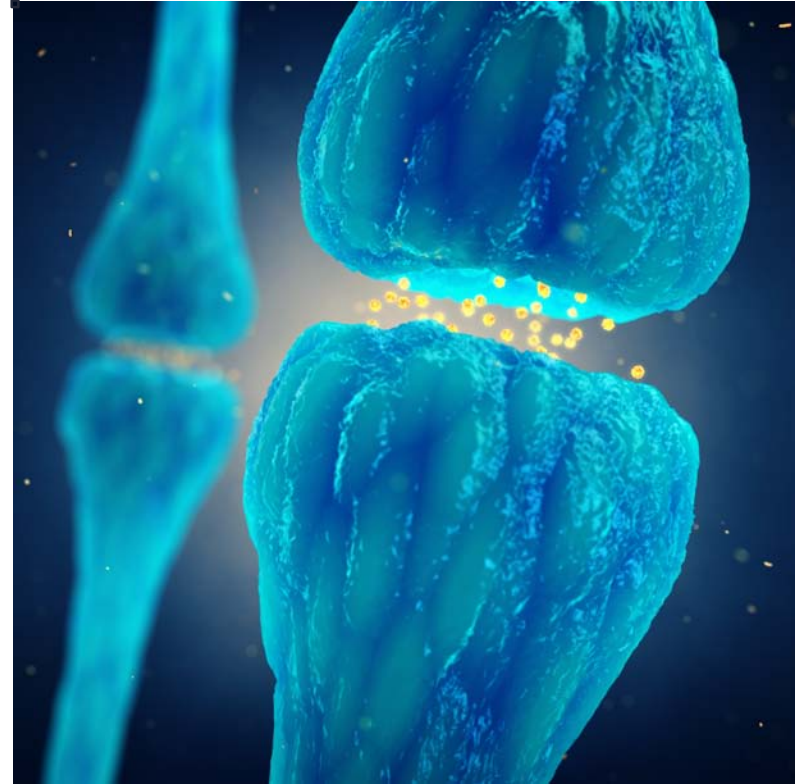
Rats can also display conditioned gaping upon re-exposure to a nausea-paired context and this model is similar to the development of anticipatory nausea in humans [1].

As in human anticipatory nausea, a 5-HT3 receptor antagonist *does not reduce* contextually elicited conditioned gaping. [2]



Research: Chemotherapy-Induced Nausea

- $\Delta 9$ -THC and THCa reduced contextually elicited conditioned gaping [1], suggesting that CB1 receptor agonism reduces anticipatory nausea in rats.
- CBD and CBDa suppressed contextually elicited gaping in the absence of any locomotor impairments [2], suggesting that 5-HT1A agonism reduces anticipatory nausea in rats.



Research: Chemotherapy-Induced Nausea

Cannabinoids demonstrate a synergistic potential in vomiting, acute nausea, and anticipatory nausea when combined with other anti-emetics:

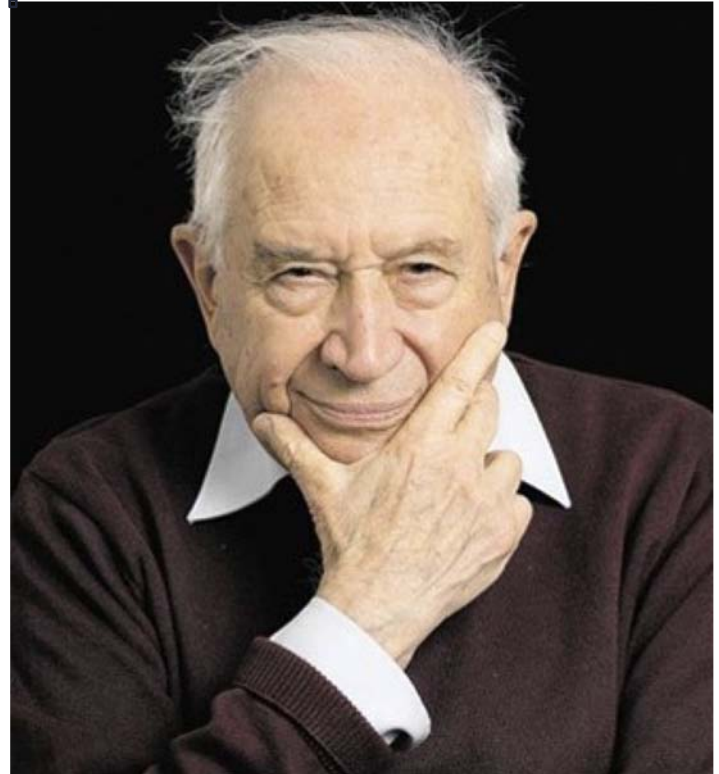
- Δ 9-THC + tropisetron, Δ 9-THC + ondansetron, and Δ 9-THC + CBD combinations demonstrate enhanced reduction of vomiting.
- CBDa + Δ 9-THC, CBDa + ondansetron, CBDa + D2 receptor antagonist combinations demonstrate enhanced reduction of anticipatory nausea.



Research: Δ 8-THC Clinical Trial

A 1995 study led by Raphael Mechoulam to test whether Δ 8-THC would prevent vomiting from antineoplastic therapy:

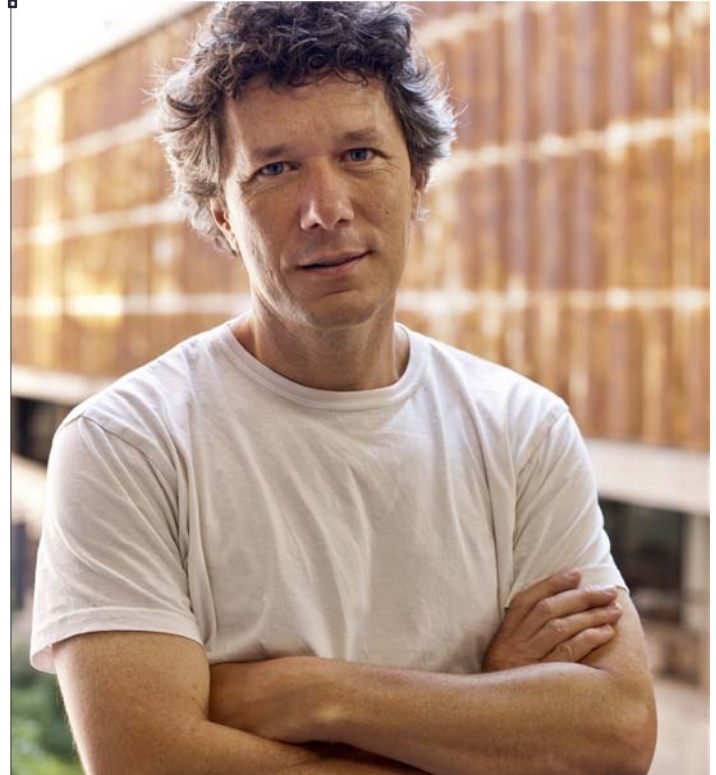
- 8 pediatric cancer patients treated with a variety of anticancer drug protocols
- Administered doses of Δ 8-THC that were much higher than doses of Δ 9-THC given to adult patients and without major side effects (5-10 mg/m² of Δ 9-THC for adult patients versus 18 mg/m² of Δ 8-THC)
- Success rates were 100%, regardless of the cancer protocol used
- Total number of treatments = 480 (8 patients treated during a 2-year period)



Research: Glioblastoma Clinical Trial

In 2006, a clinical trial tested whether cannabinoids can treat cancer in patients:

- Led by Dr. Manuel Guzman and his team in Spain
- 9 patients with advanced, terminal glioblastoma multiforme were given highly purified THC through a tube directly into their brain
- 8 patients' cancers showed a positive response to the treatment
- All patients died within a year, as expected for people with this type of cancer



Research: Glioblastoma Clinical Trial

In 2017, GW Pharmaceuticals announced the results from a small Phase II study with Δ 9-THC + CBD in 21 patients with recurrent glioblastoma multiforme (GBM):

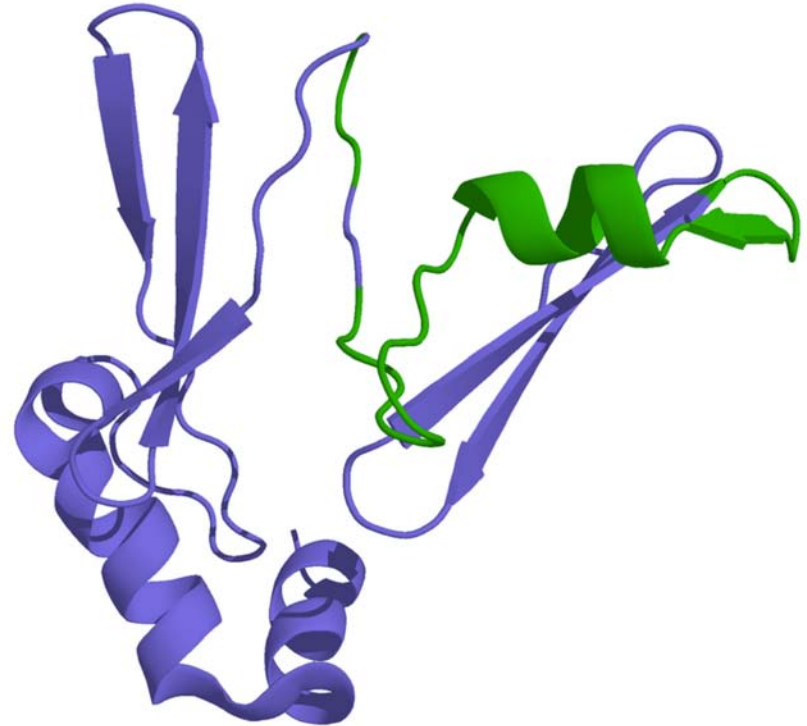
- Patients with THC:CBD had an 83% one-year survival rate compared with 53% for patients in the placebo cohort
- Median survival for the THC:CBD group was greater than 550 days, compared with 369 days in the placebo group



Research: Appetite Stimulation Clinical Trial

CB1 activation can stimulate appetite. [1] This process may also be associated with the release of ghrelin, a peptide hormone that is secreted from the stomach and intestines to increase hunger.[2]

- Ghrelin can increase food intake by increasing the activity in area of the hypothalamus that is responsible for nutrient sensing. [3] [4]
- In one study, HIV patients who inhaled cannabis tested for higher in serum ghrelin as well as reduced levels of the appetite suppressing peptide PYY. [5]



Research: Chemotherapy-Induced Peripheral Neuropathy

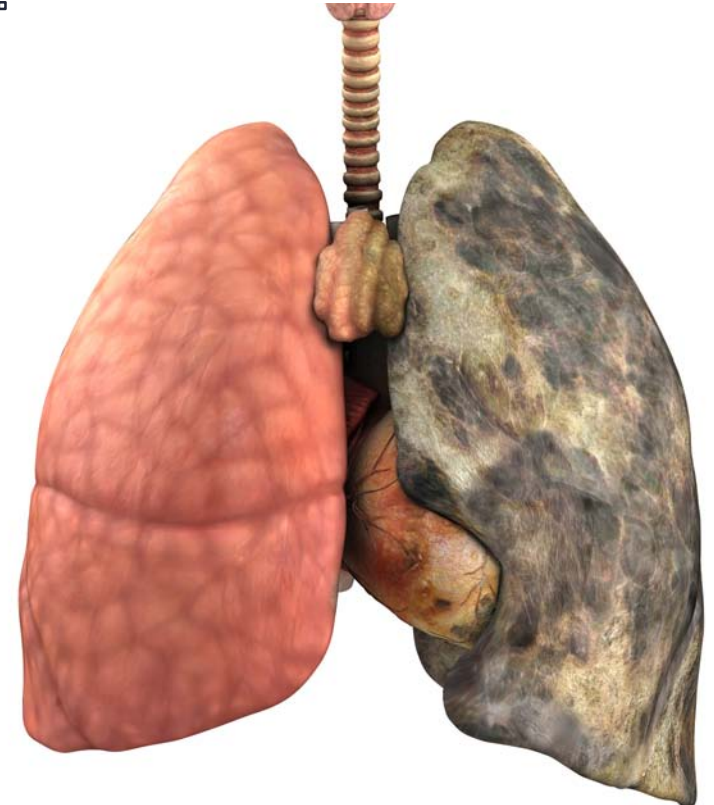
CIPN can limit chemo dose if symptoms are severe:

- One study [1] assessed whether CBD can prevent CIPN from Paclitaxel (PAC) in mice
- 2.5mg-5mg/kg of CBD was administered 15 minutes before each PAC injection
- Development of CIPN was prevented in the rodents that received CBD without compromising the anti-tumor effects of PAC on breast cells
- A 2nd study determined that CBD and THC prevented Oxaliplatin- and Vincristine-related CIPN [2]



Research: Lung Cancer

- The National Academies of Sciences, Engineering, and Medicine reviewed the literature in 2017 and determined that smoking cannabis does not increase the risk for cancers often associated with tobacco use, such as lung and head and neck cancers. [1]
- Dr. Donald Tashkin's team at UCLA in 2005 studied 1,212 cancer patients and matched them for age, gender, and neighborhood with 1,040 cancer-free controls. They found that increased cannabis use did not result in higher rates of lung and pharyngeal cancer (whereas tobacco smokers were at greater risk the more they smoked). Tobacco smokers who also smoked cannabis were at slightly lower risk of getting lung cancer than tobacco-only smokers.



Clinical Implications: Cancer

Cannabis side effects are challenging at higher doses: 70% of patients fail to complete treatment because of the side effects, which include paranoia, anxiety, hallucinations, and extreme lethargy. Many patients are using cannabis without their HCP's knowledge.

Clinical Implications: Cancer

Many patients experience adverse drug reactions due to increased toxicity of pharmaceuticals. Thoroughly review all medications to assess for potential drug-drug interactions, as cannabis can decrease the effectiveness of other treatments.

Immunotherapy and high-dose THC is contraindicated.
Suppositories are not effective for most cancer treatment.

Patient Concerns:

- Most patients want information about cannabis from their cancer care team, yet few patients reported receiving it (15% in one survey)
- Cost: nearly universal lack of insurance coverage for cannabis therapies, with typical out-of-pocket costs to patients of \$200-\$300 per month



Oncology Clinician and Patient Surveys

Clinician Concerns:

- Absence of standards around cannabis dosing
- No formal training and lack of ability/autonomy to provide guidance about cannabis type and dosing
- No confidence with respect to discussing risks and benefits of cannabis use
- Need more training, especially online training programs



A starting dose depends on patient experience, route, frequency, and time of day.




DOSING

Begin with a low dose, especially with patients who have little experience with cannabis.



An average dose is between 1mg and 5mg.



Discuss with your patients how much of a medicine to take, how frequently to take it, and for how long. Discuss when and under what circumstances the patient should increase her dose, as well as the predicted length of therapy. And, consider whether the route of administration is one that will be the most effective at treating her condition.

Drug interactions have been noted with the following:



Opiates
Anti-psychotics
Warfarin
Benzodiazepines

Muscle relaxers
Hypnotics
Anticholinergics
Antihypertensives



Additional documented drug interactions include:

lorazepam, quetiapine, sertraline, dexamethasone, tamoxifen, diltiazem, pembrolizumab (Keytruda), dabrafenib (Tafinlar) and trametinib (mekinist)

Other possible interactions are seen with antidepressants, AED's, and opiates.
In one case, dexamethasone may have decreased the effectiveness of cannabis.

Consider whether a single cannabinoid or a blend of cannabinoids is appropriate.

Medical Use Only

Strain Name

THC %

CBD %

THC

CC1=C(C(=O)OC2C=CC(=C2)C)C3CC4=C(C)C=CC=C4C31

Medical Use Only

Strain Name

THC %

CBD %

CBD

CC1=C(C(=O)OC2C=CC(=C2)C)C3CC4=C(C)C=CC=C4C31

Medical Use Only

Strain Name

THC %

CBD %

CBN

CC1=C(C(=O)OC2C=CC(=C2)C)C3CC4=C(C)C=CC=C4C31

Patients should take a few small doses throughout the day.



Patients can use the same dose and ratio for several days and record the effects.



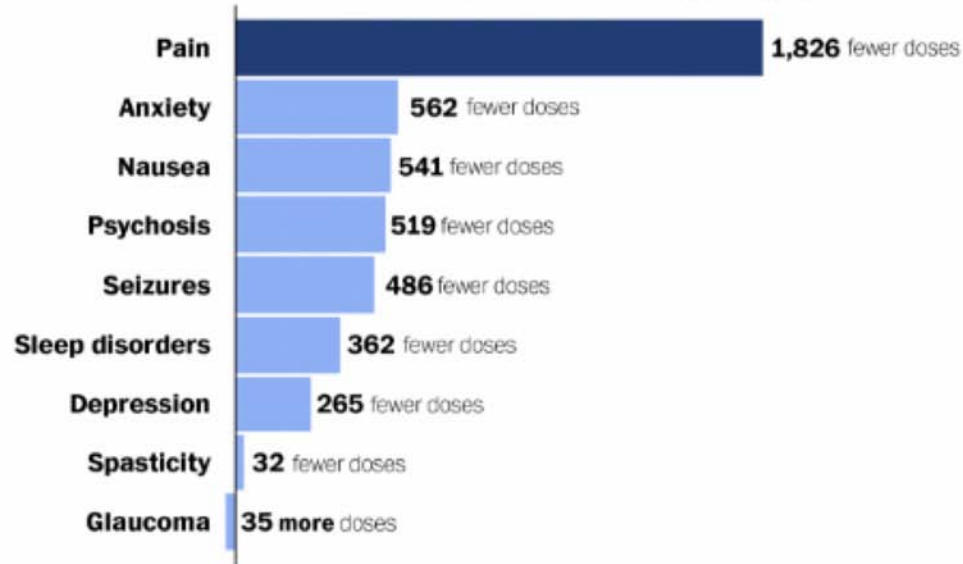
Talk about possible side effects.



In legal cannabis states, patients are weaning themselves off dangerous pharmaceuticals.

Fewer pills prescribed in medical pot states

Difference between annual drug doses prescribed per physician in medical marijuana states, and in states without medical marijuana laws, by drug category



WAPO.ST/WONKBLOG

Source: Bradford and Bradford, Health Affairs, July 2016

Questions?

Resources

American Cannabis Nurses Association

www.americancannabisnursesassociation.org

Society of Cannabis Clinicians

www.cannabisclinicians.org

Patients Out of Time

www.medicalcannabis.com

NORML

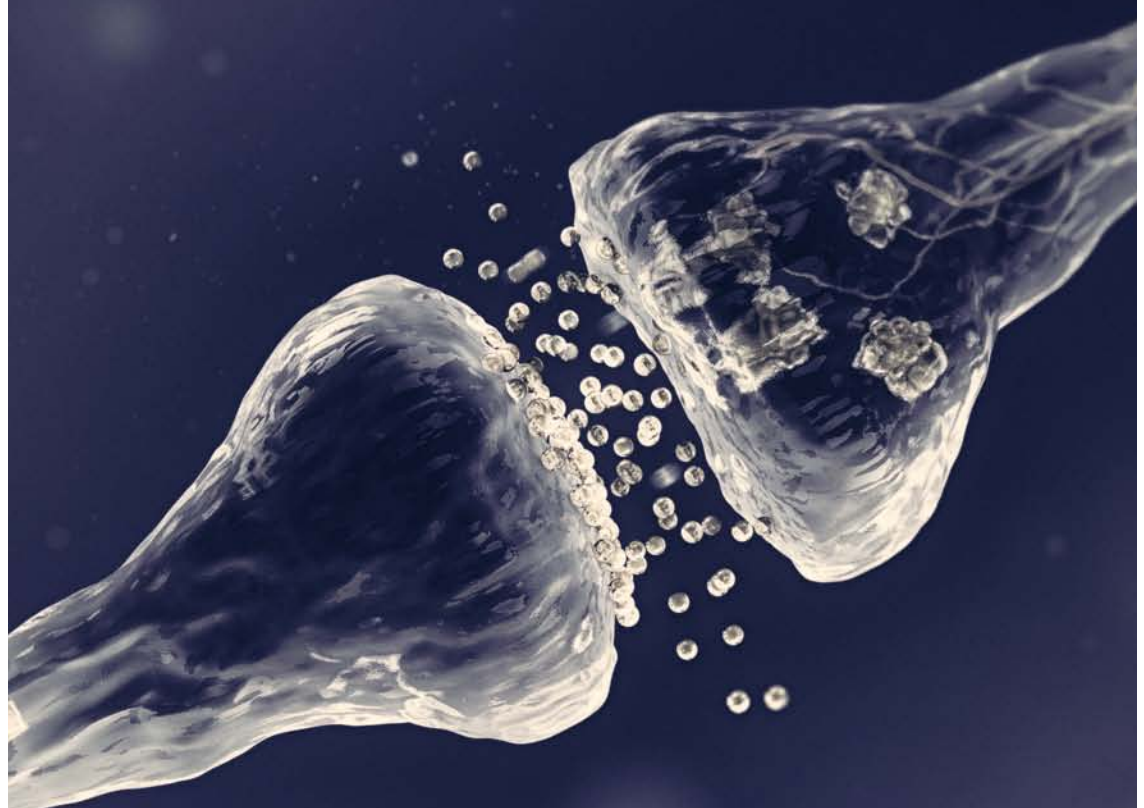
www.norml.org

Americans for Safe Access

www.safeaccessnow.org

United Patients Group

www.unitedpatientsgroup.com



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health care back to
healthcare professionals.*

