MEDICAL MARIJUANA & THE ROLE IN MANAGING THE CANCER PATIENT

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DISCLOSURE

- No disclosures
- Some mention of off-label use of dronabinol and other cannabinoid products

OBJECTIVES

- History of medicinal cannabis and cannabis laws in the United States
- Biochemistry of the cannabis plant
- Pharmacology of cannabis and cannabinoids
- Minnesota medical cannabis program
- Role of cannabis in management of cancer-related and cancer treatment-related symptoms

Cases:

1. 63yo with locally advanced breast cancer on fulvestrant. C/o aching pain in back, hips, legs, knees since starting treatment. Similar symptoms in the past with letrozole. No relief from tramadol or APAP. NSAIDs contraindicated.
2. 48yo with squamous cell carcinoma of the right anterior tongue, s/p resection and adjuvant XRT, now with recurrent disease. On palliative chemo/immunotherapy. Experiencing severe mouth pain from tumor, anxiety, and nausea.
3. 55yo with metastatic lung cancer on docetaxel. Complaints of back pain related to vertebral mets, managed with opioids. Complaints of anxiety and severe insomnia.
4. 66yo with metastatic renal cell carcinoma on 3rd line cabozantinib. Longstanding CIPN with severe neuropathic pain in b/l feet. Pain uncontrolled despite pregabalin, methadone, TENS, acupuncture.
5. 65yo with metastatic pancreatic cancer on 3rd line pemigatinib. Suffers from chronic abdomen pain, bowel cramps, anorexia, and CIPN.

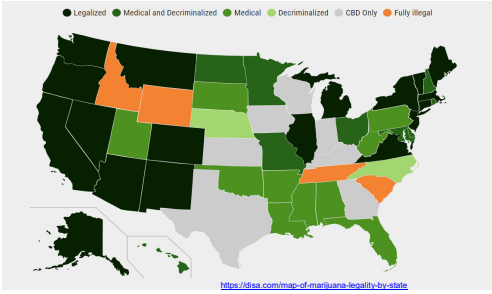
HISTORY OF MEDICINAL CANNABIS and LEGALITY

- 1840s: Introduced to Western medicine
  - Surgeon W.B. O'Shaughnessy reported analgesic, anti-inflammatory, antispasmodic, and anticonvulsant properties
  - Psychiatrist Jacques Joseph Moreau conducted studies showing benefit for headaches, appetite, sleep
- 1850: Introduced into US Pharmacopeia
  - Labor pain, nausea, rheumatism
- 1937: Criminalized by US Congress (Marijuana Tax Act)
- 1942: Removed from US Pharmacopeia
- 1970: Cannabis became a Schedule I drug

HISTORY OF MEDICINAL CANNABIS and LEGAL STATUS

- 1996: California re-legalized marijuana for AIDS, cancer, serious illness
- 2014: MINNESOTA Medical Cannabis Therapeutic Research Act
- 2015: MDH opens medical cannabis program
- 2018: Agriculture Improvement Act / Hemp Farming Act: redefined marijuana vs hemp (hemp being Cannabis containing < 0.3% THC) and removed hemp from the US list of scheduled substances.

Where we are today…

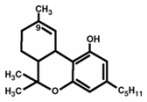


Cannabis Sativa

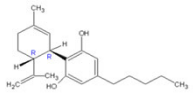
- Complex plant with >400 chemical entities
  - 80+ cannabinoids
  - Terpenes, flavonoids, fatty acids
- Cannabinoids
  - 21-Carbon molecules
  - Endocannabinoid system: endogenous homeostatic regulatory system
    - Regulatory roles in neuronal, vascular, metabolic, immune and reproductive systems
    - Involved in pain perception, appetite, mood, inflammation
    - Cannabinoid receptors
      - CB1 - brain and PNS, mediate neurotransmitters
      - CB2 - immune cells

Cannabis Sativa: Cannabinoids, Effects on HES

- THC: Delta-9-tetrahydrocannabinol
  - Psychotropic, antiemetic, muscle relaxant, appetite stimulant, sedative, antioxidant
  - Decreased gastric motility and intraocular pressure
  - Increased heart rate and BP



- CBD: Cannabidiol
  - Anticonvulsant, antipsychotic, anxiolytic, antiemetic, antioxidant
  - Decreased heart rate and BP



Cannabis Sativa

- Entourage Effect
  - Synergistic effect when all the cannabinoids, terpenes, and flavonoids of the plant are consumed together.
  - The other compounds modulate negative THC effects
    - Ex: CBD inhibits THC binding to CB1 receptors in CNS (mitigating THC psychosis)
  - Increased benefit when the compounds are combined
    - Ex: Increased analgesia with THC+CBD than THC alone

Cannabis Sativa: "Marijuana" vs "Hemp"

- A *legal* distinction based on **THC content**
- "Marijuana": Cannabis sativa with > 0.3% THC (Avg ~15-20%)
  - Psychoactive, potential for abuse
  - federally illegal, Schedule 1 drug
- "Hemp": Cannabis sativa with < 0.3% THC
  - Not psychoactive
  - Federally legal (Farm Act of 2018)
  - Source of commercial CBD

CBD from Hemp

- Legal in the US since 2018 Farm Act
- Each state has its own regulations
- Commercially available in Minnesota
- For patients using CBD
  - Recommend it be third-party tested
  - Educate on potential side effects and drug interactions

Medical Cannabis: Clinical uses in the cancer patient

- Antiemetic
  - 5-HT3 receptors
  - Anticipatory and refractory CINV
  - Alone or in conjunction to other anti-emetics
- Analgesic
  - THC+CBD better than THC alone
  - May prolong opioid effects
  - May delay opioid tolerance
  - CIPN

Cannabis: Clinical uses in the cancer patient

- Appetite Stimulant
  - Dronabinol studies
  - Promotes weight gain
- GI distress
  - Decrease gastric motility
  - Bowel spasms
- Insomnia
  - Sedating effects

Cannabis: Clinical uses in the cancer patient

- Tumor Suppression
  - Studies with cancer cell lines
  - Evidence for inhibiting tumor proliferation and invasion
  - Different cancers have different cannabinoid receptors
  - More research needed

Cannabis: Risks and adverse effects

Whole plant / THC-dominant effects:

- Dizziness, euphoria, sedation – fall risk, driving
- Mood changes – anxiety, agitation
- Psychosis – high risk groups (family hx, schizotypal PD, genetic mutations)
- Anticholinergic effects - dry mouth, blurry vision, urinary retention, constipation, tachycardia, hypertension
- Cognitive dysfunction – tied to use before adulthood
- Immune suppression (CD8 cells, ?concern with immunotherapy)
- Cannabis Hyperemesis Syndrome
  - Genetic abnormality in CB1 receptor

CBD-specific effects:

- Diarrhea, transaminase elevations, decreased appetite

Cannabis: Risks and adverse effects

- Cannabis use disorder
  - ~20% of users
  - DSM-5 diagnosis: meeting criteria for abuse + dependence
  - Genetic and environmental factors
- Cannabis overdose
  - No known cases of fatal cannabis overdose in epidemiologic literature
  - No respiratory depression
- Cannabis Withdrawal (DSM-5)
  - Anxiety, restlessness, depression, irritability
  - Insomnia / odd dreams
  - Physical symptoms (tremors)
  - Decreased appetite

FDA-approved / Prescription cannabinoids

- Dronabinol: synthetic THC
  - AIDS anorexia, CINV, PONV
  - Off-label use for anorexia in cancer, chronic nausea in cancer
  - Sometimes a starting point (access, cost)
- Nabilone: synthetic cannabinoid, similar to THC
  - CINV
- Nabiximols: 1:1 THC:CBD, whole plant extract, oral mucosal spray
  - Investigatory use only in US
  - Approved for MS spasticity (Canada/Europe)
  - One study showed effect on cancer pain greater than THC or placebo
- Cannabidiol: CBD from plant
  - Seizure disorders
  - First non-synthetic FDA-approved cannabis drug

Minnesota Medical Cannabis Program

Minnesota Medical Cannabis Program

- Minnesota Department of Health, Office of Medical Cannabis
- Qualifying conditions:

1) Cancer*
2) Glaucoma
3) HIV/AIDS
4) Tourette's syndrome
5) Amyotrophic lateral sclerosis (ALS)
6) Seizures
7) Severe and persistent muscle spasms
8) Inflammatory bowel disease, including Crohn's disease
9) Terminal illness with life expectancy of under one year*
10) Intractable pain
11) Post-traumatic stress disorder
12) Autism spectrum disorder
13) Obstructive sleep apnea
14) Alzheimer's disease
15) Chronic pain
16) Sickle cell disease
17) Chronic motor or vocal tic disorder
18) Any other condition or its treatment approved by the commissioner (subject to legislative oversight)

* Illness or treatment must produce one or more of the following: (1) severe or chronic pain; (2) nausea or severe vomiting; or (3) cachexia or severe wasting.

[1] Laws 2014, ch. 311; codified as Minn. Stat. §§ 152.22 to 152.37.

https://www.health.state.mn.us/people/cannabis/

Minnesota Medical Cannabis Program

Medical Cannabis Weekly Updates of Registration Data

The Office of Medical Cannabis (OMC) will be posting updated registration data on this site. The cumulative statistics (June 1, 2015 - October 14, 2021) in the Minnesota Medical Cannabis Patient Registry are:

Role in Registry	Number of People
Health Care Practitioners	
Number of health care practitioners who are registered and authorized to certify patients:	2,013
Patients	
Number of patients with approved enrollment who are currently active in the registry:	27,146
Total number of approved patient enrollments to date:	53,361
Caregivers	
Number of patient caregivers who have received their background checks and are approved in the registry:	1,274

This information is updated weekly at 9 a.m. on Fridays.

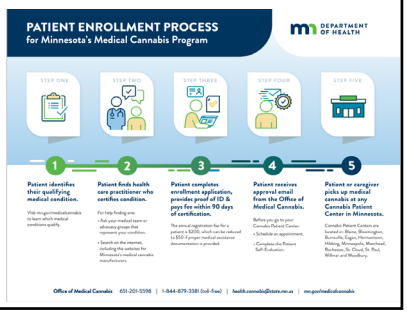
https://www.health.state.mn.us/people/cannabis

Minnesota Medical Cannabis Program

- Provider Roles
  - Cannabis knowledge base
  - Register with MDH (MD, APRN, PA)
  - Be aware of institutional policies
  - Counsel patients on MMCP when appropriate
    - discuss and document risks (DRIVING)
  - Certify patient's QUALIFYING CONDITION
    - PROVIDER IS NOT PRESCRIBING CANNABIS
    - Update med list and problem list
    - Tennessen Warning
  - Monitor patient regularly, know products
  - Report effects to MMCP

Minnesota Medical Cannabis Program

- Patient Experience
  - Discuss certification with provider
  - Complete application, registration fee
  - Await approval from OMC
  - Schedule appointment at dispensary
  - Meet with Pharmacist
  - Purchase product
  - Report effects to MMCP



Minnesota Medical Cannabis Program

COST

- No insurance coverage
- Prohibitive for many

- $200 Annual registration fee
  - $50 Reduced fee: SSI/SSD, MA, MN Care, IHS, Railroad Disability, VA
- Dispensary purchases

Products: LeafLine Labs

Tangerine (THC Dominant)

Medications in the Tangerine product family contain high levels of THC and low/trace levels of CBD. Tangerine medications can help reduce chronic pain, improve sleep, alleviate anxiety, and help improve appetite.

This benefit comes *without* the risk of respiratory depression and high levels of addiction that current prescription opioid pain medications do.

Heather (1:1 THC/CBD)

Medications in the Heather product family contain equal levels of THC and CBD. Combining THC and CBD in similar amounts reduces the sedating/psychoactive effects without diminishing the therapeutic effect of the medication.

Our pharmacists commonly advise this type of medication for painful muscle spasm disorders, neuropathic pain, select cancer related pain and other conditions.

Cobalt (20:1 CBD/THC)

Medications in the Cobalt product family contain high levels of CBD and low levels of THC. CBD is less sedating and has minimal psychoactive effects. CBD is well known for its anti-seizure properties and thus Cobalt is recommended for patients with epilepsy and other seizure disorders.

Because CBD is also known for its neuroprotective and anti-inflammatory properties, Cobalt products are also recommended for patients with chronic pain. Patients have reported that Cobalt products can help with anxiety, depression, and other mental health conditions.

https://leaflinelabs.com/

Products: LeafLine labs

Product	Volume/Qty	CBD (mg)	THC (mg)
Lozenges - Root Beer – 5mg each / 10ct. [COMING SOON]		Trace*	75
Lozenges - Mango Passion Fruit – 5mg Each / 10ct. [COMING SOON]		Trace*	75
Tangerine Vaporization (Cartridge)	0.5 mL	20	400
Tangerine Vaporization (Cartridge) 2-pack	1 mL	40	800
Tangerine Sublingual (Spray) - Vanilla Mint	15 mL	Trace*	300
Tangerine Oral Suspension ES - Unflavored	60 mL	Trace*	1200
Tangerine Oral Suspension - Unflavored	120 mL	Trace*	240
Tangerine Oral Suspension - Orange Cream	120 mL	Trace*	240
Tangerine Oral Suspension - Orange Cream (2)	240 mL	Trace*	480
Tangerine Capsule - 5mg	30 / Capsule	Trace* / Capsule	150
Tangerine Capsule - 10mg	30 / Capsule	Trace* / Capsule	300
Tangerine Topical	30 mL	Trace*	150
Heather Vaporization (Cartridge)	0.5 mL	218	218
Heather Sublingual Spray - Vanilla Mint	15 mL	225	225
Heather Oral Suspension - Unflavored	60 mL	300	300
Heather Oral Suspension - Cherry Vanilla	60 mL	300	300
Heather Oral Suspension - Cherry Vanilla (2)	120 mL	600	600
Heather Topical	30 mL	150	150
Cobalt Vaporization (Cartridge)**	0.5 mL	413	22
Cobalt Oral Suspension - Unflavored	60 mL	1200	60
Cobalt Oral Suspension - Unflavored	30 mL	600	30

https://leaflinelabs.com/

Products: Vireo (Greengoods MN)

- VIOLET — CBD Only Product
- INDIGO — 19:1 CBD:THC Cannabis Product
- BLUE — 6:1 CBD:THC Cannabis Product
- GREEN — 1:1 CBD:THC Cannabis Product
- YELLOW — 1:6 CBD:THC Cannabis Product
- RED — 1:19 CBD:THC Cannabis Product
- BLACK — THC Dominant Cannabis Product

https://minnesotamedicalsolutions.com/product-category

MMCP: Adverse effects reports

- Published data from *"Adverse Side Effect Overview: July 2015 – June 2017 Cohort"*
  - 15-25% enrolled reported a negative physical or mental side effect
    - 90% mild to moderate
    - 10% severe side effects : no clear association with age, medical condition, product
  - Most common: Dry mouth, drowsiness, fatigue, and mental clouding.
  - 1 serious adverse event (out of 7,294 patients enrolled)
    - Cannabis hyperemesis syndrome requiring hospitalization
- Vaping Associated Lung Injury
  - Tied to vitamin E acetate found in illicit THC
  - "People vaping medicine from Minnesota's medical cannabis program should talk with their health care provider about whether another delivery method may be right for them."

Minnesota Department of Health. Important Information and Warnings about Using Medical Cannabis. Oct 2019. Found at https://www.health.state.mn.us/people/cannabis/docs/patients/patientinfosheet.pdf

Symptom Management in Cancer Care

- Return to our cases
- Patient experiences with cannabis through MMCP

Symptom Management

- 63yo with locally advanced breast cancer on fulvestrant. C/o aching pain in back, hips, legs, knees since starting treatment. Similar symptoms in the past with Letrozole. No relief from tramadol or APAP. NSAIDs contraindicated.
  - Cannabis regimen:
    - Heather Oral suspension (5mg THC/5mg CBD per mL). 0.25mL - 2mL BID.
    - Heather Vape Oil (218mg THC/218mg CBD per 0.5mL). 1-4 puffs up to 5 times daily PRN.
    - Heather Topical Gel Cream. Apply 1-3 pumps to affected area up to 5 times daily PRN.
    - Tangerine Vape Oil (400mg THC/20mg CBD per 0.5mL). Inhale 1-4 puffs up to 5 times daily PRN.
  - Results:
    - "Surprisingly helpful for pain"
    - "Keeps me moving"

Symptom Management

- 48yo with squamous cell carcinoma of the right anterior tongue, s/p resection and adjuvant XRT, now with recurrent disease. On palliative chemo/immunotherapy. Experiencing severe mouth pain from tumor, anxiety, and nausea.
  - Cannabis regimen:
    - Red THC 25mg / 1mL oral solution, 0.5mL per Gtube qhs
    - Green 25mg THC + 25mg CBD / 1mL oral solution, 0.4mL per Gtube BID
  - RESULTS:
    - Modest benefit for pain. PRN oxycodone use decreased slightly
    - Beneficial for anxiety, sleep, and chemotherapy-induced nausea
    - Continued to lose significant weight

Symptom Management

- 55yo with metastatic lung cancer on docetaxel. Complaints of back pain related to vertebral mets, managed with opioids. Complaints of anxiety and severe insomnia.
  - Cannabis regimen:
    - Heather Oral Suspension (5mg THC 5mg CBD / 1 mL) 0.5-2mL po BID.
    - Tangerine Sublingual Spray 20 mg THC/1 mL). 1-4 sprays sublingually up to 5 times daily PRN
  - Results:
    - Did not help pain
    - Did not like psychoactive effects with daytime use, felt paranoid, made anxiety worse
    - Effective for sleep, less hangover effect than other sleep aids

Symptom Management

- 66yo with metastatic renal cell carcinoma on 3rd line cabozantinib. Longstanding CIPN with severe neuropathic pain in b/l feet. Pain not well controlled despite pregabalin, methadone, TENS, acupuncture.
- Cannabis regimen:
  - Red topical balm. 75mg THC per 1.5oz jar. Apply to affected area every 4 to 8 hours as needed.
- Results:
  - "It definitely helped some"
  - Did not decrease opioid needs or need for other medications / interventions

Symptom Management

- 65yo with metastatic pancreatic cancer on 3rd line pemigatinib. Suffers from chronic abdomen pain, bowel cramps, anorexia, and CIPN.
- Cannabis regimen
  - Red Tablets, 4.75mg THC/0.25mg CBD per tablet. 0.5-2 tablets every evening PRN.
  - Green Tablets, 2.5mg THC/2.5mg CBD per tablet. 1-2 tablets BID PRN.
  - Red Distillate prefilled vaporizer cartridge (380mg THC, 20mg CBD per cartridge). 1 – 2 puffs every 4 – 6 hours as needed.
- Results
  - Not effective for abdomen pain
  - Preferred hyoscyamine for bowel cramps
  - Did not feel difference in appetite but "helps me eat more"

Take homes:

- Cannabis can be beneficial for many cancer-related symptoms.
- "Natural" does not equal innocuous.
- More research needed. Evidence thus far low to moderate quality.
- MMCP provides some clinical expertise, guidance, and monitoring for patients.
- Cannabis is here to stay.

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