

Medical Marijuana Use

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Objectives

- Discuss the available evidence supporting the use of marijuana for weight gain, appetite stimulation, chemotherapy induced nausea and vomiting, and cancer related anorexia-cachexia syndrome (CACS)
- Describe various safety concerns with marijuana use in cancer patient population
- Discuss the limitations of marijuana use in cancer patients
- Provide recommendations for improving the efficacy and safety of marijuana use in cancer patients

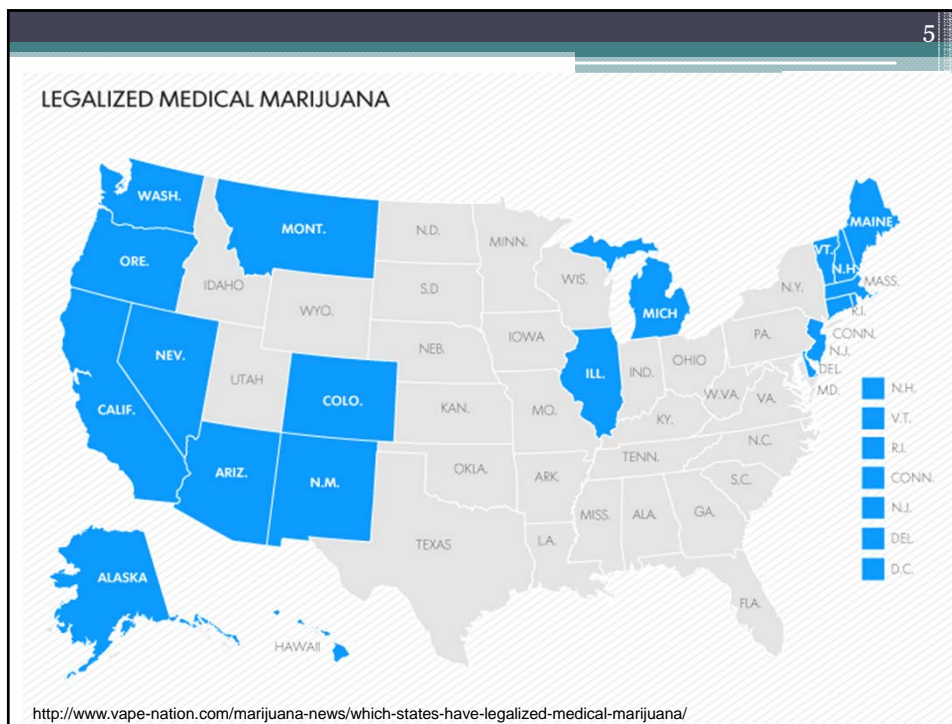
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Marijuana History^{1,2}

- 2737 BC in China
 - Chinese emperor prescribed marijuana
- 18th Century
 - British East India Company - Dr. William O'Shaughnessy
 - Used for pain of rheumatism and discomfort and nausea in cases of rabies, cholera and tetanus
- 20th Century
 - 1937: Marijuana Tax Act – made its use illegal
 - Marijuana classified as Schedule I controlled substance

Current Availability

- 21 US States and Canada have laws that allow marijuana use in some form
- 2 states (CO, WA) allow recreational use
- FDA approved
 - Nabilone (Cesamet)
 - Dronabinol (Marinol)
- Health Canada approved
 - Delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) (Sativex)



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Routes of Administration³

- **Inhalation:** cannabis cigarette (not FDA approved)
 - Peak level: 3-10 mins
 - Systemic bioavailability: 10-35%
 - Elimination: ~3-27 hrs
- **Ingestion (*PO*):** liquid concentrate, capsules (FDA approved), or food
 - Peak level: 60-120 mins
 - Hepatic first-pass metabolism
 - Systemic bioavailability: 2-14%
 - Elimination: ~20-30 hrs
- **Other:** PR, topical, SL

Possible Utility in "Medicine"

- Cannabinoids are a class of > 60 compounds derived from the plant *Cannabis sativa*
- Tetrahydrocannabinol (THC) is most widely studied
- Produces mood alterations, sedation, increased appetite, hallucinations and impairment of memory, coordination & executive function
- Analgesia occurs at higher concentrations
- Role in the palliation of neuropathic pain, muscle spasms & appetite (approved for the management of cancer/neuropathic pain in Canada)
- Adjunctive in managing nausea/vomiting associated with chemotherapy
- Potential direct anti-tumor and & anti-angiogenic properties

Cridge BJ, Rosengren RJ. Critical appraisal of the potential use of cannabinoids in cancer management. *Cancer Manag Res* 2013;5:301-13

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Pharmacology

- Primary components (cannabinoids)
 - **Delta-9-tetrahydrocannabinol (THC)**
 - Cannabinol (CBD)
- Cannabinoid (CB) receptors
 - CB1: mainly located in Central nervous system
 - CB2: mainly located in Peripheral nervous/immune systems

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Supporting Evidence

*FDA approved

Indication	Product	Patient	Study Type	Outcome(s)
Weight Gain ⁴	Dronabinol	AIDS-related anorexia	Prospective placebo controlled	At 6 weeks, improvements were seen versus placebo (5mg/day)
Appetite stimulation ⁴	Dronabinol*	AIDS-related anorexia	Prospective placebo controlled	At 6 weeks, significant improvement in appetite versus placebo (5mg/day)
CINV ^{5,6}	Dronabinol*	Cancer patients	Prospective active control (Compazine)	At doses 2.5 to 40mg/day improved emesis, especially with MOPP chemotherapy
	Nabilone *	Cancer patients receiving cisplatin or analogues	Prospective active control (dex + metoclopramide vs. nabilone + compazine)	Nabilone + compazine preferred carboplatin containing regimens
CACS ⁷	THC, Cannabis extract	Cancer patients	Prospective active control and placebo	At 6 weeks, no significant difference between treatments

CINV = Chemotherapy Induced Nausea/Vomiting, CACS = Cancer-related Anorexia-Cachexia Syndrome

Safety Concerns

Type	Product	Outcome
Cancer risk	Marijuana smoke	Increased risk of SCC of head/neck with marijuana use ⁸
		Increased risk in development of testicular germ cell tumor (TGCT) ⁹
Infection risk ¹⁰	Marijuana smoke	Aspergillosis associated with marijuana use after Stem Cell Transplant (SCT)
Physical Symptoms ¹¹	Marijuana smoke, or oral ingestion	Hypotension, tachycardia, dizziness, cardiac arrhythmia
Psychiatric Symptoms ¹¹	Marijuana smoke, or oral ingestion	Depression, paranoia, and hallucinations, addiction?

Megestrol versus Marijuana

Product	Mechanism	Availability	Benefits	Risks
Marijuana	Binds to CNS CB1 receptors	Currently available in 21 US states	<ul style="list-style-type: none"> • May reduce nausea/vomiting associated with high emetogenic chemotherapy • May improve appetite stimulation ? effects on weight gain 	<ul style="list-style-type: none"> • May cause intolerable side effects – ataxia, hallucinations, anxiety, disorientation • Not-FDA approved • Long-term risks not known
Megestrol	Progestin analogue with antiestrogenic properties	Available in all 50 US states	<ul style="list-style-type: none"> • FDA approved for anorexia, cachexia, or unexplained significant weight loss in patients with AIDS 	<ul style="list-style-type: none"> • Thromboembolic events may limit utility in cancer patients. Chronic use may lead to HPA suppression, diabetes

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Dronabinol, Megestrol, or Both?

- Prospective double-blind study of 469 cancer patients randomized to megestrol, dronabinol or the combination for cancer-associated anorexia
- Interventions
 - Megestrol 800mg/day liquid suspension+ placebo
 - Dronabinol 2.5mg twice daily + placebo
 - Megestrol 800mg/day liquid suspension + dronabinol 2.5mg twice daily
- Measurements
 - Baseline questionnaires for appetite and weight at baseline then weekly for 4 weeks then monthly (Functional Assessment of Anorexia/Cachexia Therapy (FAACT) instrument
 - Patients could remain in study as long as they and healthcare professional felt was beneficial

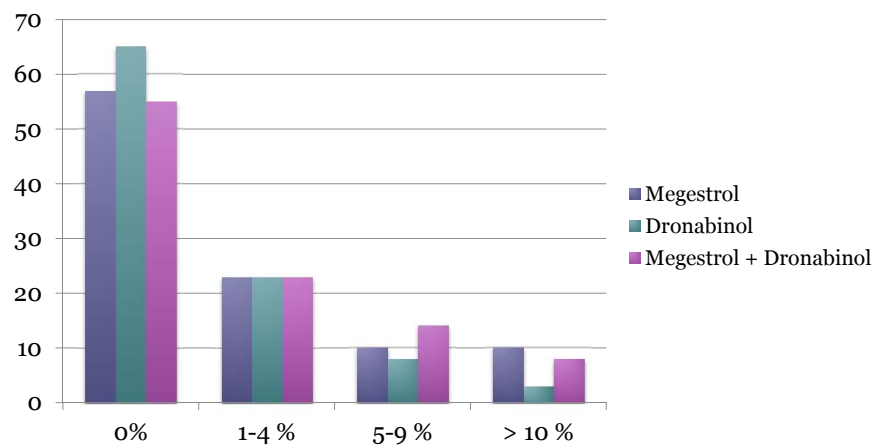
Jatoi A, Windschitl HE, Loprinzi CL, Sloan JA, et al. Dronabinol versus megestrol versus combination therapy for cancer-associated anorexia: A north central cancer treatment group study. *Journal of Clinical Oncology*. 20(2):2002:567-573

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Maximum Weight Gain from Baseline

*Percentage of patients in each treatment arm



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Dronabinol, Megestrol, or Both?

- Study conclusions
 - Megestrol superior to dronabinol in the treatment of cancer-associated anorexia
 - Addition of dronabinol adds no additional benefit
- Adverse events
 - Significantly more male patients in megestrol group reported impotence than other modalities (p=0.032)
 - No difference found in thromboembolic events or drop outs
- Additional thoughts
 - Should megestrol be reserved for females patients?

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Frequently Asked Questions

- Since marijuana is not FDA approved is it safe?
- Will it be covered by health insurance?
- Why do some patients prefer inhaled versus FDA approved oral (dronabinol)?
- What are common side effects that may occur?
- What about long term side effects?

Treatment Recommendations

- In refractory patients, with limited life expectancy, inhaled/oral marijuana should be considered
- Safety and purity concerns remain with non-approved products (inhaled, food, etc.)
- Caution with pre-existing psychiatric disorders and with immunosuppressive cancer treatment (i.e. stem cell transplant)
- Inhaled may be more helpful but potential more risk
- Combining marijuana with other approved agents may provide additional benefit

Conclusions

- Use of cannabinoids in cancer treatment or prevention unclear
- Studies suggest potential increased risk for cancer development (inhaled)
- Benefits are not without risks
- Oral marijuana ingestion may pose less risk
- Combination therapy may be superior to individual agents
- Caution is warranted with overlapping CNS active agents

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References

1. Marijuana. UXL Encyclopedia of Drugs and Addictive Substances. Bigelow BC, Thomson Gale; Detroit. Vol 4; 2006. Pgs. 491-514.
2. Stack P. A Brief History of Medical Marijuana. TimeHealth. Available at <http://www.time.com/time/health/article/0,8599,1931247,00.html>. Accessed April 10, 2014
3. Grotenhermen F. Pharmacokinetics and Pharmacodynamics of cannabinoids. Clin Pharmacokinet 2003; 42 (4):327-60
4. Marinol® prescribing information found at http://www.rxabbvie.com/pdf/marinol_PI.pdf Accessed April 20th, 2014
5. Beal JE, Olson R, Laubenstein L, Morales JO, et al. Dronabinol as a treatment for anorexia associated with weight loss in patients with AIDS. J Pain Symptom Manage. 1995 Feb;10(2):89-97.
6. Cunningham D, Bradley CJ, Forrest GJ, Hutcheon AW, et al. A randomized trial of oral nabilone and prochlorperazine compared to intravenous metoclopramide and dexamethasone in the treatment of nausea and vomiting induced by chemotherapy regimens containing cisplatin or cisplatin analogues. Eur J Cancer Clin Oncol. 1988 Apr;24(4):685-9.
7. Strasser F, Luftner D, Possinger K, Ernst G, et al. Comparison of orally administered cannabis extract and delta-9-tetrahydrocannabinol in treating patients with cancer-related anorexia-cachexia syndrome: a multicenter, phase III, randomized, double blind, placebo-controlled clinical trial from the Cannabis-In-Cachexia-Study-Group. J Clin Oncol 2006 Jul 20;24(21):3394-400.
8. Zhang ZF, Morgenstern H, Spitz MR, Tashkin DP, et al. Marijuana use and increased risk of squamous cell carcinoma of the head and neck. Cancer Epidemiol Biomarkers Prev. 1999;8:1071-1078
9. Lacson JCA, Carroll JD, Tuazon E, Castela EJ, Bernstein L, Cortessis VK. Population-based case-control study of recreational drug use and testis cancer risk confirms an association between marijuana use and nonseminoma risk. Cancer. 2012;118:5374-5383.
10. Hamadeh R, Ardehali A, Locksley RM, York MK. Fatal aspergillosis associated with smoking contaminated marijuana, in a marrow transplant recipient. Chest 1988 Aug;94(2):432-3.
11. American Cancer Society, Herbs, Vitamins and Minerals: Marijuana. Found at <http://www.cancer.org/treatment/treatmentsandsideeffects/complementaryandalternativemedicine/herbsvitaminsandminerals/marijuana> Accessed April 22, 2014

Questions?