

Medical Cannabinoids in Maryland: An Overview

Dr. Francisco Ward
Medical Director: Seton Pain & Rehabilitation Center
MEDCHI: BOT; Co-Chair Medical Economics Council, Chair Medical
Cannabis Task Force

Medical Marijuana: Legalized?

- House Bill 881 signed into law June 01, 14
- Create Commission that will be independent and sustained to license Academic Medical Centers, Growers
- Commission to regulate and oversee – can collect fees to monitor
- Indemnity: Safe haven created for those compliance with Commissions regulatory guidelines (TBA)
- Access to patients delayed several years

THE TWO FACES OF MC

- MARINOL – SYNTHETIC THC IN SESAME OIL: APPROVED BY FDA IN 1985 TO TREAT NAUSEA AND VOMITING; IN 1992 APPETITE STIMULATION ADDED.
- CANNABIDIOL: LEGAL FROM HEMP
- the FDA has not yet approved a marketing application for a drug product containing or derived from the whole cannabis plant. It has, however, **approved** three cannabinoid-based medicines derived from isolated synthetics: Marinol, Syndros, and Cesamet.

Marinol legally available in MD for years

Clin J Pain. 2013 Nov 25. [Epub ahead of print]

The Subjective **Psychoactive** Effects of Oral **Dronabinol** Studied in a Randomized, Controlled Crossover Clinical Trial For Pain.

Issa MA, Narang S, Jamison RN, Michna E, Edwards RR, Penetar DM, Wasan

AD.*Department of Anesthesiology, Perioperative, and Pain Medicine, Brigham and

Women's Hospital and Harvard Medical School, 75 Francis Street, Boston, MA 02115

US PATENT #: 6630507 B1
FILED APRIL 21, 1999

- **Cannabinoids as antioxidants and neuroprotectants**
- ASSIGNEE: US GOVERNMENT
- INVENTORS: [Aidan J. Hampson](#), [Julius Axelrod](#), [Maurizio Grimaldi](#)
- SPECIFICALLY LOOKS AT THC AND CANNABIDIOL

6630507 B1 - ABSTRACT

Cannabinoids have been found to have antioxidant properties. This new found property makes the cannabinoids useful in the treatment and prophylaxis of wide variety of oxidation associated diseases, such as ischemic, age-related, inflammatory and autoimmune diseases.

The cannabinoids are found to have particular application as neuroprotectants, for example in limiting neurological damage following ischemic insults, such as stroke and trauma, or in the treatment of neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease and HIV dementia. Nonpsychoactive cannabinoids, such as cannabidoil, are particularly advantageous to use because they avoid toxicity that is encountered with psychoactive cannabinoids at high doses useful in the method of the present invention.

Medical Use of Cannabinoids

- Chronic or debilitating disease or medical condition, or treatment, that causes:
 - Cachexia (THC)
 - Anorexia (THC)
 - Wasting Syndrome (THC+ CBD)
 - Severe or chronic pain (CBD +- THC)
 - Severe nausea (THC)
 - Seizures (experience with tremors) CBD
 - Severe or persistent muscle spasm (CBD, THC)
 - Glaucoma (no experience)
 - Post Traumatic Stress Disorder (PTSD) (CBD, Elixer THC)

EFFECTS OF THC

- Psychodelic (judgment/perception) impaired
- Anti emetic
- Appetite stimulant
- Anti-oxidant
- Euphoric
- Anxiety (tachycardia, MI)
- Memory loss / STM

EFFECTS OF “CBD”

- Non-Psychoactive and high safety margin
- Neuroprotectant / anti-oxidant (stroke, MS, neuropathy, dementia, TBI)
- Anti: inflammatory, autoimmune, aging
- Anti-anxiolytic, anti-osteoporotic
- Cannabidiol inhibits paclitaxel-induced neuropathic pain through 5-HT1A receptors
- Curbs addiction craving (opioids, tobacco, cannabis)

Marijuana Ingestion

- Classic combustion inhalation (pipe, “joint”, water pipe)
- Oral consumption (elixir, capsule)
- Transdermal (ointment / cream)
- Vaporizer (wax, oil, buds)
- Mixed with tobacco or alone
- Continuous, daily, bid, qh, prn

CBD Use

- Classic combustion inhalation (pipe, “joint”, water pipe – hemp buds)
- Oral consumption (elixir, oil, capsule)
- Transdermal (ointment / cream / roll on)
- Vaporizer
- Mixed in with food items
- Mixed in cosmetic items

First things first: Do no harm !

Schizophr Res. 2013 Nov 4: S0920-9964(13)00564-1. 10.1016/j.schres.2013

- Association between Tetrahydrocannabinol use, psychosis, and schizotypal personality disorder: Findings from the National Epidemiologic Survey on Alcohol and Related
- Conditions. Davis GP, Compton MT, Wang S, Levin FR, Blanco C.
- Department of Psychiatry, Division on Substance Abuse, Columbia University Medical Center/NYSPI, 1051 Riverside Drive, Unit 66, New York, NY 10032, United States

Marijuana: research highlights

- **Cell. 2013 Nov 21;155(5):1154-65. doi: 10.1016/j.cell.2013.10.042.**
- Δ⁹-THC-Caused Synaptic and Memory Impairments Are Mediated through COX-2 Signaling.
- Chen R, Zhang J, Fan N, Teng ZQ, Wu Y, Yang H, Tang YP, Sun H, Song Y, Chen C.
- Neuroscience Center of Excellence, School of Medicine, Louisiana State University, Health Sciences Center, New Orleans, LA 70112, USA.
- These results suggest that the applicability of MM would be broadened by concurrent inhibition of COX-2.

Do no harm continued

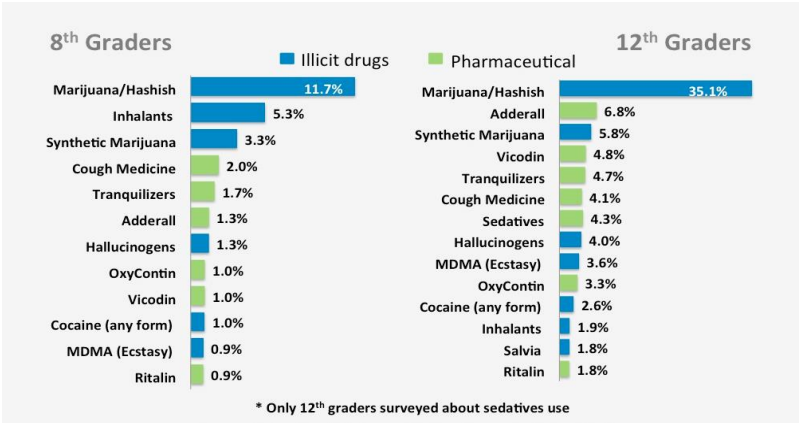
- **Driving impaired – Australia studies**
- Opioid sharing data: Most people will share!
- Immature brains / minds (already high use)
- Gateway drugs (tobacco, alcohol, cannabis)
- Consider psychosocial parameters
- Consider risk of misuse / abuse / diversion
- Myocardial infarcts, Pulmonary diseases
- Drug / drug interactions

% of Students Reporting Marijuana use in the past year -

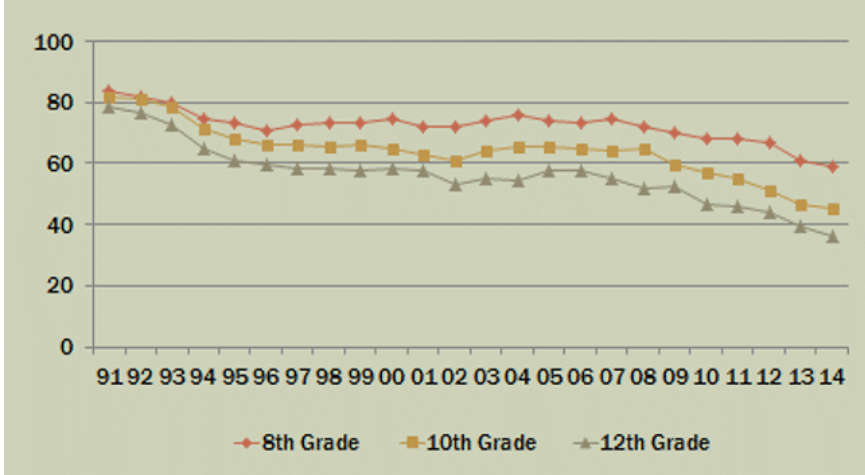
2017



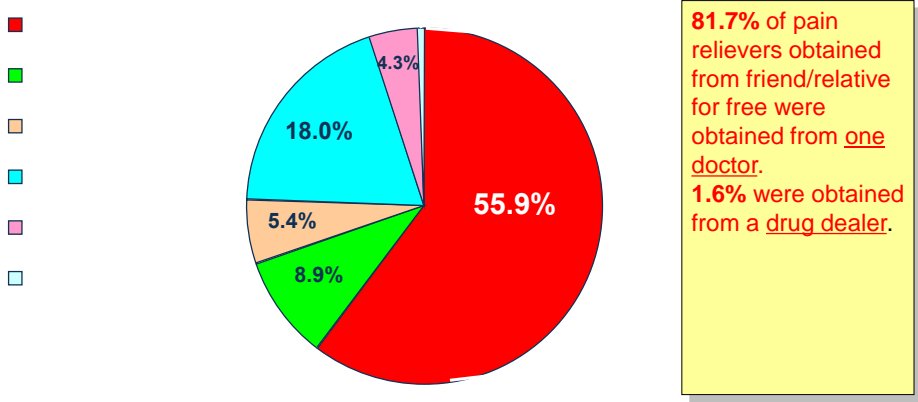
Past Year Drug Use 2014



% Perceiving great risk of smoking Marijuana regularly



Source Where Pain Relievers Were Obtained for Most Recent Non-medical Use among Past Year Users Aged 12 or Older: 2008



81.7% of pain relievers obtained from friend/relative for free were obtained from one doctor. 1.6% were obtained from a drug dealer.

Note: Totals may not sum to 100% because of rounding or because suppressed estimates are not shown. Source: NSDUH 2008

Legitimate medical purposes?

MM

- Pain (myofascial, muscle spasms, neuropathic, chronic)
- Wasting / Anorexia / Nausea / Cancer, AIDS (wasting, neuropathy), Multiple Sclerosis, **Anhedonia: Loss** of the capacity to experience **pleasure**. **Anhedonia** is a core clinical feature of depression, schizophrenia, and some other mental illnesses.
- Anxiety, insomnia, dysthymia,
- Severe childhood epilepsy, Tourettes, Neurodegenerative, Stroke, Trauma
- Crohn's Disease, Pancreatitis, Hep C
- Glaucoma (no personal experience)

What your patient can get !

- **Basic quantity limit of 30-day supply**
- 30-day supply defined as:
 - Up to 120 grams of usable cannabis or
 - 36 grams of Delta9-THC in a medical cannabis infused product
- Physician may authorize greater quantity on determination that those amounts inadequate to meet patient's medical needs

Product Parameters

- Every batch and lot must be analyzed and labeled with cannabinoid ingredients:
 - THC
 - THCA
 - CBD
 - CBDA
 - Certain terpenes
 - CBG
 - CBN

Written Certification

- Physician* shall terminate certification if
 - Patient meets exclusion criteria
 - Treatment no longer medically necessary
 - Adverse effects outweigh medical benefits
 - Evidence patient is diverting cannabis
- May terminate for abuse of any substance
- Notify Commission of termination in one (1) business day

Written Certification

- **Patient may seek renewal** not less than 30 calendar days after issuance
- Physician may renew if
 - Patient is still registered
 - Bona fide physician-patient relationship still exists
 - Patient meets inclusion criteria
 - Patient does not meet exclusion criteria
 - Medical benefits likely outweigh health risks
- Cannot renew without full in-person patient assessment within 365 days before renewal

Security - Safety

- **Control of cannabis**
 - Demanding inventory controls from “seed to sale”
 - Any diversion reported to Maryland State Police
 - All transactions recorded
 - Strict transportation security
 - Strict control in dispensaries
 - Vaults for cannabis
 - Exclusion of persons other than patients
 - Commission review of security plans

Security - Safety

- No one can obtain cannabis from a licensed dispensary without a written certification from a Maryland physician who is registered with the Commission
- Physician must be licensed with the Maryland Board of Physicians
- Physician license must be **“active, unrestricted, and in good standing”**

Security - Safety

- Patients and patient use of cannabis not excluded from offenses of:
 - Operating vehicles under the influence
 - Smoking cannabis in a motor vehicle
 - Smoking cannabis in a public place

Security - Safety

- Package Warnings:
 - Keep away from children
 - Illegal for any person to possess or consume the contents other than the patient
 - Illegal to transfer (other than caregiver to transfer to patient)
 - Poison Control Center telephone number
 - Telephone number to report adverse patient event

Quality

- Goal to produce medicine that is consistent, batch to batch, lot to lot
- Growers and processors encouraged to produce cannabis in a range of means and routes of administration
- Growers and processors to produce plant varieties and products containing high CBD levels, in addition to other plants & products

Quality

- Strict horticultural controls set forth in regulations
- Incoming materials must be segregated and inspected to prevent contamination
- Every batch and lot must be analyzed by a registered, accredited Independent Testing Laboratory, which provides a certificate of analysis for every batch and lot

Quality

- Every batch and lot must be analyzed and labeled with cannabinoid ingredients:
 - THC (consider defining max amount mg)
 - THCA
 - CBD (high safety margin); 15-100mg / day
 - CBDA
 - Certain terpenes
 - CBG
 - CBN

Quality

- **Prevention of contamination**
- Analysis must look for:
 - Heavy metals, mercury, lead, arsenic, cadmium
 - Foreign matter (insects, hair, other adulterants)
 - Microbiological impurity

Physician “provider” Registration

- To issue “written certifications” to qualifying patients, physician registers at Commission website
- No Registration fee
 - Registration valid for two years
 - No specialized or minimum additional training required
- Attest that Maryland medical license is Active, Unrestricted, and In Good Standing
- Is registered to prescribe Controlled Dangerous Substances in Maryland

Physician Registration

- On Web form physician affirms to follow practice standards:
- Will complete standard patient evaluation
 - History
 - Physical examination
 - Symptom review
 - Gather other pertinent information
- Will assess patient outcome, provide follow-up care, and collect/analyze data

Physician Registration

- Check off medical conditions for which physician might issue certifications for medical cannabis
- Identify other patient inclusion criteria
- Specify any reasons physician may deny issuing a certification to a patient

Physician Registration

- **Physicians encouraged to register to treat:**
- Chronic or debilitating disease or medical condition, or treatment, that causes:
 - Cachexia
 - Anorexia
 - Wasting Syndrome
 - Severe or chronic pain
 - Severe nausea
 - Seizures
 - Severe or persistent muscle spasm
 - Glaucoma
 - Post Traumatic Stress Disorder (PTSD)

Qualifying Patients

- Patient must register with Commission before physician can issue written certification
- Patient must
 - Live in Maryland; or
 - Be physically present in Maryland for the purpose of receiving medical care from a medical facility in Maryland
- If younger than 18 years old, parent or guardian must be caregiver
- No fee for patient unless patient desires ID card

Qualifying Patients

- **Physician and patient must have a “bona fide” relationship:**
- Treatment or counseling relationship
- Physician has
 - Reviewed patient’s relevant medical records
 - Completed an in-person assessment of the patient’s medical history and current medical condition
 - Created and maintained records of patient condition in accord with medically accepted standards

Qualifying Patients

Bona fide relationship (Continued)

- Reasonable expectation physician will
 - Monitor patient progress while using medical cannabis
 - Take medically indicated action
 - To provide follow-up care
 - Regarding efficacy of medical cannabis as treatment
 - Report any adverse event associated with use of medical cannabis

Written Certification

- **Issue by logging onto commission website**
 - Physician's name, license number, telephone number
 - Patient's name, DoB, address, county
 - Condition(s) requiring medical cannabis
 - Date patient is qualified
 - (Optional) Print out certification for patient use
 - Define 30 day supply (flower 120 g / THC 36 g)

Written Certification

- **Basic quantity limit of 30-day supply**
- 30-day supply defined as:
 - 120 grams of usable cannabis or
 - 36 grams of Delta9-THC in a medical cannabis infused product
- Physician may authorize greater quantity on determination that those amounts inadequate to meet patient's medical needs

Written Certification

- Physician shall terminate certification if
 - Patient meets exclusion criteria
 - Treatment no longer medically necessary
 - Adverse effects outweigh medical benefits
 - Evidence patient is diverting cannabis
- May terminate for abuse of any substance
- Notify Commission of termination in one (1) business day

Dispensaries “politics in play”

- Dispensaries to be located throughout the state:
 - Up to two per each of 47 state senatorial districts
 - Up to 15 associated with licensed growers (not counted in senatorial district allocation)

Dispensaries (per MMCC)

- **Extensive training of dispensary agents** in:
 - Pharmacology of cannabis
 - Potential therapeutic and adverse effects of cannabis
 - Dosage forms and pharmacodynamics
 - Potential drug interactions
 - Recognition of symptoms of substance use disorders and acute intoxication

At Dispensary

- Patient also must acknowledge:
 - It is illegal to transfer the cannabis to any person
 - Obtaining medical cannabis does not exempt patient from prosecution under federal law
 - Scientific research has not established the safety of the use of medical cannabis by pregnant women
 - Use of medical cannabis to treat a medical condition is not approved by the U.S. FDA

Elderly

- 98 y.o. with disinterest, loss of appetite and progressive social withdrawal.
- 96 y.o. woman with appetite loss, weight loss and chronic back pain. Marinol d/c paranoid
- 82 y.o. male with metastatic prostate CA, opioids, depression – responded well.

Middle Age

- 48 y.o. woman with chronic LBP ->fusion, infx, advanced OA-> TKA, diabetic neuropathy – developed pancreatic cancer > chemo / radx
- Nausea, weight loss, dysthymia, anxiety, pain
- Marinol plus Cannabidiol 50mg / .6 ml
- 60 y.o. woman with chronic knee pain, opioid dependent for pain control. CBD vape for anxiety successful to d/c benzo

Young Adult

- 16 y.o. with chronic facial pain felt to be neuropathic (secondary to extensive computer screen time), PTSD
- Trial of CBD with initial AE reported at low doses.
- I didn't provide Rx for Marinol – too off label

- 25 y.o. with history of chronic opioid addiction currently in methadone program, chronic marijuana smoker, personality disorder came in with father seeking medical cannabis access.
 - Discussed CBD, Avoidance of THC initially or in elixir non vape preparation, father would have to be “caretaker” given my discomfort with allowing patient access to dispensary with my recommendation

- 21 working electrician apprentice, lives with girl friend – chronic myofascial pain and difficulty relaxing – non tolerant of Rx to treat

Disclaimer

- Patients and patient use of cannabis not excluded from offenses of:
 - Operating vehicles under the influence
 - Smoking cannabis in a motor vehicle
 - Smoking cannabis in a public place
- Package Warnings:
 - Keep away from children
 - Illegal for any person to possess or consume the contents other than the patient
 - Illegal to transfer (other than caregiver to transfer to patient)
 - Telephone number to report adverse patient event

Physician Protection

- In 2014, Congress enacted a law barring the U.S. Department of Justice from interfering in the implementation of state medical cannabis laws (Section 538 of Continuing Appropriations Act of 2016, P.L. 114-53, sec. 103, 129 Stat. 502 (2015))
- Re-enacted on Dec. 18, 2015 for 2016 (Sec. 542 of P.L. 114-113)
- In October 2015, interpreting that law, a Federal Court blocked U.S. Department of Justice from trying to stop a California dispensary from operating (*U.S. v. Marin Alliance for Medical Marijuana*, U.S.D.C., No. Dist. Cal., Case No. C-98-00086-CRB, Oct. 19, 2015)

Protect Your License: Continued

Initiation of an appropriate trial of opioid/MM therapy with or without adjunctive medications. Treatment plans should begin with a “trial” of therapy when controlled substances are contemplated. This allows a stable therapeutic platform from which to base treatment changes.

Reassess the pain score / treatment success and level of function. Regular reassessment of the patient, combined with corroborating information from family or other knowledgeable third parties, will help to document the reasons to continue or modify the current therapeutic trial.

Regularly assess the “4 A’s” of pain medicine. Routine assessment of analgesia, activity, adverse effects and aberrant behaviors will help to direct therapy and support the selection of pharmacologic options.

Periodically review the pain diagnosis and any comorbid conditions, including substance use disorders. Underlying illnesses and diagnoses evolve and as they do, the focus of treatment may need to change as well. If an addictive disorder presentation develops, the treatment should include the addictive disorder being addressed.

Document careful and complete initial evaluations and each follow-up visit. This is clinically and legally indicated and in the best interest of all parties.

Protect your House

- Policy and Procedures Manual (include physician training – CME)
- Clinical guidelines for what conditions you will treat and how you will monitor progress. EBM & Appropriate Consultations.
- Informed consent (legal, potential for harm etc), and compliance contract. Length of treatment & Exit plan?
- Risk assessment: Low – Medium - High for misuse, abuse, diversion.
- Medical records: comprehensive initial H&P (PMH, Social Hx, Mental health, Vocational, Family HX, ROS, labs, imaging, Assessment with DDX, Plan, Monitoring – Universal Precautions

Questions