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Sang Choi, R.Ph
Etain Health, LLC
(914) 437 – 7898
schoi@etainhealth.com

Disclosure:

Downstate Dispensary Manager
Etain Health, LLC



AGENDA

- The Plant
- Pharmacology of Cannabinoids
 - Cancer and Cannabinoids
 - NYS Regulations
 - Approved Uses
 - Available Products
 - Questions



GENERAL & HISTORICAL BACKGROUND

- The cannabis plant (*Cannabis sativa*, *C. indica* and *C. ruderalis*) is an annual flowering herb
- It has more than 60 unique compounds (~480 total)
- Δ -9-tetrahydrocannabinol (THC) is psychoactive
- Cannabidiol (CBD) is “not”; may ameliorate some THC effects
- Earliest recorded use of medicinal cannabis (“ma”) dates back to 2900BC – Emperor Fu Hsi

CANNABINOID SYSTEM: CLINICAL RELEVANCE

- Endogenous cannabinoid system (ECS) is a signalling system that includes cannabinoid receptors and endocannabinoids
- Core functions of the ECS have been described as “relax, eat, sleep, forget and protect.” ECS regulates neuronal excitability and inflammation in pain circuits and cascades.
- Cannabinoid receptors: CB1 and CB2.
- CB1-found in brain, CB2-found in immune cells where they play an important role in regulating immune function and inflammation.

- Affects opioid, 5HT, NMDA receptors-relevant in pain modulation.
- Effects – TNF, ILs, NO, oxygen radicals, anti-oxidant

Homeostatic super-modulatory system

CANNABINOIDS AND TERPENES

- Cannabinoids:
 - Endocannabinoids, phyto-cannabinoids, and synthetic cannabinoids
- Most Therapeutic Interest:
 - Endocannabinoids
 - Anandamide (AEA) and 2-Arachidonoylglycerol (2-AG)
 - Phytocannabinoids
 - Δ^9 -Tetrahydrocannabinol (THC) and Cannabidiol (CBD)
- Terpenes:
 - β -caryophyllene, myrcene, limonene, and pinene

CB1 Receptors

- Primarily expressed in the Central Nervous System
- Modulate neurotransmitter release
 - GABA, Glutamate, Dopamine and Serotonin
- Medical application
 - Stress, anxiety and PTSD
 - Depression
 - Insomnia
 - Inflammation
 - Analgesia

CB2 Receptors

- Expressed in immune tissues and intestines
- Inhibit cytokine release
- Medical application
 - Analgesia
 - Inflammation
 - Nausea and appetite

Anandamide (AEA) and 2-Arachidonoylglycerol (2-AG)

- AEA
 - “Bliss molecule”
 - Binds to CB1 and CB2 receptors
- 2-AG
 - Binds to CB1 and CB2 receptors

THC

(Δ 9-tetrahydrocannabinol)

- Interacts with both CB1 and CB2 receptors
- Psychoactive component of the plant
- Medical application
 - Analgesic
 - Inflammation
 - Appetite stimulant
 - Anxiolytic
 - Antiemetic

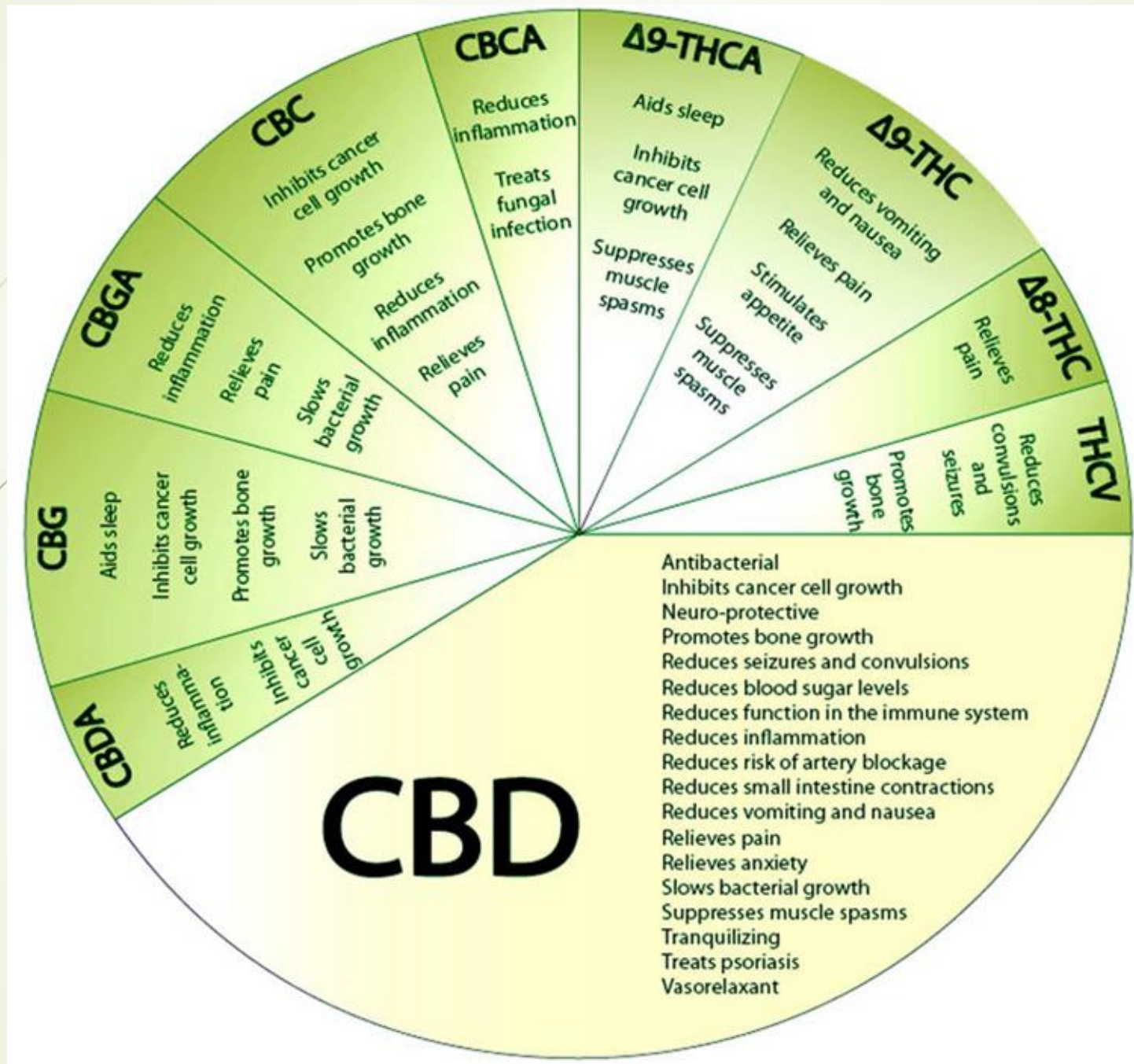
CBD

(Cannabidiol)

- Non-psychoactive
- Doesn't interact with CB1 or CB2 receptors but Inhibits Fatty Acid Amide Hydrolase (FAAH)
- Medical application
 - Inflammation
 - Muscle spasms
 - Anxiolytic
 - Anticonvulsant
 - Antiemetic
 - Analgesia
- CBD does not bind directly to cannabinoid receptors. Instead, CBD works by inhibiting an enzyme called FAAH, which is responsible for the breakdown of anandamide. When FAAH is inhibited, it cannot break down anandamide at its normal rate, making anandamide more readily available in the brain.

Cannabinoids

- ▶ Cannabinoids are present in the stalk, leaves, flowers, seeds and resin (hash) secreted by the female plant.
- ▶ During smoking, 50% of the THC is absorbed in the mainstream smoke via the lungs, enters rapidly the blood stream and reaches the brain in minutes.
- ▶ After oral intake, blood concentration reaches 25-30% of those obtained by smoking the same dose, onset is delayed (0.5-2 hours) but the duration is prolonged.



Pharm, con't

- ▶ Once absorbed, THC And Other Cannabinoids Are Rapidly Distributed To All Other Tissues, Accumulate In Fatty Tissues, Reaching Peak Concentration In 4 To 5 Days.
- ▶ Elimination Half Life Is 7 Days And Completely Eliminated In 30 Days.
- ▶ Metabolism is In the liver. A major metabolite, 11-hydroxy THC Is more potent than THC and may be responsible for some of the effects of cannabis. More than 20 other metabolites are known.
- ▶ The metabolites are excreted in the gut (65%) and urine (25%)
- ▶ Poor relationship between urine and plasma levels and degree of THC intoxication

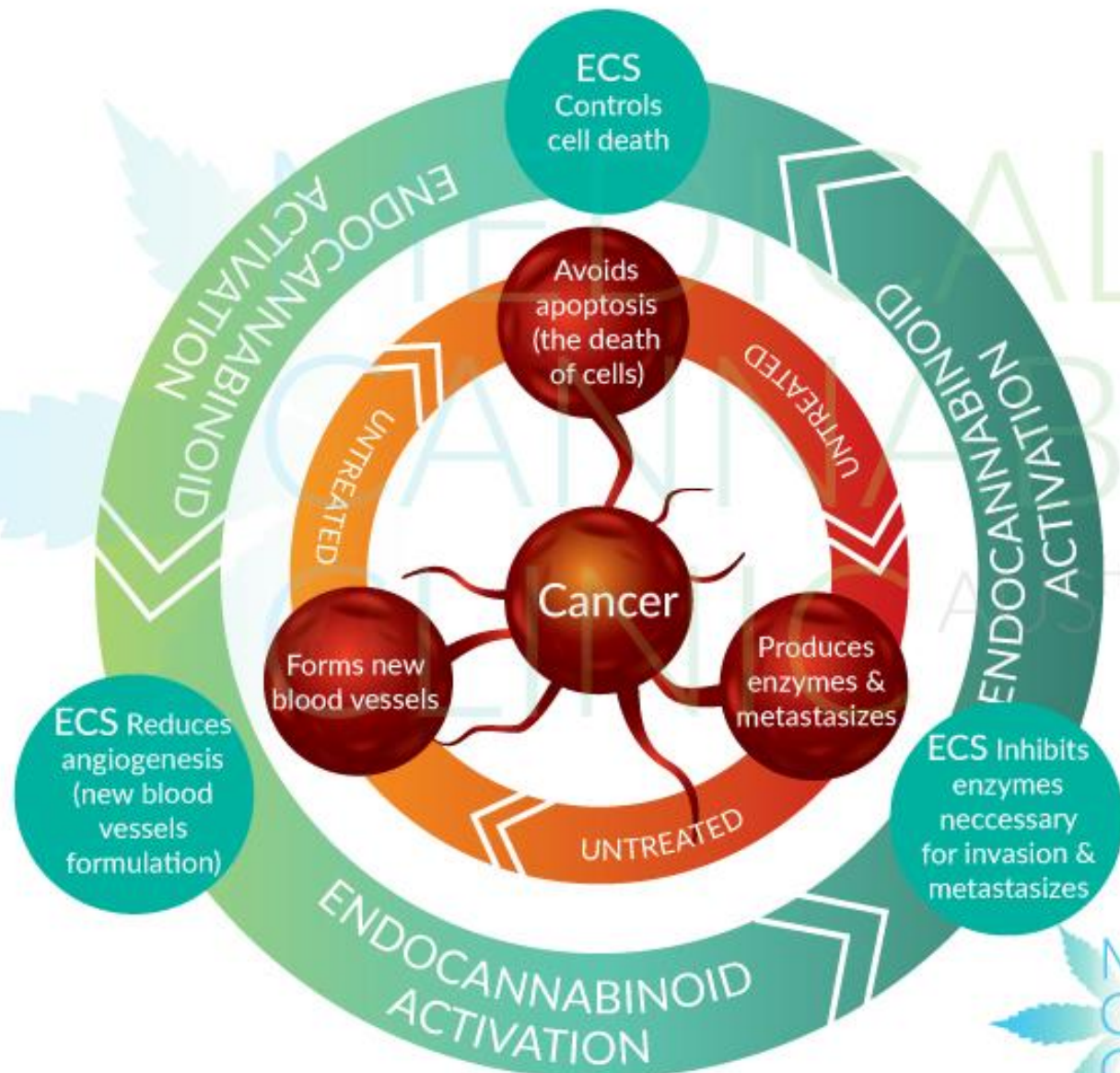
Cancer and Cannabis

- A 2014 poll conducted by Medscape and WebMD found that more than three-quarters of U.S. physicians think cannabis provides real therapeutic benefits. And those working with cancer patients were the strongest supporters: 82 percent of oncologists agreed that cannabis should be offered as a treatment option.
- It is estimated that one in eight women will develop breast cancer.
- Breast cancer is tricky to treat because there are few biomarkers that signal when someone has the disease, and many patients show or develop resistance to current therapies.
- Moreover, several specific types of breast cancer respond poorly to modern treatment. These difficulties underscore the importance of exploring new treatments for breast cancer.

Appraising the "entourage effect": Antitumor action of a pure cannabinoid versus a botanical drug preparation in preclinical models of breast cancer.

Blasco-Benito S¹, Seijo-Vila M², Caro-Villalobos M², Tundidor I², Andradas C³, García-Taboada E³, Wade J⁴, Smith S⁴, Guzmán M⁵, Pérez-Gómez E², Gordon M⁴, Sánchez C⁶.

- Extensive preclinical research has demonstrated that [cannabinoids](#), the active ingredients of [Cannabis sativa](#), trigger antitumor responses in different models of cancer. Most of these studies have been conducted with pure compounds, mainly Δ^9 -tetrahydrocannabinol (THC).
- Compared the antitumor efficacy of pure THC with that of a botanical drug preparation (BDP). The BDP was more potent than pure THC in producing antitumor responses in cell culture and animal models of ER+/PR+, HER2+ and [triple-negative breast cancer](#)
- While pure THC acted by activating cannabinoid CB2 receptors and generating [reactive oxygen species](#), the BDP modulated different targets and mechanisms of action. The combination of cannabinoids with estrogen receptor- or HER2-targeted therapies (tamoxifen and [lapatinib](#), respectively) or with [cisplatin](#), produced additive antiproliferative responses in cell cultures
- Together, our results suggest that standardized cannabis drug preparations, rather than pure cannabinoids, could be considered as part of the therapeutic armamentarium to manage breast cancer.



ECS = Endocannabinoid System

www.medicalcannabisclinic.com.au

MEDICAL
CANNABIS
CLINIC AUSTRALIA

Cancer and Cannabis Continued..

- Two biomarkers frequently used to diagnose breast cancer are hormonal receptors (the estrogen receptor and progesterone receptor) and the HER2 oncogene (a gene which can transform a normal cell into a tumor cell). But a more aggressive malignancy, known as “triple-negative breast cancer,” doesn’t express hormonal receptors or the HER2 oncogene. No targeted therapy exists for triple-negative breast cancer, so patients are treated with harsh chemotherapies that indiscriminately kill proliferating cells, whether cancerous or not.
- These three types of cancer – hormone-sensitive, HER2, and triple-negative – were used as models for “Appraising the entourage effect.”
- In all models of breast cancer studied, *in vitro* as well as *in vivo*, the whole plant extract was significantly more effective at producing anticancer effects than single-molecule THC. These results were largely consistent for type of cancer and type of model. Researchers tested the compounds in cell cultures (petri dishes) and in rodent models (mice).

Cannabidiol Induces Programmed Cell Death in Breast Cancer Cells by Coordinating the Cross-Talk Between Apoptosis and Autophagy.

CBD induces concentration-dependent cell death in breast cancer cell lines in a receptor-independent manner

- The sensitivity of breast cancer cells to anticancer agents depends in part on estrogen receptor status (18). We analyzed the effects of CBD on breast cancer cells by using both estrogen receptor+ve (MCF-7 and ZR-75-1) and estrogen receptor-ve (MDA-MB-231 and SK-BR-3) cell lines with an MTS viability assay. Cells were treated with CBD (0–10 $\mu\text{mol/L}$) for 24 hours. CBD significantly decreased cell viability of both estrogen receptor+ve and estrogen receptor-ve cell lines in a concentration-dependent manner
- This study showed that CBD induced both apoptosis and autophagy-induced death in breast cancer cells.
- In summary, we showed that CBD, a plant-derived cannabinoid, preferentially kills breast cancer cells by inducing ER stress, inhibiting mTOR signaling, enhancing ROS generation, and mediating a complex balance between autophagy and mitochondria-mediated apoptosis in MDA-MB-231 breast cancer cells. These findings support the continued exploration of CBD as an alternative agent for breast cancer treatment.



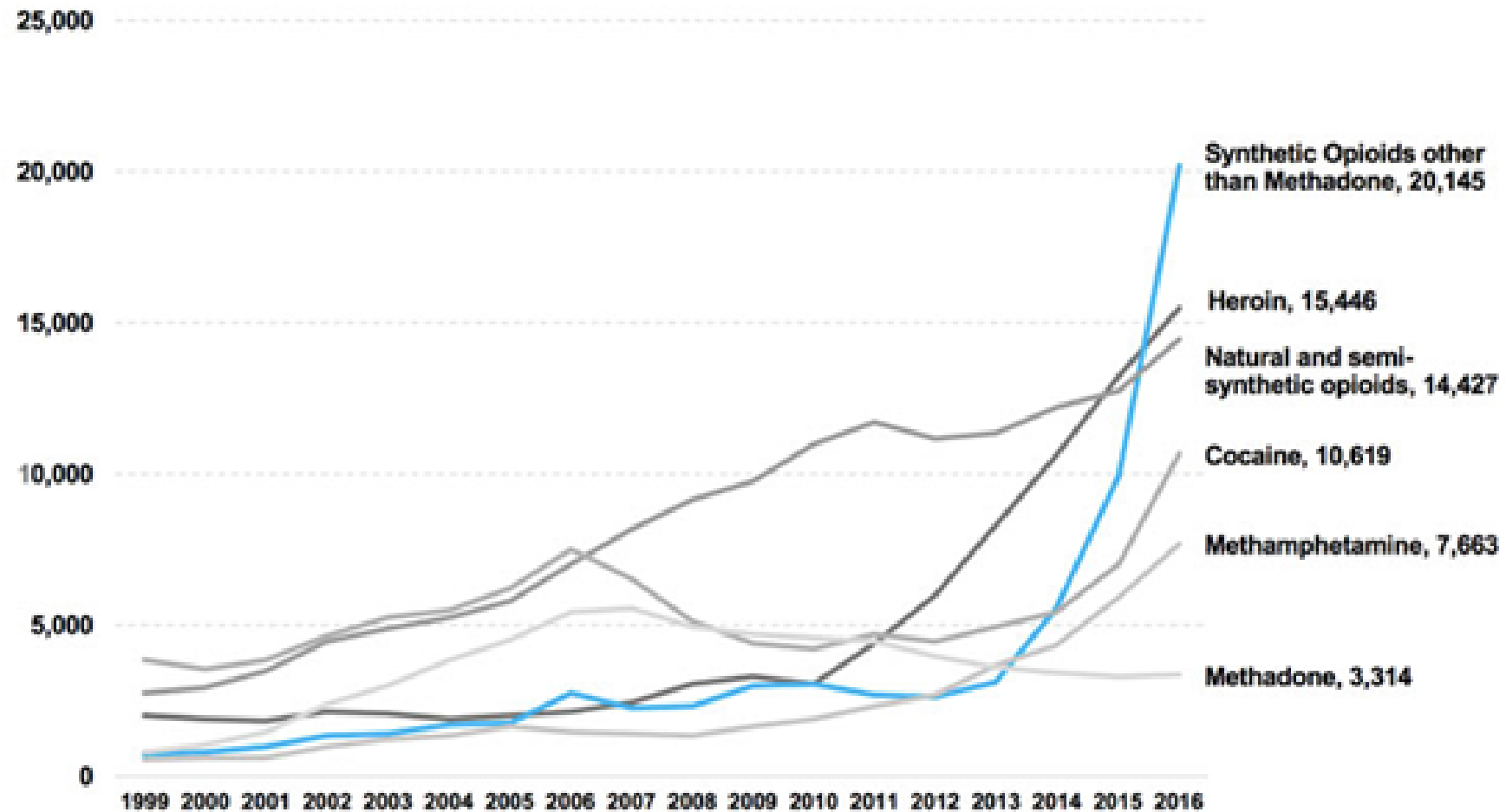
Cannabis and Opioids

- ▶ SINCE 1999 – PRESCRIPTION OPIOIDS SOLD IN THE USA HAS QUADRUPLED – REPORTED PAIN IS THE SAME – NO CHANGE
- ▶ SINCE 1999 - DEATH FROM PRESCRIPTION OPIOIDS HAS QUADRUPLED
- ▶ STATES WITH MEDICAL CANNABIS HAVE LOWER OPIOID OVERDOSE RATES BY 25 – 30%

Center for Disease Control. Injury Prevention and Control: Opioid Overdose. www.cdc.gov/drugoverdose/epidemic

Bachhuber MA et al. Medical Cannabis Laws and Opioid analgesic Overdose Mortality in the US 1999-2010 JAMA 2014;174:1668-1673

Drugs Involved in U.S. Overdose Deaths, 2000 to 2016



Drugs Involved in U.S. Overdose Deaths - Among the more than 64,000 drug overdose deaths estimated in 2016, the sharpest increase occurred among deaths related to fentanyl and fentanyl analogs (synthetic opioids) with over 20,000 overdose deaths. Source: CDC WONDER

ANNUAL DEATHS

Tobacco	435,000
Poor Diet/Exercise	365,000
Alcohol	85,000
Prescription Drugs	32,000
Motor Vehicle Crashes	26,347
Homicide	20,308
Aspirin	7,600
Peanuts	100
Marijuana	0



MARIJUANA: Safer Than Peanuts!



Other Tidbits

- ▶ 44% reduction in opioid pain medication usage in chronic pain patients utilizing medical cannabis*
- ▶ Patients using medical marijuana to control chronic pain reported a 64 percent reduction in their use of more traditional prescription pain medications known as opioids, a University of Michigan study finds**

*[Clin J Pain](#). 2016 Feb 17

The Effect of Medicinal Cannabis on Pain and Quality of Life Outcomes in Chronic Pain: A Prospective Open-label Study.

[Haroutounian S¹](#), [Ratz Y](#), [Ginosar Y](#), [Furmanov K](#), [Saifi F](#), [Meidan R](#), [Davidson E](#).

****Medical Cannabis Use Is Associated With Decreased Opiate Medication Use in a Retrospective Cross-Sectional Survey of Patients With Chronic Pain**, Kevin F. Boehnke, Evangelos Litinas, Daniel J. Clauw

MEDICAL CANNABIS CAUTIONS

- Cannabis is generally well-tolerated, and serious adverse effects, including increased risk of cardiovascular events, are rare.
- Adverse changes in cognitive function, especially executive function, may occur, especially with fetal or adolescent exposure.
- Cannabis should be avoided by adolescents, pregnant women, and nursing mothers.
- Cannabis should be avoided in those at risk of psychosis.
- Many studies show driving impairment, but on a much lower scale than alcohol.
- Drug interactions are a concern.
 - Cannabis enhances CNS depressant effects when combined with alcohol, barbiturates and benzodiazepines, but probably not opioids
 - THC induces CYP1A2, and can reduce levels of drugs metabolized by CYP1A2.
 - CBD inhibits CYP3A4 and CYP2D6, and can increase levels of drugs metabolized by these isoenzymes. CYP3A4 metabolizes about a quarter of all drugs.


Contraindications

- ▶ THC has been shown to have an association with aggravating or precipitating a psychotic episode in persons with a susceptibility to such effects *
- ▶ THC can cause vasodilation, lower blood pressure and increase cardiac demand; smoking cannabis has been associated with a four-fold increase in the risk of myocardial infarction in the hour following cannabis smoking. Therefore, cannabis should be avoided in patients with **active unstable ischemic heart disease****
- ▶ Cannabis use is also contraindicated in **women who are pregnant or breastfeeding**, as cannabis use has been associated with premature labor and low birth weight***

*Moore TH, Zammit S, Lingford-Hughes A, Barnes TR, Jones PB, Burke M, Lewis G. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet*. 2007 Jul 28; 370(9584): 319-28

**Mittleman MA, Lewis RA, Maclure M, Sherwood JB, Muller JE. Triggering myocardial infarction by marijuana. *Circulation*. 2001 Jun 12; 103(23): 2805-9

***Park B, McPartland JM, Glass M. Cannabis, cannabinoids and reproduction. *Prostaglandins Leukot Essent Fatty Acids*. 2004 Feb; 70(2): 189-97



Physiologic and Adverse Effects


- ▶ Psychological
 - ▶ Euphoria, anxiety, or paranoia
 - ▶ Drowsiness or somnolence
- ▶ Cognitive and psychomotor*
 - ▶ Impairment of cognitive function
 - ▶ Impairment of complex motor skills
 - ▶ Impairment of working memory, executive functions & information processing
- ▶ Perception and sensory
 - ▶ Hallucinations, time distortion and intensification of sensory experiences

*<http://www.hc-sc.gc.ca/dhp-mps/marihuana/med/infoprof-eng.php> -Health Canada website



Cannabis Use Disorder

- Acute intoxication- euphoria, sense of calm, increased awareness of sensory experience, craving foods, enhanced perceptions, increased salience of stimuli, impaired shifting of focus.
- Neurocognition- deficits in processing speed, attention, working memory, decision making, motivation, time perception, reality testing (Atkinson, 2015)
- Risk of anxiety with cannabis intoxication- female, personality traits, infrequent use, high dose, high THC/low CBD varieties, history previous reaction, basal anxiety states (Crippa, 2009)
- Cannabis withdrawal associated with lower ECS tone mediated by release of stress hormones and reduced dopamine levels
- Increasing risk of rebound anxiety upon cessation and fostering cannabis dependence.



Safety of Medical Cannabis

- ▶ There is no record in the extensive medical literature describing a proven, documented cannabis-induced fatality.
- ▶ Marijuana cannot induce a lethal response as a result of drug related toxicity.
- ▶ Massive use of THC may lead to Medical Cannabis Hyperemesis Syndrome
- ▶ Reported deaths were due to concomitant use of other drugs.
- ▶ In contrast, in 2015, over 52,404 annual deaths have been reported due to drug overdose, 20,101 overdose deaths due to prescription pain relievers and 12,990 overdose deaths due to heroin (ASAM data)
- ▶ JAMA report (2014): In states where medical marijuana is legal, there is a 25% reduction in opioid related deaths.

DRUG INTERACTIONS

1. SSRIs

2. TCAs

3. NSAIDs

4. Barbiturates

5. BZDPs

6. β -Blockers

7. ETOH

8. Opioids

9. Theophylline

1. THC can increase the effect of fluoxetine.

2. THC can increase the side effects of amitriptyline (i.e. tachycardia, hypertension and sedation).

3. Indomethacin and acetylsalicylic acid (aspirin) reduce the effects of THC.

4. These increase the depressive effects of THC and also increase tachycardia associated with THC consumption.

5. These drugs can increase depression of the nervous system and also of the respiratory system.

6. These reduce tachycardia associated with THC.

7. This can increase nervous system deterioration.

8. Increased sedation and analgesia.

9. Cannabinoids increase theophylline catabolism. A dosage increase is thus required in such cases.

10. Atropine and scopolamine can increase tachycardia produced by THC.

11. THC interacts with disulfiram causing an unpleasant reaction. Combination should be avoided.

QUALIFYING CONDITIONS

- Prescribers must be qualified to treat ≥ 1 of the following :

Cancer

HIV/AIDS

Epilepsy

Neuropathies

Amyotrophic lateral sclerosis (ALS)

Huntington's disease

Parkinson's disease

Multiple sclerosis (MS)

Inflammatory bowel disease (IBD)

Damage to spinal cord nervous tissue with intractable spasticity

Chronic Pain

PTSD, Opioid Reduction

SECONDARY QUALIFYING CONDITIONS

- One or more of the conditions must include:
 1. Severe or chronic pain causing a substantial limitation of function
 2. Severe nausea
 3. Seizures
 4. Cachexia or wasting syndrome
 5. Severe or persistent muscle spasms

**The Commissioner may add
or remove approved
conditions and disease
accompanying symptoms**

ENDOCANNABINOID
IMBALANCE

Migraine
Fibromyalgia
Post-traumatic stress disorder (PTSD)
Bipolar disease
Autism
Epilepsy
Neurodegenerative disease
(Russo 2004)



Dolce

Primary Effects:

Seizure Prevention

Anti-anxiety

Muscle relaxation

Anti-inflammatory

Antiemetic

Mezzo

2 CBD : 1 THC

High CBD and moderate THC

Mild chance of impairment

Used to treat

Muscle spasms

Nausea

Appetite loss

Inflammation

Anxiety

PTSD

Seizures

Pain

Balance

Primary Effects:

Anti-anxiety

Muscle relaxation

Anti-inflammatory

Antiemetic

Pain relief

Appetite stimulation

Norte

Primary Effects:

Pain relief

Appetite stimulation

Muscle relaxation

Antiemetic

eTain

Dosage Forms

- Oral Capsule:
 - Onset: 1-2 hours duration 6-8 hours.
- Tincture:
 - Onset: 30 minutes; duration 4-6 hours.
- Oral Spray:
 - Onset: 30 minutes; duration 4-6 hours.
- Vaporization:
 - Onset: Immediate to 5 minutes; duration 2-4 hours.



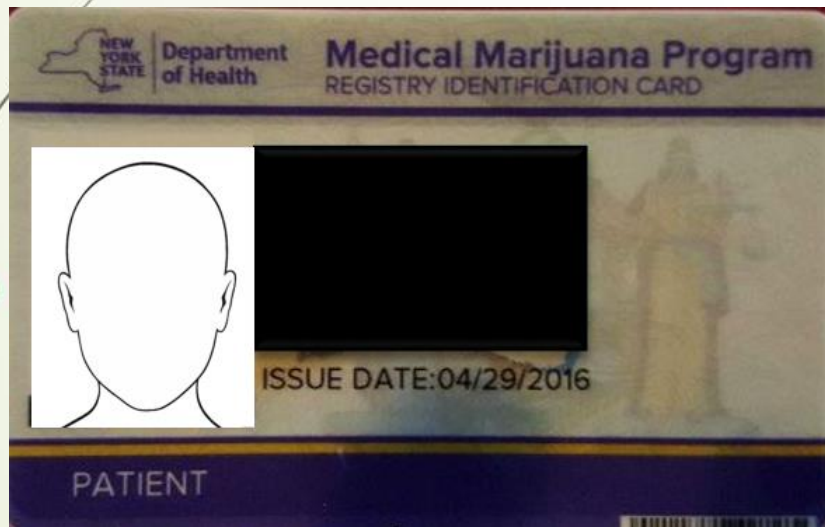
WHO CAN CERTIFY MMJ IN NEW YORK ?

MDS NPS PAS

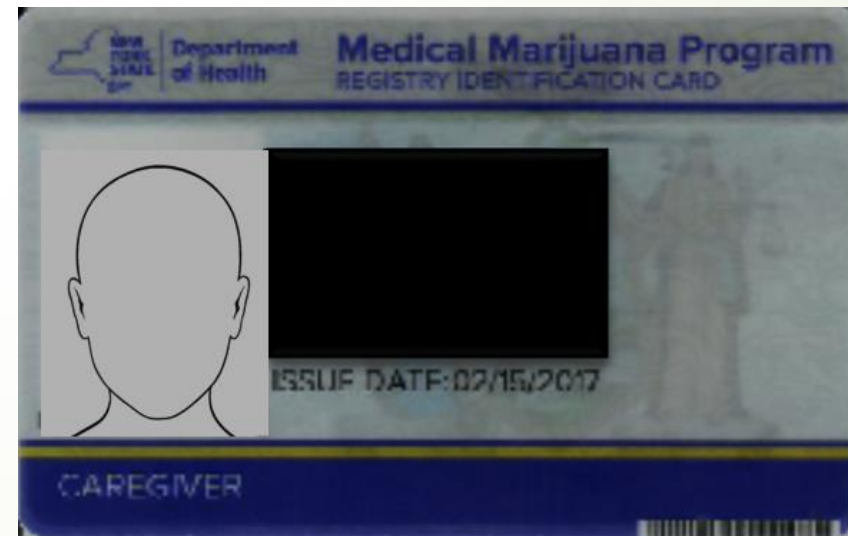
- Must complete a four hour DOH Approved online course.
- Register with the NYS MMJ Program.
- Determine whether the patient meets the requirements for certification.
 - Cancer, HIV/AIDS, ALS, Parkinson's Disease, MS, Spinal Cord Nerve Injury with Intractable Spasticity, Epilepsy, IBD, Neuropathy, Huntington Disease, Chronic Pain, PTSD

WHO HAS ACCESS TO MMJ
DISPENSARIES IN NEW YORK?

Patients & Caregivers with a valid New York MMJ Registry Card, Photo ID, and Certification



Patient Card



Caregiver Card

SAMPLE CERTIFICATION FORM



Department of Health

**Medical Marijuana Program
Patient Certification #:**

Practitioner Information	
First Name:	Last Name:
Business Address:	
City: NEW YORK	State: NY ZIP Code:
Phone:	Email:
NYS Physician License Number:	DEA Registration Number:
Patient Information	
First Name:	Last Name:
Address:	
City:	State: NY ZIP Code:
Phone:	Email:
Severe Debilitating Condition(s): Parkinson's disease	Associated Condition(s) or Symptom(s): Severe or persistent muscle spasms Severe or chronic pain resulting in substantial limitation of function
Temporary Resident? No	Incapable of Consent? No
Dosing Recommendations	
1	Product: No Preference Form/Administration Method: /Oromucosal/Sublingual THC/CBD Ratio: Low:High Concentration: Low THC High CBD Recommendations/Limitations: None Start Date: 11/07/2016 End Date: 11/07/2017
2	Product: No Preference Form/Administration Method: /Oromucosal/Sublingual THC/CBD Ratio: High:Low Concentration: High THC Low CBD Recommendations/Limitations: None Start Date: 11/07/2016 End Date: 11/07/2017
3	Product: No Preference Form/Administration Method: /Oromucosal/Sublingual THC/CBD Ratio: 1:1 Concentration: Equal THC: CBD Recommendations/Limitations: None Start Date: 11/07/2016 End Date: 11/07/2017
Patient Certification Issue Date: 11/07/2016 Patient Certification Expiration Date: 11/07/2017	

As the practitioner named above, I attest to the following:

- I am a licensed practitioner currently in good standing in New York State, and possess an active Drug Enforcement Administration registration;
- I am currently registered with the New York State Department of Health to issue this certification;
- I am caring for this patient in relation to the serious and associated conditions listed above;
- By training and/or experience, I am qualified to treat the serious condition(s) listed above;
- In my professional opinion and based on my review of past treatments, the patient named above is likely to receive therapeutic or palliative benefit from the primary or adjunctive treatment with medical marijuana for the serious condition(s) listed above;
- I have explained the potential risks and benefits of the use of medical marijuana to the above-named qualifying patient and/or the qualifying patient's parent or legal guardian, if applicable, and have documented in the patient's medical record that such explanation has been provided; and
- The above-named qualifying patient and/or the qualifying patient's parent or legal guardian, if applicable, have provided informed consent.

Practitioner Signature: _____ Date: _____

FALSE STATEMENTS MADE HEREIN ARE PUNISHABLE AS A CLASS A MISDEMEANOR PURSUANT TO PENAL LAW § 210.45. ISSUANCE OF A CERTIFICATION WHEN (I) THE RECIPIENT HAS NO MEDICAL NEED FOR IT, OR (II) IT IS FOR A PURPOSE OTHER THAN THOSE DEFINED IN PHL § 3360 (7) IS PUNISHABLE AS A CLASS E FELONY PURSUANT TO PENAL LAW § 179.10.

This certification, containing the practitioner's handwritten signature, must be provided to the patient and a copy of this signed certification must be included in the patient's medical record. To register, patients will need to login to <https://my.ny.gov/>, click the "Health Applications" icon, and then click the "Medical Marijuana Data Management System" link. Patients who do not have a NY.gov account will need to visit <https://my.ny.gov/> and click on the "Don't have an Account?" button to create a personal NY.gov ID first.

1	Product: No Preference	Form/Administration Method: /Oromucosal/Sublingual
	THC/CBD Ratio: Low:High	Concentration: Low THC High CBD
	Recommendations/Limitations: None	
	Start Date: 11/07/2016	End Date: 11/07/2017
2	Product: No Preference	Form/Administration Method: /Oromucosal/Sublingual
	THC/CBD Ratio: High:Low	Concentration: High THC Low CBD
	Recommendations/Limitations: None	
	Start Date: 11/07/2016	End Date: 11/07/2017
3	Product: No Preference	Form/Administration Method: /Oromucosal/Sublingual
	THC/CBD Ratio: 1:1	Concentration: Equal THC: CBD
	Recommendations/Limitations: None	
	Start Date: 11/07/2016	End Date: 11/07/2017
Start Date: 11/07/2016		End Date: 11/07/2017
Patient Certification Issue Date: 11/07/2016		Patient Certification Expiration Date: 11/07/2017

CONTINUED...

- The Certification expires in one year unless the patient is terminally ill. At which point the Certifying Practitioner must recertify the patient.
- The patient may designate up to 2 caregivers.
 - Caregivers can be a parent, family member, legal guardian, or appropriate guardian (non-family)
 - Caregivers can have up to 5 certified patients at any time.

PRODUCTS OFFERED: CONTINUED...

- Note that brands vary by dispensary.
- 2 Ratios are REQUIRED as per regulation.
- A high CBD:Low THC and 1:1 THC/CBD
 - Currently, dispensaries may have up to 5 brands.
 - All Medical Marijuana Products produced are tested by a lab licensed by the DEA and approved for analysis of Medical Marijuana.
 - The ROs MUST conform to GAPs (Good Agricultural Practices)

New Products

- Powder for reconstitution
- Dried plant material for vaporization
- Lozenge
- Topicals
- Suppositories
- Chewable tablets

Etain

Locations

New York City

Located at **142 East 39th St, New York, NY 10016**, positioned to provide easy access to medical marijuana products for the patients in Manhattan and surrounding boroughs and is conveniently located 3 blocks from Grand Central Station.

Kingston

Located at **445 State Route 28 Kingston, NY 12401**, Etain's Kingston dispensary is set to serve patients from Kingston, Saugerties, and surrounding areas.

Syracuse

Located at **2140 Erie Blvd E, Syracuse, NY 13224**, Etain's Syracuse dispensary is positioned to conveniently serve patients from Syracuse, Utica, and the surrounding areas.

Yonkers

Located at **55 Main Street, Yonkers, NY 10701**, Etain's Yonkers dispensary is conveniently located two blocks from the Yonkers Hudson Line Metro North Stop and is situated to serve patients in Yonkers and any patients who pass through on their way to and from New York City.



Thank You



Any Questions?