

# Medical Marijuana: High Expectations

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**What we know**  
**What we don't**

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# Speaker Disclosures

Dr. Ally is on the faculty of the University of Nebraska College of Pharmacy Department of Pharmacy Practice

She is the Senior Partner of BBfN,  
a health and safety consulting company

She has no conflict in regard to medical use of  
cannabinoids



# “Off Label Use”

In order to assure that there are no problems with the accreditation of this program nor problems caused for the accrediting body here goes:

There are 3 approved products containing one or more chemicals found in the marijuana plant.

Epidiolex (cannabidiol)

Marinol

Cesamet

We will NOT discuss uses for these 3 approved products beyond the labeling. We will discuss cannabinoids not found in drug products currently approved by the FDA. The concept of being “off label” for these products is illogical, as there is no label to follow.

Got it?



# A note from the CE clinical reviewers ...

*“Medical marijuana is considered a controversial topic in CME. When a CME activity includes information about an approach to diagnosis or treatment that is not generally accepted, it is allowable to facilitate debate and discussion about the approach, but it is not allowable to advocate for the test or treatment, or teach clinicians how or when to use it.”*

Trust me, I am not advocating for any test - - in fact, I'm going to slam one.

I do advocate for rational pharmacotherapy – there are clearly 3 FDA approved drugs with approved labels – the rest is presented to facilitate debate and discussion.

I asked for a resource or reference to verify that this is “not generally accepted”



# Learning Objectives

At the completion of this professional continuing education program, the alert attendee should be able to:

Define medical cannabis using the AACP standard definition. I figure the drug experts can define drugs, right?

Cite claimed and verified medical uses for cannabinoids

Discuss administration of cannabinoids

Formulate policy opinions on medical cannabinoids\*\*





**When you are asked to form an opinion, you are not asked to be “right.” There is no “right”**

**The opinions that impress me are those that are supported by evidence and science rather than by emotion and half truths. If it helps to understand me better, I believe:**

- 1. The world is round**
- 2. Vaccines are effective at preventing disease**
- 3. Humans are contributing to changes in weather and climate**

**Impressing me is neither right nor wrong.**





# The 3 FDA Approved Drugs

They have approved labels and approved labeling and proof of

1. Purity
2. Safety
3. Efficacy



# Epidiolex (cannabidiol)

FDA Approved Indications:

Treatment of Seizures associated with Lennox-Gastaut Syndrome

Treatment of Seizures associated with Dravet Syndrome

to be used in children 2 years of age or older



# Research at the University of Nebraska Medical Center

CBD was supplied by GW Pharma  
I didn't participate in the study

Tested patients from age 1 to 60 with treatment resistant seizures



# Marinol (dronabinol)

## FDA Approved Indications

Anorexia associated with weight loss in patients with AIDS

Nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments

For use in adults only



# Cesamet (nabilone)

Indication: {This is verbatim from the nabilone labeling}

Cesamet capsules are indicated for the treatment of the nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.

This restriction is required because a substantial proportion of any group of patients treated with Cesamet can be expected to experience disturbing psychotomimetic reactions not observed with other antiemetic agents.

Because of its potential to alter the mental state, Cesamet is intended for use under circumstances that permit close supervision of the patient by a responsible individual particularly during initial use of Cesamet and during dose adjustments.

Cesamet capsules are not intended to be used on as needed basis or as a first antiemetic product prescribed for a patient.



# Medical cannabinoids

What is “**medical**”

Does it mean proven?

Does it mean safe?

Does it mean appropriate?



# What does medical mean?

Of or relating to medical treatment –  
Merriam Webster

From the Latin *mederi* – to remedy or to heal

From the Greek *medesthai* – to be mindful of

Of or relating to the treatment of diseases and injuries –  
English Language Learners Dictionary



# Medical cannabinoids

## Medical Marijuana or Medical Use of Marijuana

is that use of marijuana that is specifically defined as medical in the laws of the state or jurisdiction where the cannabis is being used.



AACP Non-medical marijuana task force 2014-2015: Chairman Ally Dering-Anderson  
Members: Laura Borgelt, Frank Caligiuri, Michaelene Kedzierski, Julie Kissack, Cynthia Koh-Knox,  
Sarah Melton, Michael O'Neil, Don Stanford





# Law or Science?

Using this definition, the use of “medical” cannabis is a legal distinction, not a scientific one.

The difference between an over-the-counter product and a prescription is a legal distinction, not always a scientific one.



# Pharmacology

Cannabinoids activate cannabinoid receptors –

Endogenous cannabinoids:

- anandamide

- 2-arachidonylglycerol

Exogenous cannabinoids:

- tetrahydrocannabinol (THC)

- cannabidiol (CBD)

- cannabinol (CBN)



# 3 Exogenous cannabinoids with extensive research

THC – tetrahydrocannabinol

Stimulates primarily cannabinoid receptor type 1 (CB<sub>1</sub>)  
psychoactive

CBN – cannabinol

Stimulates primarily CB<sub>2</sub>

CBD – cannabidiol

Very limited psychoactivity, if any



# 3 cannabinoids with research, how many are there?

CBC	(Cannabichromene)
CBCV	(Cannabichromevarin)
CBD	(Cannabidiol)
CBDA	(Cannabidiol Acid)
CBDV	(Cannabidivarin)
CBE	(Cannabielsoin)
CBG	(Cannabigerol)
CBGM	(Cannabigerol Monomethyl Ether)
CBGV	(Cannabigerovarin)
CBL	(Cannabicyclol)
CBN	(Cannabinol)
CBT	(Cannabicitran)
CBV	(Cannabivarin)
THC	(Tetrahydrocannabinol)
THCA	(Tetrahydrocannabinolic acid)
THCV	(Tetrahydrocannabivarin)

**Probably more than 100 when we get done  
discovering new strains of the marijuana plant**



# Drug Testing ...

Most “marijuana” tests actually test for TCH

Can CBD use cause you to test POSITIVE?

Maybe....

Depends on the CBD – Epidiolex - no

Joe’s Bait & Tackle CBD - maybe



# Proof of efficacy for cannabinoids:

Weight gain in wasting syndromes or cachexia

Decreased intra-ocular pressure (glaucoma)

Pain control

- nerve based

- stress based

- cancer based

Relief in myo-spastic conditions

Decreased nausea and vomiting

Seizure control

Control of anxiety and social phobias



# Weight Gain in wasting syndromes and cachexia

Megace (megestrol)

diarrhea

hyperglycemia

insomnia

anorexia/dyspepsia

Anabolic Steroids – Winstrol® (stanozolol)

Controlled Substance in Schedule III

WADA banned – ask Ben Johnson

gynecomastia

hepatic failure

acne

aggression

Cannabinoids – THC causes “the munchies”

WADA banned

Controlled Substance

psychoactive

habit forming?

**No clearly superior product**



# Glaucoma

Beta blockers - Timoptic®

Adrenergic agonists - Alphagan®

Carbonic Anhydrase inhibitors - Diamox®

Cholinergics – Isopto Carpine®

Prostaglandin analogs – Xalatan®

Cannabinoids – mostly a THC phenomenon  
CBD may increase intraocular pressure<sup>1</sup>

**Traditional pharmaceuticals work better than cannabinoids**

Sally Miller, Laura Daily, Emma Leishman, Heather Bradshaw,  
Alex Straiker. **Δ9-Tetrahydrocannabinol and Cannabidiol  
Differentially Regulate Intraocular Pressure.** *Investigative  
Ophthalmology & Visual Science*, 2018; 59 (15): 5904  
DOI: [10.1167/iovs.18-24838](https://doi.org/10.1167/iovs.18-24838)





# Glaucoma and the VA

Marijuana is grown at the University of Mississippi

Technically the Federal Government (therefore you and me) owns the copyright/patent on the strain of cannabis grown at the Coy W. Waller Laboratory Complex in Oxford, Mississippi. (Approximately 4% THC)

There is still a living patient in Omaha

Here's a weird thing - - the VA suspended the study, but didn't kick anyone out, so using cannabis on VA property is illegal, but they are still shipping it to a few homes...



# Dosing Challenge - Note

The Ole Miss cannabis is ~4% THC

There is a strain “Bruce Banner #3” that is ~28% THC



# Pain Control

The greatest concern for legislators: medical use for pain

Pain cannot be measured

Pain can be faked

Pain patients are already “addicts”

Every legislator, like every other adult, knows a malingerer



# Options for Pain Control

Opiates – marijuana does not claim to treat pain perception, at least not yet

NSAIDs – research shows that CBD may be anti-inflammatory  
Gabapentin / Pregabalin – CBD certainly does the same thing for nerve pain

P.R.I.C.E. – perhaps these are more likely if the patient is calm, relaxed, unafraid



# Myospastic Conditions

CBD has direct nerve effect

May relieve muscle spasms and the pain that goes with them

Key to the research in Multiple Sclerosis

**NOTE: CBD Oil is NOT  
legal everywhere**



# Anxiety & Social Phobias

Cannabidiol is likely the active agent in this therapy

Improved mood

Improved sense of well-being

Improved sleep (CBN)

Decreased anxiety have been reported in studies

**Do not be led astray  
CBD Oil is NOT legal  
everywhere!**



# Study Published January 2019

Potential of THC to slow or remove amyloid plaques & reduce neural inflammation

Older research from 2006, Scripps showed that there may be an inhibition of a neural enzyme.

Schubert is now showing a reduction in inflammatory response – slowing or eliminating nerve damage



# Claims with no proof

No proof means no research

If a claim has been **PROVEN** false, it is not included in this program





# Other Claims ...

**No attempt was made to be all inclusive**

- \* Cancer – direct antineoplastic
- \* Anti-viral activity
- \* Lung protection
  - Anti-inflammatory effects
- \* Creativity and Artistic Stimulation



# FDA Issues Warning

You may not claim that any component of marijuana “treats or cures” cancer without the proof to support these claims.

“Substances that contain components of marijuana will be treated like any other products that make unproven claims to shrink cancer tumors. We don’t let companies market products that deliberately prey on sick people with baseless claims that their substance can shrink or cure cancer and we’re not going to look the other way on enforcing these principles when it comes to marijuana-containing products,” said FDA Commissioner Scott Gottlieb, M.D. “There are a growing number of effective therapies for many cancers. When people are allowed to illegally market agents that deliver no established benefit they may steer patients away from products that have proven, anti-tumor effects that could extend lives.”



# Are cannabinoids antiviral?

No research to show that they are.

BUT – they have been shown to improve sleep (CBD and CBN) in acute viral infections, sleeplessness is a common complaint.

!!! If it helps with sleeplessness, it causes drowsiness !!!



# Lung Protection??

Many marijuana opponents point to the “dangers of smoking”  
These have NOT been shown in marijuana smokers

That led to a theory that smoking may actually be lung protective.  
Studies are on-going focusing on the anti-inflammatory components of marijuana.

No definitive results at this time.



# Improved artistic or musical ability?

**Impossible to prove or disprove**

Art and Music are emotional media, there are no “quality criteria” on which to measure them.



# How to “use” medical cannabinoids

This becomes a societal question, as well as a medical question

There are very few drugs when I use them, that I put you at risk, simply by being in my presence

**\*\*\* From the CE Reviewers: It is okay to discuss the routes of administration, but please do not discuss specific doses or dose titration.**

**\*\*\* From Dr. Ally: I don't think they're talking about FDA approved drugs, but they didn't say that**



# Dosing / Administering

Smoked (toked, if you're old enough to remember the term)

Vaporized

Oral – traditional dosage form or food

Sublingual



# Inhaled - Vaped

For quick onset of drug action

Perhaps for muscle spasms

Maybe for sleep

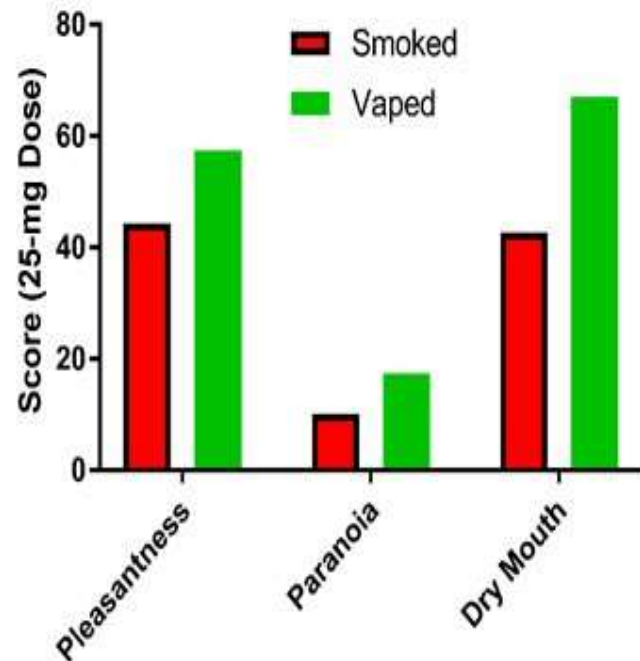
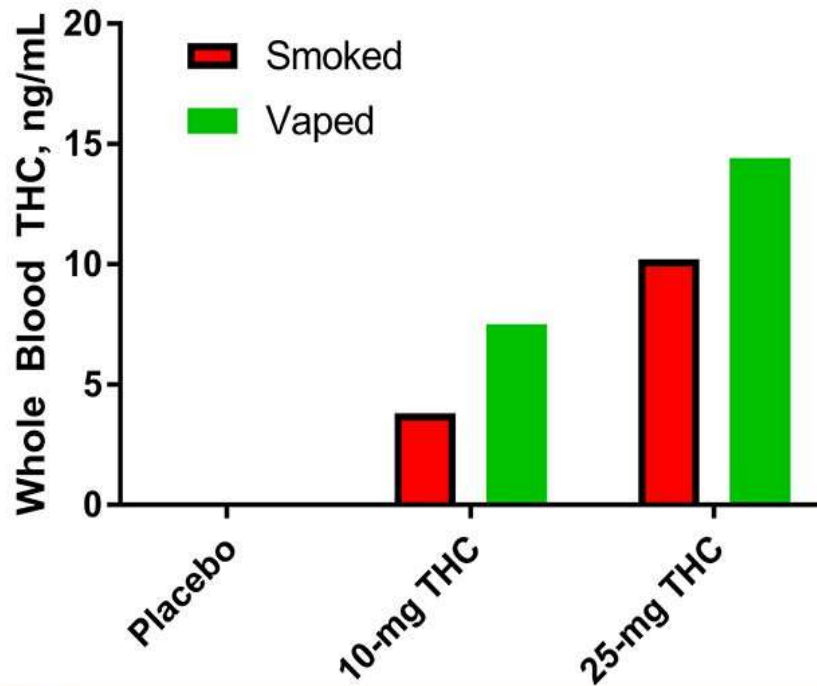
Might work for migraine

You are still going to exhale





# Johns Hopkins Study



# Multiple Lessons from the study

Vaping provides much higher blood levels

Blood levels correlate to the sensations induced by THC

These were people who hadn't smoked marijuana in the last year - - the drug is more powerful than it was when you tried it in college

Spindle TR, Cone EJ, Schlienz NJ, et al. Acute effects of smoked and vaporized cannabis in healthy adults who infrequently use cannabis: a crossover trial. *JAMA Netw Open*. 2018;1(7):e184841. doi:10.1001/jamanetworkopen.2018.4841.



# Oral – also called edibles

Slowest onset

Lasts the longest

Appropriate for chronic disease management

**Drugs should NEVER look like candy - - - not ever!**

**Does any state restrict this??**



# Sub-lingual



# Selecting a route

Inhaled is the fastest onset and the shortest duration

THC is metabolized differently when introduced via the gut

Colorado “Stop Sign” proposal

Sublingual misses 1<sup>st</sup> pass effect without smoking



# Big Business

The Altria Group just bought 45% of the Cronos Group  
The Cronos Group is a provider of marijuana for  
medical and recreational use in Canada.

Consumers are expected to spend \$57 BILLION  
worldwide on LEGAL cannabis by 2027 with  
\$47.3 BILLION being spent in North America.



# Business requires business acumen ...

Oregon:

In the past 2 years, 150 cannabis businesses have closed

Farmers grew 3x more marijuana than the consumer demanded

1lb of marijuana in 2014 sold for \$2,000  
today it's <\$600



# 11 January 2019

FDA Commissioner Scott Gottlieb:

“Additionally, it’s unlawful ... to introduce food containing added CBD or THC into interstate commerce, or to market CBD or THC products as, or in, dietary supplements, regardless of whether the substances are hemp derived,”

He said that this restriction exists because both CBD and THC are active ingredients in FDA-approved drugs and were subject to clinical investigations before they were marketed as foods or supplements.





# Understand why we ask

All drugs have side effects

All drugs have drug to drug interactions

This isn't judgmental, it's simply information gathering



**Bring on the Questions**

# A shortened bibliography is attached

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5. Structure-Activity Relationship of Cannabis Derived Compounds for the Treatment of Neuronal Activity-Related Diseases; Prandi C, Blangetti M, Namdar D, et al; Molecules; 25 June 2018; 1-17.
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23. Cannabidiol modulates serotonergic transmission and reverses both allodynia and anxiety-like behavior in a model of neuropathic pain; De Gregorio D, McLaughlin RJ, Posa L, et al; PAIN; 10.1097; 2018
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36. The Dispensary of the United States of America, 9<sup>th</sup>; edited by George B Wood and Franklin Bache; Lippincott; 1851

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