Medical Marijuana: High Expectations
Dr. Ally Dering-Anderson, RP
University of Nebraska College of Pharmacy

Speaker Contact Information
Dr. Ally Dering-Anderson, RP
Clinical Associate Professor of Pharmacy
University of Nebraska College of Pharmacy

986145 Medical Center
College of Pharmacy
Department of Pharmacy Practice
Omaha, NE 68198-6145

Ally.DeringAnderson@UNMC.edu
Check the Date!!

Please note:
This program was presented on 11 June 2019

Law regarding cannabinoids change rapidly

There may be an earth shaking new research paper published on 12 June 2019

“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.
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.

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 evidence 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

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:
  - anadnamide
  - 2-arachidonylglycerol

Exogenous cannabinoids:
  - Found in the plant known as marijuana
  - Hemp is marijuana
3 Exogenous cannabinoids with extensive research

THC – tetrahydrocannabinol
Stimulates primarily cannabinoid receptor type 1 (CB₁)
psychoactive
CBN – cannabinol
Stimulates primarily CB₂
CBD – cannabidiol
Very limited psychoactivity, if any

3 cannabinoids with research, how many are there?

CBC (Cannabichromene)
CBCV (Cannabichromevarin)
CBD (Cannabidiol)
CBDA (Cannabidiolic 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 (Tetrahydrocannabinavin)

Probably more than 100 when we get done discovering new strains of the marijuana plant
Drug Testing …

Most "marijuana" tests actually test for **TCH**
Nobody tests positive for "poppy" they test positive for
heroin or morphine or some other opiate.
Nobody tests positive for this plant either.

Can CBD use cause you to test POSITIVE?

Maybe….
Depends on the CBD – Epidiolex - no
Joe’s Bait & Tackle CBD - maybe

Evidence 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

Glucoma

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 pressure¹

Traditional pharmaceuticals work better than cannabinoids

¹ Sally Miller, Laura Daily, Emma Leishman, Heather Bradshaw, Alex Striker. Δ9-Tetrahydrocannabinol and Cannabidiol Differentially Regulate Intraocular Pressure. Investigative Ophthalmology & Visual Science, 2018; 59 (15): 5904 DOI: 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

---

**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

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
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 evidence to support them

No evidence means no research

I don’t care what worked for your sister’s neighbor’s cousin’s dog-walker.

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
* Creativity and Artistic Stimulation

FDA Issues Warning
You may not claim that any component of marijuana “treats or cures” cancer without the evidence 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.

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 measure

Art & 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
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
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


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 1st 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.

Associated Press; New York; 7 December 2018

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 Jan 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.

3 Questions to ask yourself

1. Do I have an opinion concerning medical use of cannabinoids?

2. Did I learn something new about “marijuana” during this program? What did I learn?

3. Can I name 3 diseases or conditions where there is evidence that cannabinoids are useful?
Recommended or additional readings

These are not all peer reviewed, nor are they all scientifically rigorous, but they do represent the variety of points of view on the issue of medical cannabis. All citations used during the lecture part of this presentation are from robust sources unless otherwise noted.

GW Pharmaceuticals Continues to be the best cannabis play: [http://seekingalpha.com/article/3426716-gw-pharmaceuticals-continues-to-be-the-best-cannabis-play?ifp=0]

Places with more marijuana dispensaries have more marijuana-related hospitalizations: [http://www.sciencedaily.com/releases/2015/08/150810110907.htm?utm_source=feedburner&utm_medium=email&utm_campaign=Feed%3A+sciencedaily%2Fmind_brain%2Fmarijuana+%28Marijuana+News+-+ScienceDaily%29]

Shakespeare may have been a cannabis user: [http://www.cnbc.com/2015/08/09/shakespeare-may-have-been-a-cannabis-user-report.html]

Using cannabis in your teens is not linked to depression or psychotic symptoms, study says: [http://metro.co.uk/2015/08/06/using-cannabis-in-your-teens-is-not-linked-to-depression-or-psychotic-symptoms-study-says-5329603/]

Juicing Cannabis for Cancer: [https://greenrushinvestors.com/juicing-cannabis/]


Cannabinoids in the treatment of glaucoma: Jarvinen, T; Pate, DW; Laine K; Pharmacology & Therapeutics; Vol 95, Issue 2; August 2002; pp 203-220; doi 10.1016/S0163-7257(02)00259-0

references continue

S. Mercadante; Oral morphine consumption in Italy and Sicily; 2004


When Weed is The Cure: A Doctor’s Case for Medical Marijuana: [http://www.npr.org/sections/health-shots/2015/07/31/422876970/when-weed-is-the-cure-a-doctor-s-case-for-medical-marijuana]

Was Marijuana Really Less Potent in the 1960’s?: [http://www.theatlantic.com/technology/archive/2015/03/was-marijuana-really-less-potent-in-the-1960s/387010/]

Can we Open More than 100 Pot Shops as It Becomes the Second Country to Legalize Marijuana: [http://time.com/5421431/canada-legal-marijuana-sales/]


Pharmacists take on medical cannabis dispensing role in three states. (2016, January 13) Retrieved September 28th from [https://www.pharmacist.com/node/9659475_ssd-called=1]

Keep on reading, it’s how you learn & how you form an educated opinion…

Mike Tyson breaks ground on marijuana farm and luxury resort https://m.sfgate.com/bayarea/article/Mike-Tyson-marijuana-cannabis-weed-california-12467556.php

JPMorgan Lends Credibility to Cannabis Stocks https://www.barrons.com/articles/jpmorgan-recommends-cannabis-stock-51546450672