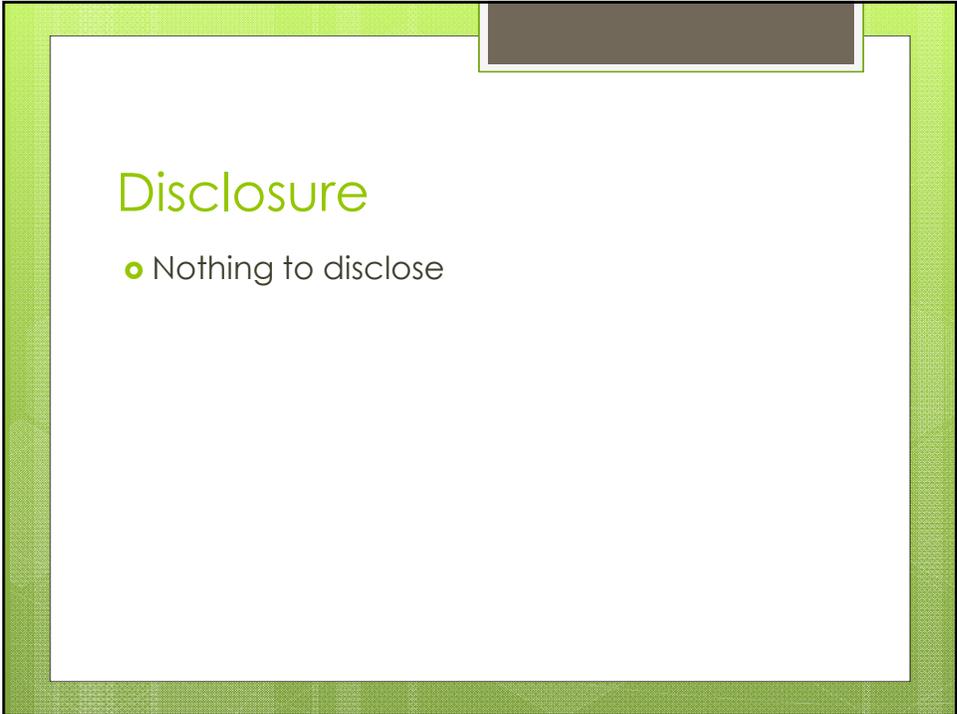


## Medical Marijuana Updates

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## Disclosure

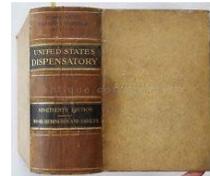
- Nothing to disclose

## Objectives

- Describe the biology of medical marijuana
- Describe possible indications for the use of medical marijuana in CKD
- Discuss legality of medical marijuana in the state of Florida and Federally

## History of Marijuana

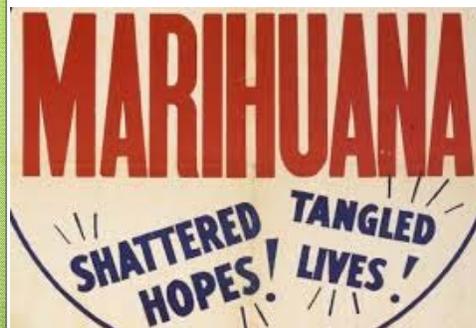
- References to marijuana have appeared in the medical literature throughout history.
- W.B O'Shaughnessy's 1830 paper on "Indian hemp"
- Mid 19th century medical marijuana was included in the US Dispensatory



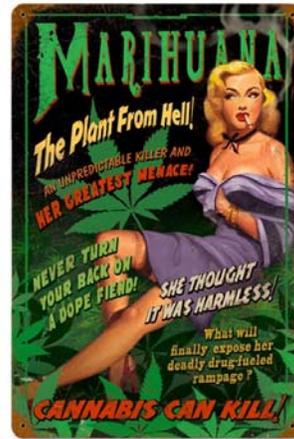
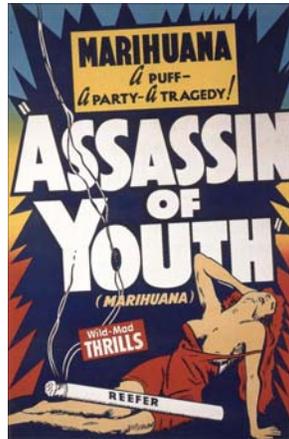
## History of Marijuana

- 1920's Marijuana hysteria begins....
  - Great Depression and Stock Market crash
  - Poor economic climate fueled anti-immigrant stance
  - Immigrants were thought to use marijuana

## Reefer Madness



## Reefer Madness



## Epidemiology

- 2014: 182 million globally
- 3.8% of the global population aged 15-64
- 38.5 million users in North America

## Marijuana Biology

- *Cannabis sativa* plant,  
*Cannabis indica*,  
*Cannabis ruderalis*

- Composed of 400 compounds

- 66 Cannabinoids

- Interact with CB1R and CB2R

### types of cannabis



S. indica



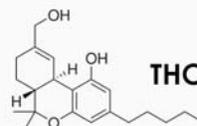
S. sativa



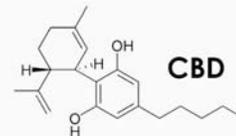
S. ruderalis

## Marijuana Biology

- $\Delta^9$ -tetrahydrocannabinol (THC)
  - CB1R/2R agonist
  - Antiemetic
  - Appetite stimulation
  - Psychotropic effects



- Cannabidiol (CBD)
  - Anticonvulsant effects
  - Anxiolytic effects
  - Antipsychotic effects
  - Neuroprotection
  - Anti-inflammatory effects



Both: Analgesia, Muscle relaxation

## Endocannabinoid System

- Receptors
  - Cannabinoid-1 (CB1)
  - Cannabinoid-2 (CB2)
- Endogenous ligands
  - Anandamide
  - 2-arachidonoylglycerol (2-AG)

## Synthetic Formulations

- Dronabinol (Marinol®) CIII
  - Active Agent: Synthetic THC
  - Indication: Anorexia/Wasting in HIV Pts, Chemo induced N/V
- Nabilone (Cesamet®) CII
  - Active Agent: Analog of THC
  - Indication: Chemo induced N/V
- **THC:CBD Buccal Spray (Sativex®)**
  - Active Agent: Cannabis extract of THC and CBD
  - Indication: Adjunctive for neuropathic or cancer pain

## Non-traditional forms of Medical Marijuana

- Vaporizers- less exposure to toxins than smoking, risk unknown
- Tinctures/Sprays- for sublingual use
- Edibles- longer onset of action
- Pills- contains marijuana oil
- Topical wax/balms- for localized pain, longer onset of action

## Which form of marijuana contains the highest conc. Of THC?

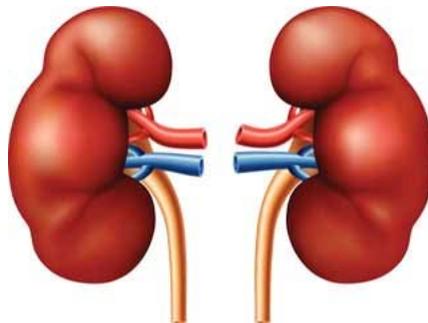
- A. Dab
- B. Hashish
- C. Cannabis
- D. Sinsemilla

Dab/Earwax contains  
80% THC

## Marijuana Types (% [THC])

- Cannabis 6%
- Sinsemilla 13%
- Hashish 40%
- Hash oil 50%
- Dabs/Earwax 80%

## Possible indications of Medical Marijuana in CKD



## Chronic Pain in CKD

- 50% of hemodialysis patients complained of pain
- Musculoskeletal pain most common cause at 63.1%
- 18% of patient reported more than one cause of their pain
- 82.5% of patient reported mod-severe pain

Davison SN. Pain in hemodialysis patients: prevalence, cause, severity, and management. Am J Kidney Dis 2003;42:1239-1247

## Chronic Pain in CKD

- Management:
  - No Tx 35%
  - Nonopioid 30%
  - Weak opioid 27%
  - Strong opioid 10%
- Effectiveness:
  - 94.8% of patients responded that pain Tx was neutral or negative

Davison SN. Pain in hemodialysis patients: prevalence, cause, severity, and management. Am J Kidney Dis 2003;42:1239-1247

## Chronic Pain in CKD

- Five RCTs revealed a statistically significant reduction in pain when comparing THC:CBD with placebo
- Two RCTs did not support a statistically significant difference
- Authors concluded THC:CBD, are modestly effective in reducing pain among patient with chronic non-cancer pain

Lynch ME, Campbell F. Cannabinoids for treatment of chronic non-cancer pain; a systematic review of randomized trials. Br J Clin Pharmacol. 2017;81(1):1-11.

## Chronic Pain in CKD

- The effectiveness of cannabinoids in the management of chronic nonmalignant neuropathic pain: a systematic review
- Assessed the therapeutic effect of THC:CBD in patients with non-cancer neuropathic pain
- Statistically significant reduction in mean pain intensity
- Authors concluded that THC:CBD may provide an effective analgesic effect in chronic neuropathic pain conditions that are unresponsive to other treatments

## Chronic Pain in CKD

- Cannabinoids for medicinal use: a systematic review and meta-analysis
  - Found that on average patients reported >30% reduction in pain control, but the results of the pooled analyses were not statistically significant
  - Authors concluded there was a moderate quality of evidence supporting the use of cannabinoids in the management of chronic pain

## Chronic Pain in CKD

- Two studies found that cannabinoids are safe treatment options for chronic non-cancer pain
  - No serious life threatening adverse effects
  - Very few risks were associated with the use of cannabinoid products

Lynch ME, Ware MA. Cannabinoids for the treatment of chronic non-cancer pain: an updated systematic review of randomized controlled trials. *J Neuroimmune Pharmacol*. 2015 Jun;10(2):293-301.

Lynch ME, Campbell F. Cannabinoids for treatment of chronic non-cancer pain; a systematic review of randomized trials. *Br J Clin Pharmacol [Internet]*. 2011 Nov [cited 2016 Apr 7];72(5):735-44.

All of the following are street names of marijuana, except?

- A. Mary Jane
- B. Aunt Mary
- C. Spider
- D. Roach

Spider is NOT a slang term for marijuana

## Appetite Stimulant

- Patients with CKD have a decline in nutritional status as they progress to ESRD
- 10-25% of CKD patients experience a loss of appetite or loss of desire to eat (*J Ren Nutr.* 1999; 9:129-132)
- 32% of dialysis patients have fair or poor appetites (Nephrol Dial Transplant. 2005;20:2765-2774)

## Appetite Stimulant

- Marijuana users represented 38% of patients in the Coronary Artery Risk Development in Young Adults (CARDIA) study
- These patients had an average caloric intake of 3365 kcal/day vs 2746 kcal/day in non marijuana users.

Marijuana Use, Diet, Body Mass Index, and Cardiovascular Risk Factors. The American Journal of Cardiology, Volume 98, Issue 4, Pages 478-484)

## Appetite Stimulant

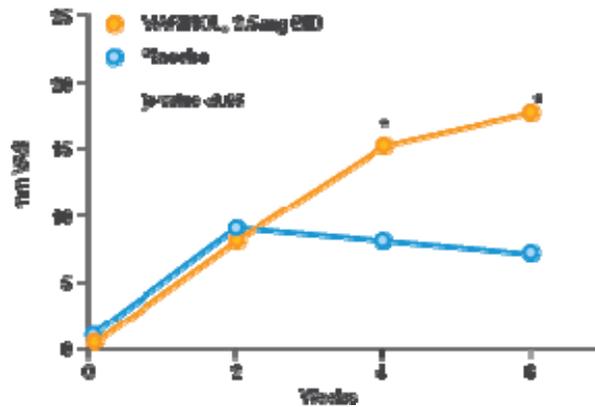
- Protein Energy Wasting (PEW): multiple nutritional and catabolic alterations that occur in CKD
  - Correlation between PEW and the risk of hospitalization/death
- Protein catabolism is stimulated by decreased nutrient intake

T. Alp Ikizler. Optimal Nutrition in Hemodialysis Patients. Adv Chronic Kidney Dis. 2013 Mar; 20(2): 181-189

## Appetite Stimulant

- Marinol (dronabinol)
  - Appetite stimulation in the treatment of AIDS-related anorexia associated with weight loss
  - RCT involving 139 patients
  - As compared to placebo, dronabinol capsules treatment resulted a statistically significant improvement in appetite as measured by visual analog scale. Trends towards improved body weight and mood, and decreases in nausea were also seen.

## Appetite Stimulant



MARINOL [package insert]. North Chicago, IL: AbbVie Inc.

## Depression

- 20% of CKD patient suffer from major depressive episode
- 28% of dialysis patients suffer from major depressive disorder (vs 16.2% in general population)
- Depression can affect outcomes in HD patients
- Higher rates of hospital readmission and greater likelihood of ED visits

Kiosses V, Karathanos V (2012) Depression in Patients with CKD: A Person Centered Approach. J Psychol Psychother S3: 002. doi: 10.4172/2161-0487.S3-002

## Depression

- University of Buffalo study published in the Journal of Neuroscience linked chronic stress to depletion of endocannabinoids in rats
- "the impairment of eCB signaling in the DRn (dorsal raphe nucleus) could mediate, at least in part, some of the behavioral consequences of chronic stress exposure, such as depression-like behaviors. It is noteworthy that pharmacological manipulation that increases eCB signaling has been shown to block chronic stress-induced depression-like behaviors"

● Haj-Dahmane S, Shen RY. Chronic Stress Impairs alpha1-Adrenoceptor-Induced Endocannabinoid-Dependent Synaptic Plasticity in the Dorsal Raphe Nucleus. The Journal of Neuroscience, October 29, 2014;34(44):14560–14570

## US states that allow medical marijuana see drop in other Rx

Medication Type	Before	After	%
Spasticity	2,068 doses	1,645 doses	20
Seizure	9,368 doses	8,029 doses	14
Pain	31,810 doses	28,166 doses	11

Medications for anxiety, depression, nausea, psychosis and sleep disorders were all prescribed between 8-13% less often in states that offered medical marijuana.

US states that allow medical marijuana see drop in prescriptions for other drugs, study finds. BMJ 2016;354:i3942 doi: 10.1136/bmj.i3942 (Published 14 July 2016)

## Harmful Effects of Marijuana



## Brain



- Short term:
  - Poor focus, memory and reaction time.
  - Difficulty with problem solving
  - Hallucinations, paranoia, anxiety
- Long term:
  - Memory problems and trouble learning new things
  - Hallucinations, paranoia, anxiety, worsening PTSD symptoms
  - Addiction

## Lungs



- Chemicals inhaled associated with use; Gasses, small particles and carcinogens
- Over time patients can develop similar symptoms of tobacco smokers
  - Daily cough with mucus
  - Difficulty breathing
  - Lung infections (bronchitis, pneumonia)

## Heart

- Increased risk of heart attack
- Increases heart rate
- Changes in heart rhythm



## Where does the Federal Gov't stand?

- Marijuana is NOT an FDA-approved medicine
- Schedule 1 Controlled Substance
  - *No* currently accepted medical use and a high potential for abuse.
  - Ex: Heroin, LSD



## American Medical Association

- In Nov 2013 stated that cannabis...
  - is dangerous and a public health concern
  - should not be legalized
  - additional research is needed



## American Society of Addiction Medicine

- ASAM public policy statement on medical marijuana states the following...
  - rejects smoking as a drug delivery system
  - discourages states medical marijuana programs



## Others...

- American Cancer Society: "supportive of more research"... "does not advocate legalization"
- American Glaucoma Society: "do not recommend for treatment of glaucoma"
- American Academy of Pediatrics: "opposes legalization"

## Others...

- American Academy of Child and Adolescent Psychiatry: "opposes medical marijuana dispensing to adolescents"
- National Association of School Nurses: "believe current classification is correct"
- American Psychiatric Association: "no current scientific evidence that marijuana is beneficial for treatment of psych disorders"

## Florida Right to Medical Marijuana Initiative, Amendment 2

- Guaranteed:
  - Medical use of marijuana by qualified patient OR prescribed by licensed physician OR dispensed by a treatment center would not be subject to criminal liability
- Defeated on 2014 ballot
  - 57.62% Yes to 42.38% No

## Florida Medical Marijuana Legalization, Amendment 2

- Supports the legalizing of medical marijuana for individuals with specific debilitating diseases or comparable debilitating conditions as determined by a license state physician
- Requires the Department of Health to regulate marijuana production and distribution centers and issue identification cards for patients and caregivers

## Florida Medical Marijuana Legalization, Amendment 2

Passed on 2016 ballot

- 71% Yes to 28% No

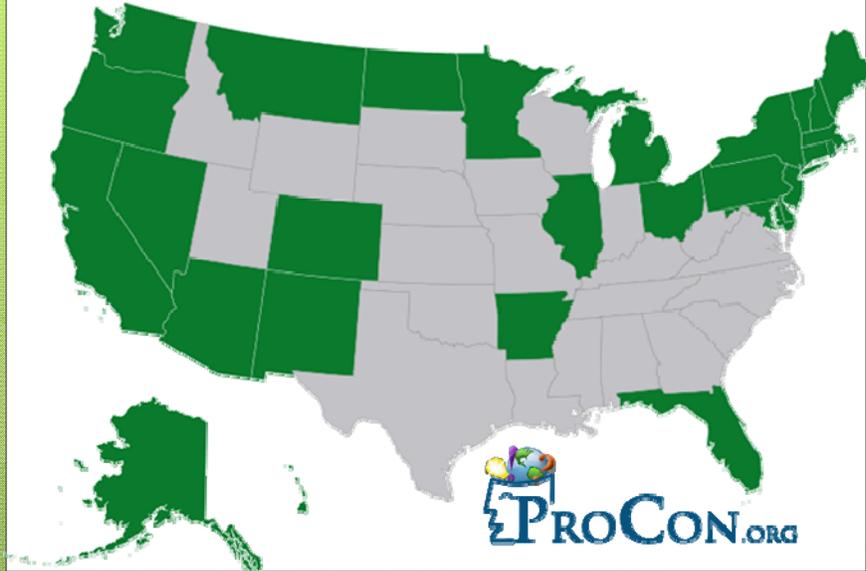
Difference:

- Added parental consent for use by minors
- Defined qualifying illnesses
- Doctors can face legal action for negligent prescribing practices and limited the number of patients that can be treated by one provider

## What does this mean?

- Effective: January 3, 2017
- Department of Health has 6 months from effective date to
  - Set qualifications and standards of care givers and medical marijuana treatment centers
  - Set regulations for the issuance of ID cards.

28 LEGAL MEDICAL MARIJUANA STATES AND DC



The first state to pass a medical marijuana law was...

- A. Florida
- B. Rhode Island
- C. California
- D. Maryland

California (1996)

## Things to consider...

- Is marijuana correctly classified as a Schedule I substance
- Can medical marijuana be effective in the CKD population?
- Can medical marijuana be used to treat multiple disease states and minimize other medications used?
- Are the benefits of medical marijuana greater than the clear risks associated with its use?

## References

- Boychuk DG, Goddard G, Mauro G, Orellana MF. The effectiveness of cannabinoids in the management of chronic nonmalignant neuropathic pain: a systematic review. *J Oral Facial Pain Headache*. 2015;29(1):7-14
- Davison SN. Pain in hemodialysis patients: prevalence, cause, severity, and management. *Am J Kidney Dis* 2003;42:1239-1247
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- T. Alp Ikizler. Optima Nutrition in Hemodialysis Patients. *Adv Chronic Kidney Dis*. 2013 Mar; 20(2): 181-189

Questions?



*Be careful who you invite to your next potluck!!!*

## Medical Marijuana Updates

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