



**Reefer Madness Revisited:
Taking the Insanity Out of Medical
Cannabinoids**

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Disclosure

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- Consultant/Independent Contractor, Speakers Bureau: kaléo
- Dr. Schatman has no other conflicts of interest, although he is a veteran of 32 Grateful Dead/Dead and Company concerts



Learning Objectives

- Lots of questions to be asked...
- Lengthy history in the US
 - California became the first state to legalize MM in 1996
- Currently there are MM laws in 33 states plus DC

National Conference of State Legislatures. State medical marijuana laws, 2/11/2019. Available at: <http://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx>.
- Individual states' medical marijuana laws are incredibly heterogeneous – varying widely in terms of process of obtaining, limits on possession, rules regulating dispensaries, allowable medical conditions, and every other parameter



What the Heck is “Medical Marijuana”?!?!

- Describe the political issues surrounding the legalization of medical marijuana
- Recognize the obstacles to conducting high-quality medical cannabinoid research in the United States
- Discuss how to modify your medical marijuana authorization patterns based on legal realities and empirical data



What is Medical Marijuana?

- In the eyes of the pro-marijuana zealots, ALL marijuana is “medical”
- In the eyes of the FDA, NO marijuana is “medical”
- Perhaps the truth falls somewhere in between...
- CSA (1970) made cannabis a Schedule I drug – “drugs with no currently accepted medical use and a high potential for abuse”
US Drug Enforcement Administration, Drug Scheduling. Available at: <http://www.usdoj.gov/dea/da/infor/ds.shtml>
- Remains federally “illegal”



What is Medical Marijuana? (cont’d)

- Is it legal or illegal?
- Should it be legal?
- Is it safe?
- Is there an evidence basis for efficacy?
- If it’s sold in a dispensary, should it therefore be considered “medical”?
- If it’s “medical,” can it be abused?



So Let's Complicate Things Even More...

- What constitutes "recreational marijuana"?
 - Washington
 - Colorado
- Again, to the FDA, legal recreational marijuana doesn't exist
 - Alaska
 - Oregon
 - California
 - Nevada
 - DC
 - Massachusetts
 - Maine
 - Vermont
 - Michigan
- However, tell this to the good citizens of:



The Future of Recreational Pot?

- Predictions for legalization in 2019:
 - Connecticut
 - Illinois
 - Minnesota
 - New Hampshire
 - New Jersey
 - New Mexico
 - New York
 - Rhode Island
 - Vermont



Angell T. Forbes, December 26, 2018. Available at: <https://www.forbes.com/sites/forbes/2018/12/26/these-states-are-most-likely-to-legalize-marijuana-in-2019/#511d299e9d41>



Politics

- 2014: Congress passes the Rohrabacher–Blumenauer amendment, defunding the DOJ from enforcement of federal law in MM states

Lopez G. Vox, May 30, 2014.
- Must be renewed every fiscal year to stay in effect

McCoy J. New Frontier Data, March 17, 2018. Available at: <https://newfrontierdata.com/marijuana-insights/rohrabacher-blumenauer-what-are-the-stakes-revisited/>.
- Has been successfully renewed each year – attached to the federal budget bill
- Every time a budget agreement can't be reached, federal protection of states' laws is threatened
- And the DOJ can theoretically run wild...



Cannabinoids

- Marijuana contains over 100 cannabinoids
National Institute on Drug Abuse. Drug Facts: Is Marijuana Medicine? Revised April, 2014.
- Δ9-tetrahydrocannabinol (THC) – the principle psychoactive constituent of cannabis
- Gets all of the press – good and bad
- Recreational marijuana – goal is to maximize THC
- Seems to be the goal of “medical marijuana” as well...
- Higher THC fetches a higher price in dispensaries



THC:CBD Ratio

- What kinds of ratios do we see in medical and nonmedical cannabis?
- Recent study of THC & CBD (medical and recreational) 2008-2017
Chandra S, et al. Eur Arch Psychiatry Clin Neurosci. 2019 [Epub ahead of print].
 - THC levels doubled (8.9% in 2008, 17.1% in 2017)
 - CBD levels decreased from 0.37% in 2008 to 0.14% in 2017
 - THC:CBD ratio increase from 23:1 in 2008 to 104:1 in 2017
 - Importance of the ratio: “CBD is nonintoxicating and has been found to offset several, harmful effects of Δ9 -THC, including memory impairment and psychotic-like symptoms”



THC:CBD Ratio (cont'd)

- Authors conclude, “These trends in the last decade suggest that cannabis is becoming an increasingly harmful product”
- The THC:CBD ratio is not examined in most studies
 - Most current data come from toxicology following seizures
Vindenes V, Morland J. Increasing plant concentrations of THC and implications on health related disorders. In: Handbook of Cannabis and Related Pathologies: Biology, Pharmacology, Diagnosis, and Treatment. Academic Press, 2017. pp. 24-32.
- Ability to understand the THC:CBD ratio and the impact of breeding the CBD out of cannabis is essential to understanding its health risks



Synthetic THC

- Available as a Schedule III drug (dronabinol/Marinol) since 1985
- Nabilone/Cesamet (Schedule II) – a synthetic THC analogue – also FDA-approved in 1985
- Common side effects include drowsiness, unsteady gait, dizziness, inability to focus thoughts, confusion, mood changes, delusions, and hallucinations

WebMD. Drugs and medications: Marinol oral. [http://www.webmd.com/drugs/2/drug-9309-Marinol-Oral-aspx?drugid=9308&drugname=Marinol%20oral&page\[number\]=6](http://www.webmd.com/drugs/2/drug-9309-Marinol-Oral-aspx?drugid=9308&drugname=Marinol%20oral&page[number]=6)

- Tolerability is dubious
 - Consequently, so is clinical utility for pain
- Issa MA, et al. Clin J Pain 2014;30:472-478.



Safety Issues Associated with Marijuana

- The myriad safety concerns identified are thought to be due primarily to THC; more THC means more risks
Fischer B, et al. Am J Public Health. 2017;107(8):e1-e12.
- Can we assume that as the THC levels continue to rise, that safety risks will do the same?
- Smoking remains the most common route of administration
Russell C, et al. Int J Drug Policy. 2016;52:87-96.
- Recent review: pulmonary effects are even worse than we'd thought – "Marijuana Lung"
Lab JS, et al. Chronic Obstr Pulm Dis. 2016;5:81-83.
- Tars from smoked marijuana contain more carcinogens than do those from tobacco
Wu TC, et al. N Engl J Med. 1988;318:347-351.



Physical Safety Issues

- 2018 review: Concludes that vaporization is safer than smoking from a pulmonary perspective
MacCallum CA, Russo EB. Eur J Intern Med. 2018;49:12-19.
- Dysregulation of the endogenous lipid mediator endocannabinoids has been implicated in a variety of cardiovascular pathologies
Pacher P, et al. Nat Rev Cardiol. 2016;15(3):151-166.
- Increases rates of acute myocardial infarction and cardiovascular mortality – doubles rate of MI
Franz CA, Frishman WH. Cardiol Rev. 2016;24:158-162.
- Predicts heart failure and CVA – whether recreational or medical
Kallia A, et al. J Cardiovasc Med (Hagerstown). 2018;19:480-484.



Physical Safety Issues (cont'd)

- Increased duration of marijuana use is associated with increased risk of death from hypertension
Yankay BA, et al. Eur J Prev Cardiol. 2017;24(17):1833-1840.
- Associated with higher rates of acute ischemic stroke
Jung JS, et al. Investig Magn Reson Imaging. 2018;22(3):168-171.
- Immunosuppressive – reduces T-cell activation
Henriquez JE, et al. J Pharmacol Exp Ther. 2018;367(1):49-58.
 - Implications for cancer, HIV, among others



Physical Safety Issues (cont'd)

- Cannabinoid hyperemesis syndrome
 - Characterized by a syndrome of cyclic vomiting, abdominal pain, and compulsive showering in some habitual users
 - Symptoms improve with cessation utilization
 - Prevalence of cannabinoid hyperemesis syndrome seen in EDs quickly doubled following the liberalization of MJ laws in Colorado
Kim HS, et al. Acad Emerg Med. 2015;22:694-699.
 - Can masquerade as an eating disorder
Brewerton TD, Anderson O. Int J Eat Disord. 2016;49:826-829.
 - Estimated 2.75 million cases in the US annually
Habibouche J, et al. Basic Clin Pharmacol Toxicol. 2018;122:660-662.
 - Fatal cases now being reported
Nourbakhsh M, et al. J Forensic Sci. 2019;64(1):270-274.



Physical Safety Issues (cont'd)

- Cannabis use is associated with higher rates of occupational injuries, injury severity, and prolonged lost workdays among construction workers
Khoshaba E, et al. Toxicol Ind Health. 2018;34:89-90.
- Drugged driving – 96% of cases involve cannabis
Bonar EE, et al. Addict Behav. 2018;78:80-84.
- Drugged driving continues to increase, with increases associated with more traffic fatalities
Robertson FD, et al. Accid Anal Prev. 2017;99(Pt A):236-241.



Physical Safety Issues (cont'd)

- French study: 1 in 2 drivers in fatal accidents under the influence of ETOH were also under the influence of cannabis
Martin JL, et al. PLoS One 2017;12(11):e0187320.
- High-risk drinking behavior recently found to be related to medical cannabis utilization
Davis AK, et al. Addict Behav. 2018;77:166-171.
- Older adults – cannabis use associated with greater physical injury risk and ED visits
Choi NG, et al. Am J Drug Alcohol Abuse. 2018;44:215-223.



Physical Safety Issues (cont'd)

- Perhaps the issue is that users of MJ have been found to have greater perceived safety than those who don't
Santor CE, et al. Addict Behav. 2017;66:114-117.
- Pregnancy: Use of marijuana among pregnant women increased by 69% between 2009 and 2016
Young-Wolf KC, et al. JAMA 2017;318(24):2490-2491.
- Currently at 22%
Oga EA, et al. Matern Child Health J. 2019;23(2):250-257.
- Cannabis use associated with preterm birth
Prunet C, et al. J Gynecol Obstet Hum Reprod. 2017;46(1):19-28.
- Likelihood of stillbirth or miscarriage 12 times higher among women using MJ during pregnancy
Coleman-Cowger VH, et al. Neurotoxicol Teratol. 2018;68:84-90.



Physical Safety Issues (cont'd)

- Addiction
 - Not as severe as opioid or benzo addiction
 - Abrupt cessation results in irritability, insomnia, anorexia
Haney M, et al. Neuropsychopharmacology 2013;38:1557-1565.
- Perceived barrier to quitting MJ – fear of severe withdrawal symptoms
Zvolensky MJ, et al. Addict Behav. 2018;76:45-51.
- When used hs, withdrawal's impact on sleep is particularly problematic
Cranford JA, et al. Drug Alcohol Depend. 2017;180:227-233.
- Reduced MJ use associate with improved sleep quality
Hser YI, et al. J Subst Abuse Treat. 2017;81:53-58.



Cognitive Safety Issues

- We've known about chronic MJ use and its impact on diminution of grey matter in the brain for years
Block RI, et al. Neuroreport 2000;11:491-496.
- Of particular concern in the developing brain
- Executive functioning deficits associated with MJ use
Clark DB, et al. Front Behav Neurosci. 2017;11:223.
- Myriad studies and review indicate that chronic MJ use results in cognitive deficits
 - Long-term and short-term



Cognitive Safety Issues (cont'd)

- Long-term deficits ("residual cannabis effect") include (from a meta-analysis):
 - Learning
 - Forgetting/retrieval
 - Abstraction/executive functioning
 - Attention
 - Motor skills
 - Verbal/language

Schreiner AM, Dunn ME. Exp Clin Psychopharmacol. 2012;20(5):420-429.



Mental Health Risks

- Most studied issue has been early-onset psychosis and recovery from it in marijuana users
- MJ-psychosis association recognized back to the 1950s
Ames F. J Ment Sci. 1958;104(437):972-999.
- High THC cannabis increases the risk of psychosis 3-fold compared to nonusers, and 5-fold among daily users
Di Forti M, et al. Lancet Psychiatry 2015;2(3):233-238.
 - Particularly problematic in patients using ultra-high-THC wax dabs
Pierre JM, et al. Schizophr Res. 2016;172(1-3):211-212.



Mental Health Risks – Psychosis

- Cannabis use in first episode psychosis is associated with failure of anti-psychotic medications
Patel R, et al. BMJ Open. 2016;6(3):e009888.
– As well as adherence to anti-psychotic medications
Schoeler T, et al. Lancet Psychiatry 2017;4(8):627-633.
- Extended abstinence from MJ doesn't seem to reverse symptoms in cannabis-dependent schizophrenics
Rabin RA, et al. Schizophr Res. 2018;194:55-61.
- A risk factor for violent behavior in early phase psychosis
Moulin V, et al. Front Psychiatry. 2018;9:294.



Mental Health Risks – Anxiety

- The acute induction of anxiety associated with THC cannot be ignored
- Early studies found an anxiolytic effect of MJ
Seftin BB, et al. Biol Psychiatry 1986;21:3-10.
- 2017 meta-analysis concludes that THC's impact on anxiety is not necessarily impressive
Turna J, et al. Depress Anxiety. 2017;34:1006-1017.
– However, that may have much to do with Indica vs. Sativa strain
- Recent study found that longitudinally, reduction of MJ use was associated with decreased anxiety
Hser YI, et al. J Subst Abuse Treat. 2017;81:53-58.



Mental Health Risks – Anxiety (cont'd)

- PTSD: once thought to be “treatable” with cannabis
- However chronic MJ use has been found to impair fear extinction
Papini S, et al. J Abnorm Psychol. 2017;126:117-124.
- MJ use in PTSD patients strongly predicts dropout from therapeutic treatment
Bedard-Gilligan M, et al. Psychol Addict Behav. 2018;32(3):277-288.
- Indicas may be helpful, activating sativas likely to exacerbate
- Good news: dispensary employees found to be more likely to recommend an indica or a hybrid for PTSD than a sativa
Haug NA, et al. Cannabis Cannabinoid Res. 2016;1:244-251.



Cannabidiol (CBD)

- Contrary to popular belief, THC is not the most relevant cannabinoid for medical application
Campos AC, et al. Philos Trans R Soc Lond B Biol Sci. 2012;367:3364–3378.
- CBD was first isolated in 1934
Robson P. Br J Psychiatry 2001;178:107-115.
- First synthesized in 1967, first easily useable form in 1985
Baek SH, et al. Tetrahedron Lett. 1985;26:1083-1086.
- Ignored for many years
- Seen as something limiting the amount of THC marijuana could potentially contain



CBD

- Of no interest to recreational users... and tragically, for many medical users
- Initially described as "nonpsychotropic"
- However, produces anxiolysis through increasing serotonergic transmission... and reverses allodynia
De Gregorio D, et al. Pain 2019;160(1):136-150.
- Appears to have a mild antidepressant effect for those with low levels of serotonin
Sales AJ, et al. Prog Neuropsychopharmacol Biol Psychiatry. 2018;86:255-261.
- More appropriately called "noneuphoriant"
Russo EB. Ther Clin Risk Manag. 2008;4:245-259.



CBD Safety Profile

- Safety has been well-established
Cunha JM, et al. Pharmacol. 1980;21:175-185.
Consero P, et al. Pharmacol Biochem Behav. 1991;40:701-708.
Zuardi AW, et al. J Psychopharmacol. 2006;20:683-686.
Zuardi AW, et al. J Psychopharmacol. 2009;23:979-983.
Zuardi AW, et al. J Psychopharmacol. 2010;24:135-137.
Bergamaschi MM, et al. Curr Drug Saf. 2011;6:237-239.
Devinsky O, et al. Lancet Neurol. 2016;15:270-278.
McQuire P, et al. Am J Psychiatry 2018;175:225-231.
- Attenuates the "high" caused by THC at 8:1 CBD:THC ratio
Kim PS, Fishman M. Curr Pain Headache Rep. 2017;21(4):19.
- The Director of NIDA wrote, "CBD appears to be a safe drug"
Volkow N. Huffington Post July 23, 2015.



CBD Availability

- Despite its safety profile and the impossibility of abusing it, CBD from whole plant MJ is still considered a Schedule I drug
- Other than recently FDA-approved Epidiolex
- Has been available in all medical marijuana states
- 13 states had the wisdom to legalize it without MM legalization
- New changes in the law allow for CBD from the hemp plant

Traynor K. Am J Health Syst Pharm. 2018;75:1088-1089.
 McGinnell SL, Maguire TC. National Law Rev. December 20, 2018.
 Available at: <https://www.refseurope.com/article/2018/farm-bill-signed-law-includes-major-changes-in-cbd-hemp>.



CBD Legal Status

- Hemp plant is in the same genus as MJ, but contains, by definition and law, <0.3% THC content
- THC will not show up in standard UDT immunoassays
- Now most commonly used for pain, anxiety, depression, and sleep disorders
- Due to lack of regulation, CBD products online are often mislabeled regarding constituents

Shannon S, et al. Perm J. 2019;23:18-041.
 Corroon J, Phillips JA. Cannabis Cannabinoid Res. 2018;3:152-161.
 Freedman DA, Patel AD. Pediatr Neurol Briefs. 2018;2:23.



CBD and Pain

- Much of the existing supportive data is preclinical
- CBD is anti-inflammatory
- Attenuation of early phase inflammation by cannabidiol prevents pain and nerve damage in osteoarthritis
- Found to be anti-inflammatory in human cell lines

Thepa D, et al. FASEB J. 2017;31(Suppl 1):Abstract 811.7.
 Philpott HT, et al. Pain 2017; 158:2442-2451.
 Petrosino S, et al. J Pharmacol Exp Ther. 2018;365:652-663.



Rat Cheating on a Forced-Swim Test



Painweek

CBD and Pain

- Relevance for back pain: CBD has anti-inflammatory effects on rat nucleus pulposus cells

Chen J, et al. Mol Med Rep. 2016;14:2321-2327.

- Reduces chemotherapy-related peripheral neuropathy, and does so to an even greater degree when combined with low-dose morphine

Harris HM, et al. Med Cannabis Cannabinoids 2018;1:54-69.

- In humans, CBD decreased anxiety and improved sleep scores

Shannon S, et al. Perm J. 2019;23:18-041.

Painweek

More CBD Research

- Safety established when co-administered with fentanyl

Manini AF, et al. J Addict Med. 2015;9:204-210.

- Enhances fracture healing

Apostu D, et al. Drug Metab Rev. 2019 [Epub ahead of print].

- Animal model: protective effects on lesion-induced intervertebral disc degeneration

Silveira JW, et al. PLoS One 2014;9:e113161.

- Animal model: synergistic with morphine

Neelakandan H, et al. Behav Pharmacol. 2015;26:304-314.

- Human research: effective for reducing chronic pain in kidney transplant patients (small study)

Cuñetti L, et al. Transplant Proc. 2018;50:461-464.

Painweek

Marijuana and Pain Research

- Extremely difficult to do in the US
- All federally-funded MM research currently had to use low-grade MJ grown at the U of Mississippi for NIDA
- 3 dose strengths available
 - Low potency (1.29% THC)
 - Moderate potency (3.53%)
 - High potency (7%)
- Why is this a problem?

Willsey B, et al. J Pain 2013;14:136-148.



Marijuana and Pain Research (cont'd)

- Oil or wax dabs available at some dispensaries have THC contents greater than 90%!!!!
 - Now being used regularly by 21.1% of cannabis users
- Medical marijuana sold in dispensaries is higher in THC than that sold on the streets
- Recent breakthrough – NIDA has approved a 13.4% THC MJ for research

Sagar KA, et al. Drug Alcohol Depend. 2016;160:133-142.

Sevigny EL, et al. Int J Drug Pol. 2014;25:308-319.



Edibles

- THC dosing in edibles has been described as "insane" by toxicologists
- Edibles are infused with almost pure THC
- They typically take 30-90 minutes to take effect, reach their peak in 1.5-3 hours, and can last for 6-8 hours
- Thus, they don't allow for titration due to a lack of immediate effect
- Labeling of constituents' contents is generally inaccurate

Gussow L. Emerg Med News 2014;36:24.

Vandrey R, et al. J Anal Toxicol. 2017;41(2):83-99.

Tsutaoka B, et al. Clin Pediatr (Phila). 2018;57(2):227-230.



Edibles (cont'd)

- This inability to titrate effectively has led to increases in ER visits due to THC intoxication
Kim HS, Monte AA. Ann Emerg Med. 2016;68:71-75. Vo KT, et al. Ann Emerg Med. 2018;71:306-313.
- Myocardial infarction
Saunders A, Stevenson FS. Can J Cardiol. 2019 ;35(2):229.e1-229.e3.
- And multiple deaths
Calandullo SP, Fulton KJ. University of Washington School of Law Research Paper No. 2019-07, 2018. Available at: https://papers.ssrn.com/sol3/cases.cfm?abstract_id=3163729.



Painweek

Science vs “Religion”

- Medical marijuana advocates tend not to let the data get in the way of their opinions
- Try discussing potential harms of MM on Twitter....
- “There is none so blind as those who will not see...”



Painweek

MM and Pain Research: What DO We Know?

- Is it effective for chronic pain?
- Depends on the properties of the marijuana being used and one’s definition of “effective”
- It also depends upon goals of treatment
 - Is analgesia sufficient, even if it incapacitates the patient?
- It also depends on the medical indication, eg, opioids are effective for many types of pain, but not for neuropathic pain

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MM and Pain Research

- Neuropathic pain: a number of studies demonstrate analgesia, but requires higher dosages, which result in cognitive deficits

Willsey B, et al. J Pain 2008;9:506-521.
 Ellis PJ, et al. Neuropsychopharmacology 2009;34:672-680.
 Ware MA, et al. CMAJ 2010;182:E694-701.
 Wallace MS, et al. J Pain 2015;16:616-627.
 Willsey B, et al. J Pain 2016;17:982-1000.

- 2013 study using low-dose (1.29% THC) MJ: efficacy for neuropathic pain, without significant cognitive effects

Willsey B, et al. J Pain 2013;14:136-148.



MM and Pain Research (cont'd)

- Conclusions of MJ for neuropathic pain:
 - Weak evidence as effective in terms of analgesia at higher doses
 - Cognitive side effects are dose-related
 - Never studied head-to-head against gabapentinoids
 - Gabapentinoids also have dose-related cognitive side effects
 - Research needed on MM with significant CBD content as well
 - Research needed on the types of MJ actually carried in dispensaries (25%+ THC)

- Recommendation: consider as a last option for neuropathic pain

- Recent Australian review suggests that CBD may be better

Casey SL, Vaughan CW. Medicines (Basel). 2018;5(3): pii: E67.



MM and Pain Research (cont'd)

- Musculoskeletal pain and arthritis – "Evidence is needed"
- Perrot S, Trouvin AP. Joint Bone Spine. 2019;88(1):1-3.
- Rheumatic conditions – no evidence for efficacy
- Fitzcharles MA, et al. J Rheumatol. 2019 [Epub ahead of print].
- Fibromyalgia – Israeli study hopeful, but inconclusive
- Habib G, Avisar I. Pain Res Treat. 2018;2018:7829427.
- Headache – very limited evidence for efficacy
- Lochte BC, et al. Cannabis Cannabinoid Res. 2017;2:61-71.
- Cancer pain – "prospective clinical trials are needed to provide the robust data required to establish the proper role of cannabinoid and cannabis-based therapy"
- Steele G, et al. Curr Oncol Rep. 2019;21(1):10.



MM and Opioids

- The most compelling evidence basis for MJ in treating chronic pain was for its opioid-sparing effect
Boehnke KF, et al. J Pain 2016;17:739-744.
Vigil JM, et al. PLoS One. 2017;12:e0187795.
- Medical cannabis laws were associated with lower opioid overdose mortality rates
Bachhuber MA, et al. JAMA Intern Med. 2014;174:1668-1673.
- Current data dispel this...
- Recent data indicate that recreational legalization does not influence compliance with opioid therapy
Lo S-Y, et al. Am J Med. 2018 [Epub ahead of print].



MM and Opioids (cont'd)

- Synergistic with opioids? Likely urban myth...
- Not associated with lower prescription rates and dosages of Schedule II opioids
Liang D, et al. Addiction. 2018 [Epub ahead of print].
- "Cannabis use appears to increase rather than decrease the risk of developing nonmedical prescription opioid use and opioid use disorder"
Olson M, et al. Am J Psychiatry. 2018;175(1):47-53.
- "Multivariable analyses indicated that medical cannabis use was significantly associated with risk of prescription opioid misuse"
Nugent SM, et al. Gen Hosp Psychiatry. 2018;50:104-110.



MM and Opioids (cont'd)

- Perioperative opioid use is significantly higher in MJ-users despite lower subjective pain scores
Bauer FL, et al. Perm J. 2018 Jul 19:22.
- MJ use recently found to be predictive of opioid dependence
Butelman ER, et al. Front Psychiatry. 2018;9:283.
- Predictive of a 2.5 fold increase in the rate of opioid aberrancy
DiBenedetto DJ, ... Schatman ME, et al. Pain Med. 2018;19:1997-2008.
- Medical marijuana users more likely to use prescription drugs – including opioids – nonmedically
Caputi TL, Humphreys K. J Addict Med. 2018 [Epub ahead of print].



“Watcha Smoking, Dude?”

- To talk about “medical marijuana” as a single entity is ridiculous
- We need to be discussing “medical marijuanas”
- Indica or sativa?
2 separate species, usually in a hybrid form
- Indicas empirically established as preferable for pain management, but cause more sedation than sativas

Cohen NL, et al. J Stud Alcohol Drugs 2016;77(3):515-520.



Indica vs Sativa – Street Reputations

- | | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> ▪ Indicas <ul style="list-style-type: none"> – Relaxing and calming – Body buzz or ‘couch lock’ – Best suited for night use | <ul style="list-style-type: none"> ▪ Sativas <ul style="list-style-type: none"> – Uplifting and energetic – Cerebral, spacey, or hallucinogenic – Best suited for day use |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
- Leaf Science, 2014, Indica vs. Sativa: Understanding The Differences. Available at: <http://www.leafscience.com/2014/03/19/indica-vs-sativa-understanding-differences/>.



Treatment Recommendation

- “The Medicinal Cannabis Treatment Agreement: Providing Information to Chronic Pain Patients via a Written Document”
B Wiley, et al. Clin J Pain 2015;31:1087-1096.
- Absolutely brilliant!!!!
- “Medical marijuana” is heavily abused
Wen H, et al. J Health Econ. 2015;42:64-80.
- “...physicians would seem to have an obligation to understand and inform their patients on key issues of the evidence base on cannabinoid therapeutics”



Medical Cannabis Agreement

- Covers reduction of diversion, particularly to vulnerable children and adolescents
- Addresses inappropriate utilization by the authorized patient
 - We must not lose sight of the data indicating that marijuana is indeed addictive
- Discusses the risks of marijuana generally and to specific populations
- Recommends vaporization over smoking



Medical Cannabis Agreement (cont'd)

- Warns against driving a car or operating machinery
- Emphasizes "start low, go slow" when dosing – particularly with new strains
- Covers potential benefits of FDA-approved cannabinoids over smoked marijuana
 - Based on empirical evidence...and clinical experience, I disagree
- Recommends withdrawing slowly if a patient wants to stop
- Addresses the need to evaluate the efficacy and appropriateness of therapy on an ongoing basis
- Covers not using MM in public places



Medical Cannabis Agreement (cont'd)

- Warns that medical authorization will NOT protect a patient's job
- Gives the physician the right to discontinue MM treatment
- Respect for patient autonomy is contingent upon the doctrine of informed consent
 - Dalla-Vorgia P, et al. J Med Ethics 2001;27:59-61.
 - This is exactly what these agreements are providing
 - Thus, they constitute ethical pain medicine practice
 - And perhaps even protect the physician as well as the patient



Closing Thoughts

- The future of medical cannabinoids in the US is uncertain
- To assume that marijuana is safe because it's "natural" is neuromysticism
- As is assuming that anecdotal evidence of efficacy provides us with "the truth"
- Improving the quality and quantity of MM research is imperative if MJ is ever to become "medicine"
- CBD, not THC, promises to be the most medically-relevant cannabinoid



Closing Thoughts (cont'd)

- If you're going to use MM in your practice, educate yourself and your patient – and do it right
- Take marijuana as a drug seriously – irrespective of what you smoked as a youth
- If you use an opioid agreement, consider using a medical cannabis agreement
- Practicing cannabinoid medicine is challenging when we know so little
- Better data are hopefully just around the corner



▪ THANK YOU


