

Medical Cannabis

Medical Marijuana Research Symposium
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History of Cannabis

- ▶ First recorded medical use in China in 2737 BC
- ▶ Introduced into America by Spaniards in 1545 as hemp fiber
- ▶ 1619 - King James ordered every colonist to grow 100 plants
- ▶ 1839 - Dr. William O'Shaughnessey brought it to England from India for use with muscle spasms (tetanus), pain, and insomnia
- ▶ Early 1900s - over 2000 medicinal preparations were available in the US
- ▶ 1937 - Marijuana Tax Act - levied taxes for both medicinal and recreational use. Was opposed by the AMA.
- ▶ 1951 - Boggs Act - added Cannabis to narcotics

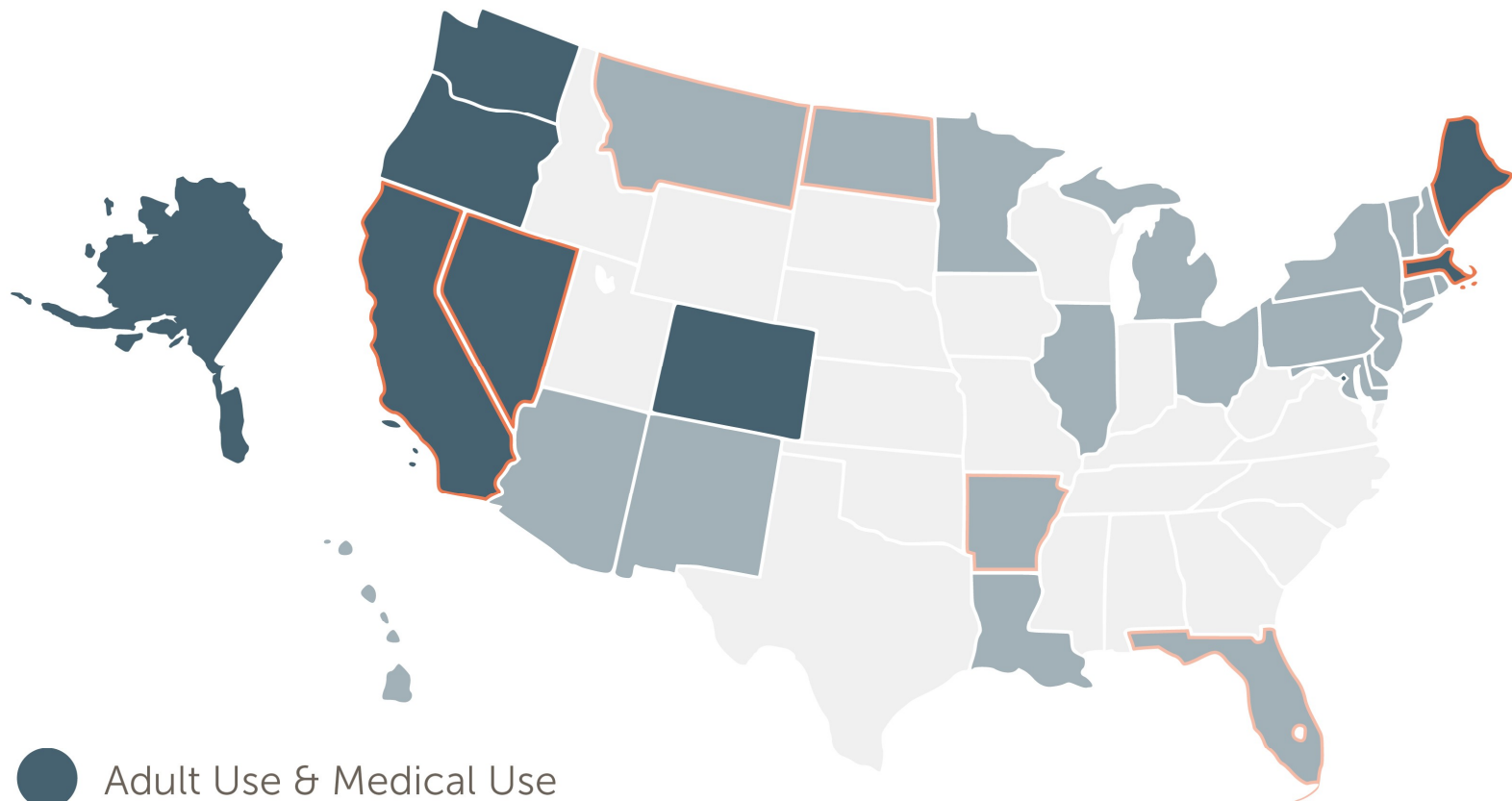


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Recent Developments

- ▶ 1970 - Controlled Substances Act - created 5 classes ("Schedules") of narcotics and "dangerous drugs"
 - ▶ Marijuana put in "Schedule 1"
- ▶ 1990 - the "endocannabinoid" system discovered - the body makes chemicals that work the same way cannabis does
- ▶ 1996 - California passes Proposition 215, allowing the use of medical cannabis
- ▶ 2016 - 28 states and DC have passed some sort of medical cannabis laws (8 states + DC have legalization)

CANNABIS LEGALIZATION NOVEMBER 9



- Adult Use & Medical Use
- Medical Use
- New Legislation

The Current FL Legal Situation

- ▶ 2009 - the US Attorney General - would not prosecute medical cannabis use when used according to state laws
- ▶ 2014 - Florida passes HB 307 - allowing for use of low-THC cannabis (CBD) for cancer, muscle spasms and seizures
- ▶ 2015 - the Compassionate Access, Research Expansions and Respect States Act (CARERS) introduced in the Senate
- ▶ 2016 - Florida passes SB 1030 allowing for use of THC cannabis for terminal illness
- ▶ 2016 - 71% of FL voters pass Amendment 2, expanding access
 - ▶ 2017 - SB 8-A passed by the legislature



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What Is Cannabis?

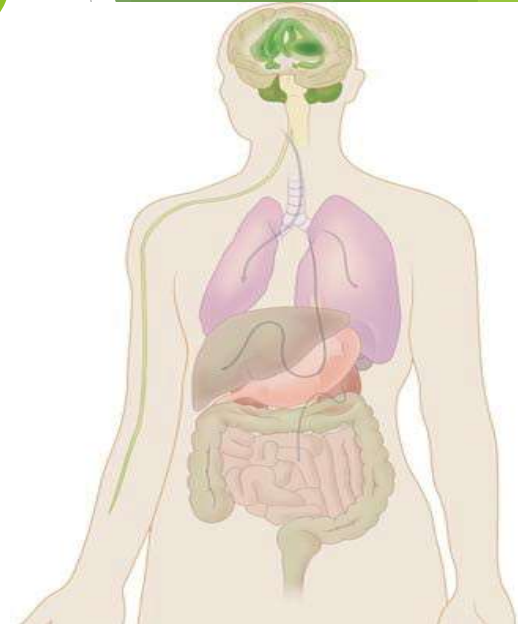
- ▶ *Cannabis Sativa* - the name of the plant species
- ▶ Two main subtypes:
 - ▶ Sativa - tall and thin plants - generally higher in THC
 - ▶ Indica - short and bushy plants - generally higher in CBD
- ▶ Currently there are hundreds of strains that have varied ratios of THC and CBD
- ▶ Current potency of plants are 10-20 times that sold in the 1960s
 - ▶ 1978 - 1.37% THC
 - ▶ 2016 - some strains may be over 25% THC



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The Endocannabinoid System (ECS)

- ▶ Cannabinoid receptors are present in brain, immune system, intestines, bone, nerves in distant body
- ▶ Responds to both internal (endocannabinoids) and external (phytocannabinoids) stimulation
- ▶ Non-lethal - there are no ECS receptors in the brain stem
 - ▶ No respiratory depression, like opioids
- ▶ Three endocannabinoids
 - ▶ Anandamide (AEA)
 - ▶ 2-arachidonoylglycerol (2-AG)
 - ▶ Palmitoylethanolamide (PEA)



Receptors and the "Entourage Effect"

- ▶ At least two main receptors
 - ▶ CB1
 - ▶ CB2
- ▶ Different cannabinoids affect how the cannabinoids act
 - ▶ CBD decreases the psychoactive effects of THC
- ▶ ECS helps control other neurotransmitters

Tetrahydrocannabinol (THC)

- ▶ Causes the “high” of marijuana
- ▶ Stimulates CB1 receptors in the brain and, to a lesser extent, the body
- ▶ When take orally 50% is changed in the liver (to 11-OH-delta-9-THC),
 - ▶ This is more potent than THC
- ▶ Continuous exposure can lead to tolerance - the person needs to take more to get the same effect
 - ▶ Not seen as often with medical use (lower doses)



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Cannabidiol (CBD)

- ▶ Doesn't cause a "high"
- ▶ Decreases the psychoactive effects of THC
- ▶ Has it's own direct effects
- ▶ Affects the brain but has more effects outside the brain than THC
- ▶ May end up having a greater medical role than THC

Cannabis Plants Are Complicated

- ▶ Over 105 plant cannabinoids have been discovered
- ▶ Natural products have varying concentrations of all these, plus
- ▶ Also has terpenes - which have medicinal effects
- ▶ CBG - CBN - THCA - THCV
 - ▶ May be beneficial in glaucoma, inflammatory bowel disease, weight loss, arthritis, diabetic neuropathy

Cannabis Delivery Systems

- ▶ Multiple types of delivery - each has benefits and risks
- ▶ Problems of dosing in other states
 - ▶ Pure plant materials have variable concentrations of cannabinoids
- ▶ General recommendations
 - ▶ **Start low and go slow**
 - ▶ **Adjust dose** ("titration") according to achievement of desired result or avoidance of side effects



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Vaporizing ("Vaping")

- ▶ Efficient - 95% of the vapor is cannabinoids
- ▶ Variety of systems available -
 - ▶ Hand-held (pens, vaporizers)
- ▶ Preferable for patients who need quicker onset of action - avoids potential breathing side-effects of smoking
- ▶ Peak effect in 5-15 minutes,
 - ▶ Declines rapidly over 30 minutes
- ▶ Can treat symptoms by taking small in inhalations every 15 - 30 minutes



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Oral Preparations

- ▶ Tinctures, oils (liquid or in capsules)
- ▶ Many variations in constituents
 - ▶ THC only
 - ▶ CBD only
 - ▶ Mixed (with varying ratios)
- ▶ Slower onset than inhalation but more prolonged action
 - ▶ Tinctures - more rapid onset, lasts 1-2 hours
 - ▶ Oils - slower onset 1-2 hours, lasts 5-6 hours



Newer Products

- ▶ Nasal sprays (Rescue spray)
 - ▶ Useful in seizure disorders
 - ▶ Delivered directly to the brain
- ▶ Topical creams and lotions
 - ▶ Have been used for thousands of years
 - ▶ Minimal systemic absorption, limited or no psychoactive effects
 - ▶ May be helpful for localized conditions - arthritis, dermatitis, dry skin, psoriasis



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Florida Qualifying Conditions (2017)

2015 (CBD)	2016 (THC)	SB 8-A (2017)
Cancer	“Terminal illness”	Cancer
Spasticity		Glaucoma
Seizures		Epilepsy
		Chronic nonmalignant pain *
		HIV
		AIDS
		Hepatitis C
		ALS
		Crohn’s disease
		Parkinson’s disease
		“Physician determination”

* Caused by a qualifying condition



Studies on medicinal cannabis effects: Whiting et al (2015) meta-analysis

# RCTs		# Reports	# Patients
28	Chronic Pain	63	2454
28	Nausea and vomiting due to chemotherapy	37	1772
14	Spasticity due to multiple sclerosis/ paraplegia	33	2280
4	HIV/AIDS	4	255
2	Sleep Disorder	5	54
2	Psychosis	9	91
2	Tourette syndrome	7	36
1	Anxiety disorder	1	24
1	Glaucoma	1	6
0	Depression		

Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for Medical Use: A Systematic Review and Meta-analysis. *JAMA*. 313:2456-2473, 2015

Chronic Pain

- ▶ Most common symptom for use (94% in CO, 85% in MI)
- ▶ Indications:
 - ▶ Neuropathy, arthritic, and muscle pain
 - ▶ Muscles stiffness, spasm and inflammation
 - ▶ Anxiety and depressed mood associated with chronic pain
- ▶ Study of neuropathic pain in a variety causes (MS, spinal cord injury, brachial plexus injury, limb amputation) showed CBD helpful
- ▶ CBD alone not helpful in cancer pain
- ▶ Can be used as adjunct to decrease or discontinue use of opioids



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Burn TL, Ann Pharmacother, 2006, Lynch ME, Br J Clin Pharmacol 2015, Neelakantan H, Behav Pharmacol 2015, JohnsonJR, J Pain Symptom Manage, 2010,

Summary - THC

- ▶ Best when used with CBD to reduce psychoactive effects.
 - ▶ 1:1 ratio is probably best for most conditions.
- ▶ Conditions potentially responsive:
 - ▶ Pain
 - ▶ Chronic pain, arthritis, cancer pain, nerve pain, fibromyalgia, myofascial pain syndrome
 - ▶ Opioid reduction
 - ▶ Anxiety
 - ▶ Insomnia
 - ▶ Spasticity
 - ▶ Appetite stimulation



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Summary - CBD

- ▶ Advantages - non-psychoactive and few side effects
- ▶ Conditions potentially responsive:
 - ▶ Pediatric seizures
 - ▶ Anxiety
 - ▶ Nausea and vomiting
 - ▶ Inflammatory conditions
 - ▶ Nerve (neuropathy) pain
 - ▶ Parkinson's disease
 - ▶ Spasticity

Side Effects

- ▶ Mostly related to THC
- ▶ Disorientation (most common), dizziness, anxiety, paranoia, depression, euphoria, drowsiness, red eyes, rapid heart rate, poor balance
- ▶ Geriatric patients may be more sensitive to the brain and heart side effects
- ▶ May lower seizure threshold
- ▶ May interact with other drugs
- ▶ Must not use with other psychoactive drugs or alcohol

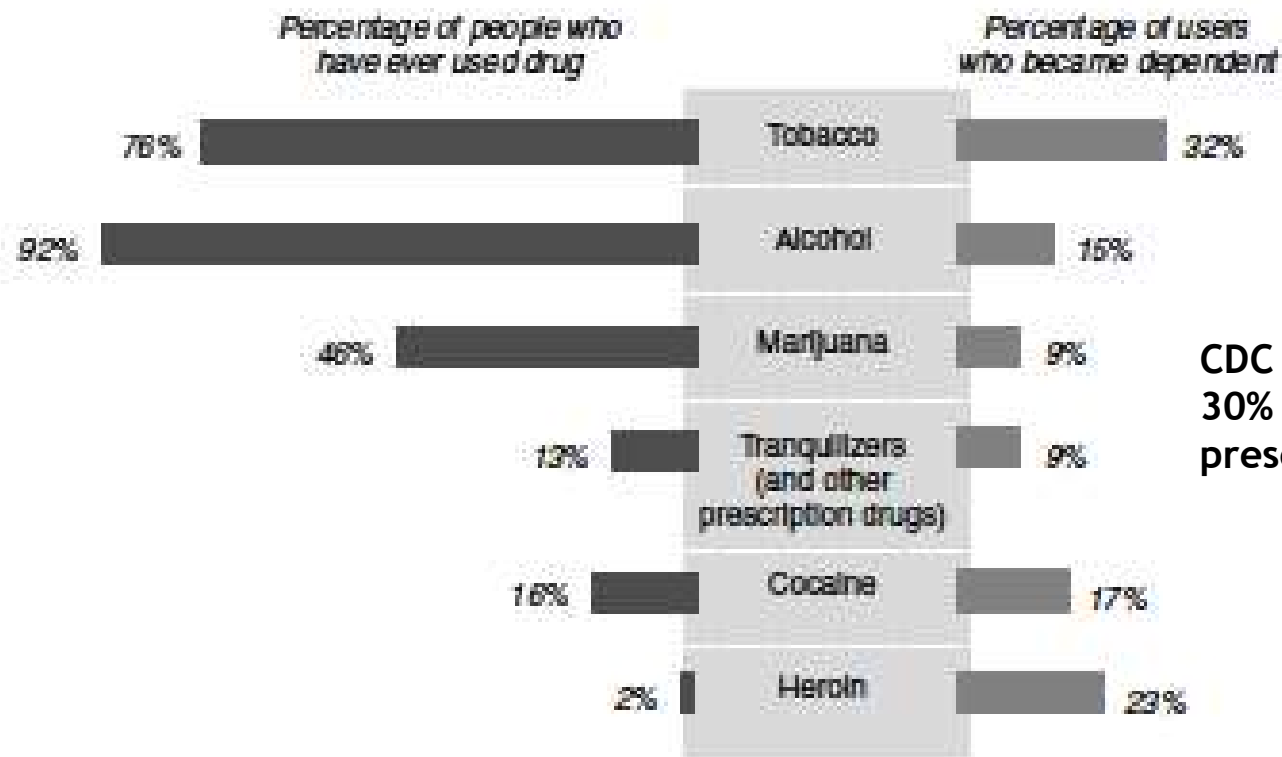
JAMA 2015;313:2456

Driving and Legal Aspects

- ▶ In states with recreational marijuana there is a significant increase in traffic stops and accidents
 - ▶ Mostly recreational users
 - ▶ Data unclear for medical only states
- ▶ Strongly advised not to drive or use mechanical equipment
- ▶ Suspicion of use for recreational or selling will lead to immediate discontinuation of certification by doctor
 - ▶ Possible legal action

BMJ 2012;344:e536; Epidemiol Rev 2012;34:65

Dependency Rates



CDC - 6% for 1 dose and 30% for 1 month use of prescription opioids

Experimental and Clinical Psychopharmacology, 1994;2:244-268; CDC MMWR 3/2017

Production and Extraction

- ▶ Very complicated
 - ▶ Multiple growth stages tightly controlled - lighting, nutrients, water, temperature
 - ▶ Avoidance of pesticides and chemicals
- ▶ Extraction
 - ▶ Depends on product (capsules, tinctures, oils)
 - ▶ Multiple steps to remove chlorophyll, lipids and fats, CO_2
 - ▶ Able to achieve a 98% pure cannabinoid state
 - ▶ Terpenes often added to duplicate natural state
- ▶ All samples tested for purity by chromatography and then sent out to an independent lab for confirmation



Resources

- ▶ Office of Medical Marijuana Use
 - ▶ <http://www.floridahealth.gov/programs-and-services/office-of-compassionate-use/>
- ▶ Florida physicians certified to order medical cannabis
 - ▶ http://www.floridahealth.gov/programs-and-services/office-of-compassionate-use/_documents/completed-cme.pdf
- ▶ Trulieve
 - ▶ <http://trulieve.com>
- ▶ Center for Medical Cannabis Research
 - ▶ <http://www.cmcr.ucsd.edu>
- ▶ Excellent articles
 - ▶ Savage SR, The Journal of Pain, Vol 17, No 6 (June), 2016: pp 654-668
 - ▶ Whiting PF, JAMA 2015;313(24):2456-2473
 - ▶ National Academies of Sciences, Engineering, and Medicine. 2017. The health effects of cannabis and cannabinoids: The current state of evidence and recommendations for research. Washington, DC: The National Academies Press



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