

“Mind the Gap” Cannabis, Cannabinoids and the Brain



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Faculty Disclosure

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Dr. J. Craig Allen has listed no financial interest/arrangement that would be considered a conflict of interest.

Learning Objectives



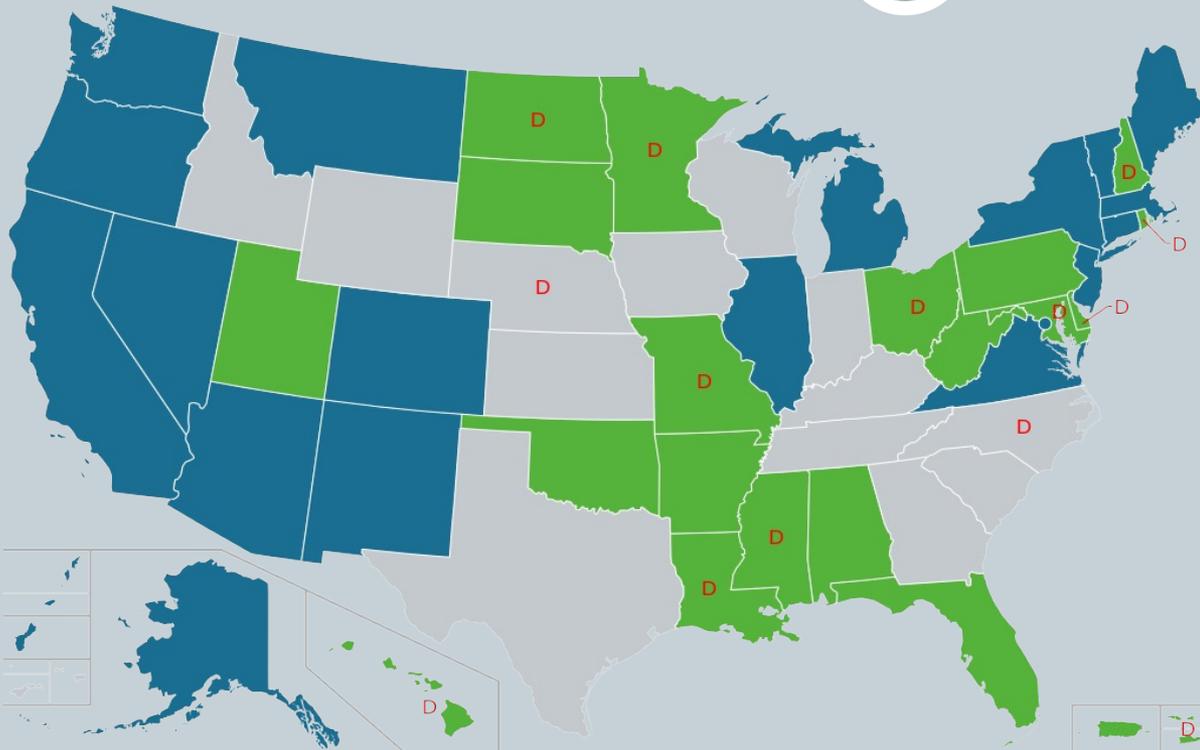
At the end of this talk you will be able to...

- Describe the current evidence supporting cannabis as medicine
- Recognize 4 high risk populations for cannabis exposure
- Understand considerations for health care professionals offering medical cannabis to their patients
- Relate recommendations to patients and their families regarding the use of marijuana and medical cannabis

Legality of Cannabis in the US



Medical Marijuana Laws



Legality of cannabis in the United States

- Legal
- Legal for medical use
- Legal for medical use, *limited THC content*
- Prohibited for any use
- Decriminalized

Notes:

- Includes laws which have not yet gone into effect.
- Cannabis *remains a Schedule I drug* under federal law.
- Some *Indian reservations* have legalization policies separate from the states they are located in.
- Cannabis is illegal in all *federal enclaves* (other than hemp).

Larry

25 yo male presents to his new PCP for a work physical with complaints of back and joint pain.

Larry shares....

HS grad, working in warehouse, lives with family.

BMI >50 with recent 50 pound diet and exercise related weight reduction.

Back pain is chronic but has flared up and negatively impacting his ability to engage in exercise activities.

Minimal relief from heating or stretching, ns aids, or course of chiropractic care.

Seeing a local psychiatrist for anxiety.



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J. Craig Allen, MD @JCAllenMD · Jul 24

"The American public has a much more favorable point of view than is warranted by the evidence," Dr. Salomeh Keyhani UC San Francisco "Perhaps most concerning is that they think that it prevents health problems" @BartAndrews @DrHowardLiu @drmanejwala @UjjRam @MDSantopietro #SUD

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WEB EXCLUSIVES

AUTHOR INFO

ORIGINAL RESEARCH | 24 JULY 2018

Risks and Benefits of Marijuana Use: A National Survey of U.S. Adults

Salomeh Keyhani, MD, MPH; Stacey Steigerwald, MSSA; Julie Ishida, MD, MAS; Marzieh Vali, MS; Magdalena Cerdá, DrPH; Deborah Hasin, PhD; Camille Dollinger, BS; Sodahm R. Yoo, BS; Beth E. Cohen, MD, MAS

Conclusion: Americans' view of marijuana use is more favorable than existing evidence supports.

What About Doctors?



- 89.5%
 - felt “not at all prepared” to prescribe medical marijuana
- 35.3%
 - felt “not at all prepared” to answer questions
- 84.9%
 - reported no education on medical marijuana
- 9%
 - of medical school curriculums teach content on medical marijuana

Physicians-in-training are not prepared to prescribe medical marijuana

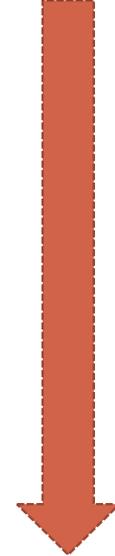
Evanoff, Anastasia B. et al.

Drug & Alcohol Dependence , Volume 180 , 151 - 155

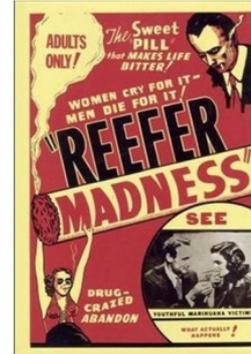
History of Cannabis as Medicine



1970
Controlled Substance Act
Schedule 1.
medical use, abuse potential
likelihood of addiction



1936



marijuana
tax act of
1937



1970

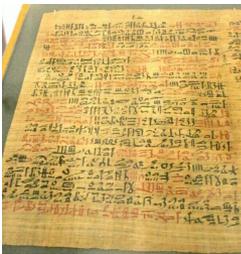


Portrait of the Red Emperor Shen Nung (2838 - 2698 B.C.)

2900-2737
B.C



1,550 BC



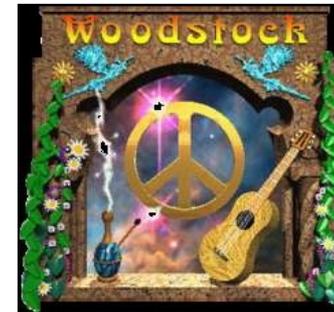
1850: U.S. Pharmacopeia. It was used as a treatment for opioid withdrawal, pain, appetite stimulation, and relief of nausea and vomiting.¹

1898
Sir William Osler
"probably the most satisfactory remedy for migraines"

1906 Pure Food and Drug Act – Required labeling over-the-counter remedies (after tobacco industry lobbying efforts, nicotine is removed from the list)



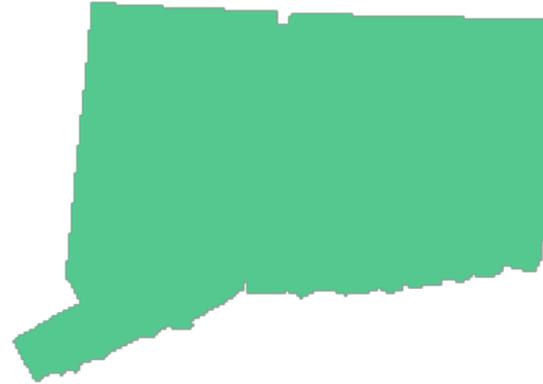
1969



1996 Medical Use Legalized in California Proposition 215 with AIDS, cancer, and other diseases.

1942: Marijuana was removed from the U.S. Pharmacopoeia

Cannabis in Connecticut

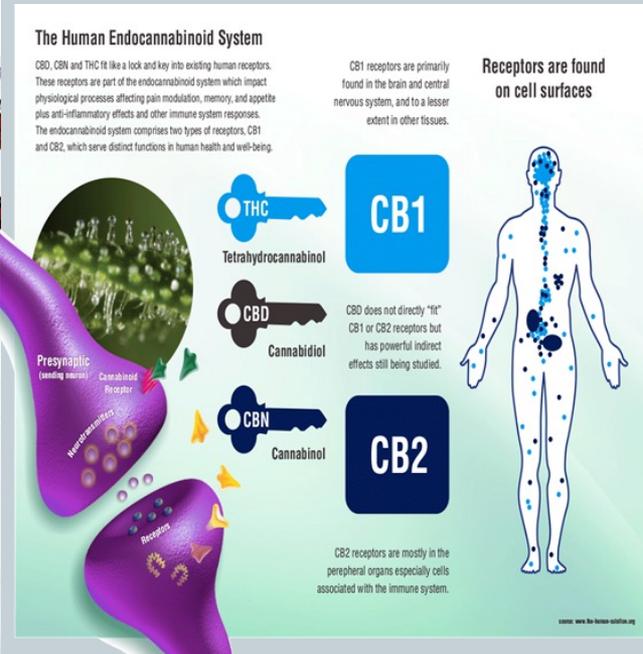
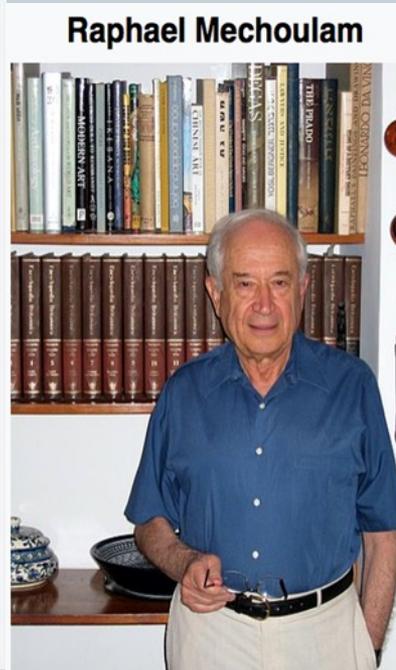
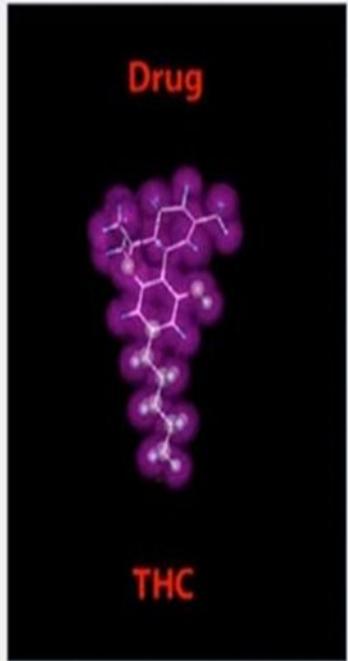
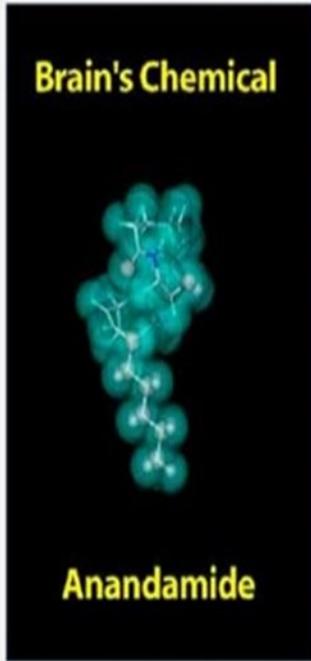


- 2012:** Medical marijuana
- 2015:** Decriminalized possession of recreational marijuana
- 2021:** 21 and older possess or consume
- 2021:** 18 and older are allowed to grow cannabis plants for personal medical use.
- 2022:** Retail (recreational dispensaries open)
- 2023:** 21 and older are allowed to grow cannabis plants for personal use.

Marijuana is federally prohibited.

- Banking commissioner (eg. electronic payments; depository banking and mortgages).
- Insurance commissioner.

Endocannabinoid System



N-arachidonylethanolamine (AEA)
2-arachidonoyl glycerol (2-AG)

Endocannabinoid System

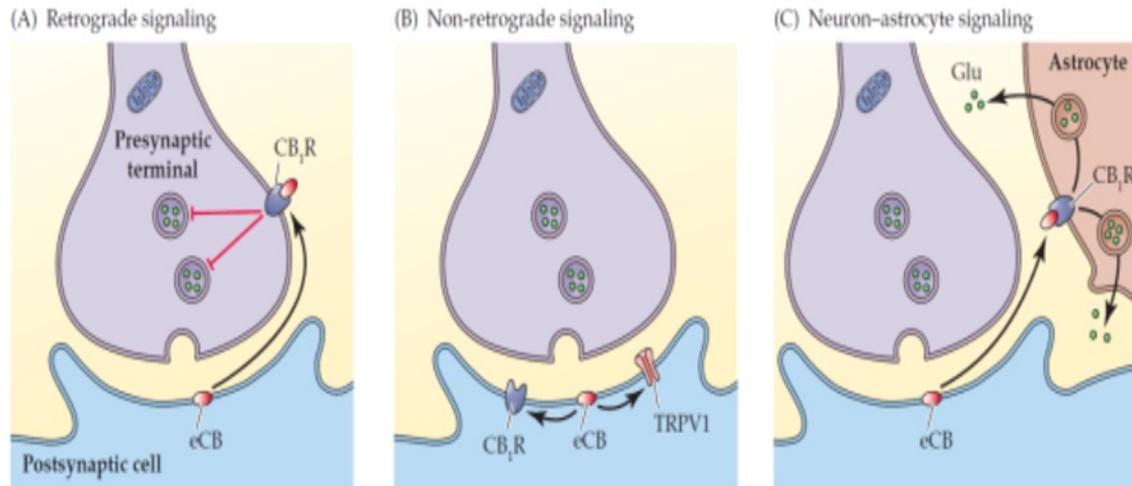


FIGURE 14.11 Mechanisms of endocannabinoid signaling (A) The most common and well-understood mechanism of endocannabinoid action is retrograde signaling. This mechanism involves release of the endocannabinoid (eCB), typically 2-AG, which diffuses from its site of synthesis in a dendritic spine to a presynaptic element where it activates CB₁ receptors (CB₁R). Such activation inhibits Ca²⁺-mediated vesicular neurotransmitter release.

(B) In the second mechanism, an endocannabinoid such as anandamide remains within the dendritic spine to activate either postsynaptic CB₁ receptors or TRPV1 cation channels. (C) The third mechanism involves endocannabinoid activation of astrocyte CB₁ receptors, which has been shown to provoke glutamate (Glu) release from the cells. (After Castillo et al., 2012.)

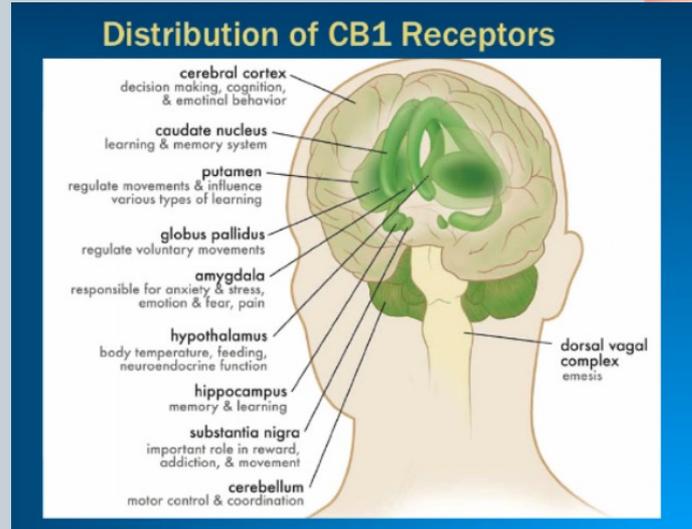
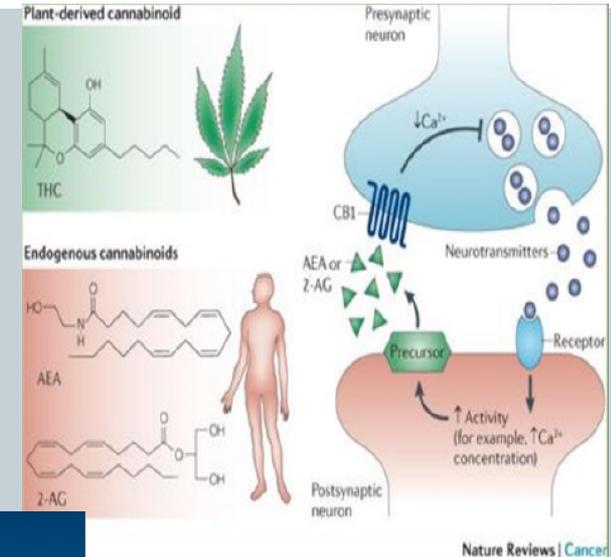
Endocannabinoid System

The Neuron's "Volume control":

- Dials down neuron activity and neurotransmitter release when too strong
- Regulates levels of neurotransmitters (mood, pain, appetite, motivation, memory, growth and reproductive hormones)
- Keeps neuronal activity in balance

Kraft, U. Scientific American Mind, 2006, p.62-65

Shapes brain development:



Endocannabinoid System

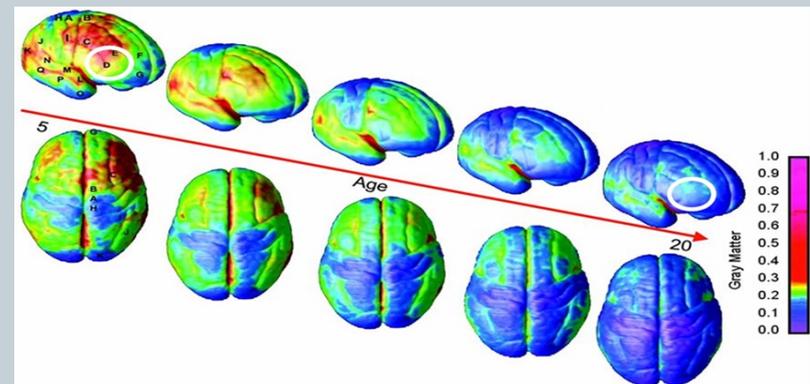
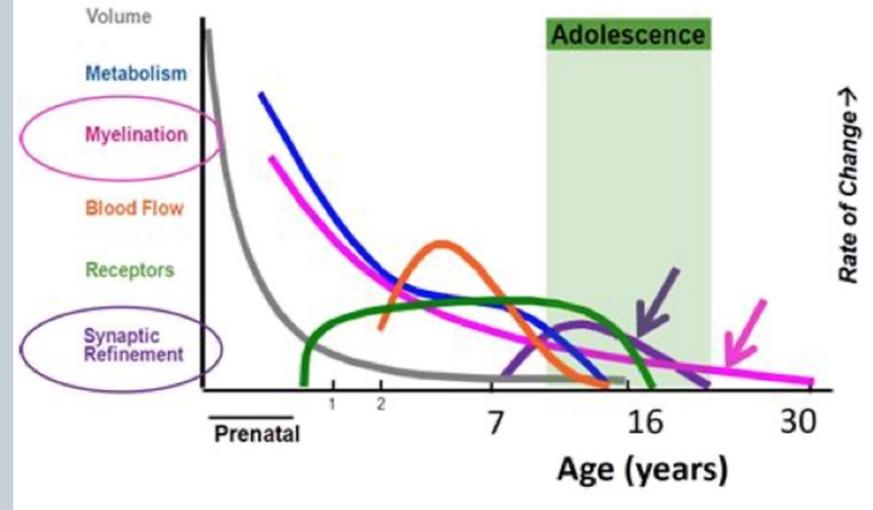
The Neuron's "Volume control":

Kraft, U. Scientific American Mind, 2006, p.62-65

Shapes brain development:

- Guides neuron grow and functioning
- Effects pruning and brain wiring
- Supports myelin growth (oligodendrocyte function)

Galve-rRoperh I, Palazuelos H, ?Aguado T, Guzman M. Eur Arch Psychiatry Clin neurosci. 2009: 371-382.



Definitions



- **FDA approved medication**
 - FDA review and approval process - ensures safety and effectiveness
 - Off label use of an FDA approved medication
- **Over the counter FDA approved products**
 - Category I Generally recognized as safe and effective (GRASE).
- **Non-FDA-approved products available under the authority of state-level programs ie. legislatively approved**
 - Connecticut's Medical Marijuana Program administered by Department of Consumer Protection
- **Non-FDA-approved products available over the counter**

FDA-APPROVED CANNABINOIDS

Medication	Type	Indication
Dronabinol (Marinol®; Syndros®)	Synthetic THC	-Chemotherapy-induced nausea and vomiting -Anorexia/wasting in HIV/AIDS
Nabilone (Cesamet™)	Synthetic substance similar to THC	-Chemotherapy-induced nausea and vomiting
Cannabidiol (Epidiolex®)	Plant-derived CBD	-Lennox-Gastaut; Dravet's