



THE SCIENCE OF MEDICAL CANNABIS AND ITS THERAPEUTIC BENEFITS



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Medical Cannabis



The New York Times
New York
When Older Age Comes With Daily Doses of Medical Marijuana

Medical Cannabis in the Elderly



<https://www.youtube.com/watch?v=0A3CRiN0hak>

Disclosures

- No financial relationships to disclose.

Objectives

- To appreciate the therapeutic benefit of medical cannabis from an historical perspective.
- To understand the science behind medical cannabis.
- To review which medical conditions can potentially benefit from medical cannabis therapy.

The Science of Medical Cannabis

- History of cannabis
- Pharmacology
- Indications
- Concerns in the elderly
- Federal vs. State laws
- Challenges in the nursing home



Cannabis sativa

History of Cannabis

- 2700 BC – China- Shen Nung first describes cannabis medicinally as treatment for malaria, constipation, and rheumatic pains.
- 1400 BC – India- *Atharva Veda* scriptures ascribe sacred virtues to cannabis for its medicinal benefits (analgesic, anticonvulsant, anti-inflammatory, anti-spasmodic, appetite stimulant, diuretic, antibiotic, anti-parasitic).
- 1000 BC –Tibet- Tantric Buddhism adopts Ayurvedic (Hindu) medicinal therapies. Cannabis becomes sacred, and use spreads through Middle East and Africa.

History of Cannabis

- 1839- UK- Dr. William O'Shaughnessy returns from service in Calcutta.
- 1842- Publishes a landmark paper on the medicinal use of cannabis for antispasmodic, antiemetic, analgesic, anticonvulsant, and appetite stimulant effects.
- 1850- United States Pharmacopeia adds *Extractum Cannabis* (tincture of cannabis sativa extract in an alcohol base).

History of Cannabis

- 1850-1900's- Cannabis is an accepted medical therapy. Over 100 scientific articles are published in Europe and US on efficacy of cannabis extract.
- Lancet article in 1880 stressing importance of dose titration to avoid "toxic effects" (Reynolds).

Challenges to Cannabis use

- Variabilities in concentration/dosage
- Bioavailability/storage stability
- Unpredictability
- Synthetic alternatives

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- Progressive Era
- Increase in recreational use (smoking)
- Marijuana
- "Reefer Madness" (1936)



Position of the AMA

• “There is nothing in the medicinal use of Cannabis that has any relation to Cannabis addiction. I use the word ‘Cannabis’ in preference to the word ‘marihuana’, because Cannabis is the correct term for describing the plant and its products. The term ‘marihuana’ is a mongrel word that has crept into this country over the Mexican border and has no general meaning, except as it relates to the use of Cannabis preparations for smoking...To say, however, as has been proposed here, that the use of the drug should be prevented by a prohibitive tax, loses sight of the fact that future investigation may show that there are substantial medical uses for Cannabis.”

-William C. Woodward MD, Legislative Council of the American Medical Association, in a report before US House of Representatives Ways and Means Committee, May 4, 1937.

Cannabis becomes prohibited


- 1937-Marihuana Tax Act is enacted.
- 1942- US Pharmacopeia removes cannabis.
- 1944- LaGuardia Committee.
- 1956- Narcotics Control Act.
- 1971- Controlled Substances Act (schedule I).
- 1973- DEA established.

Pharmacology

- 1964-THC first isolated as an active component.
- 1990-Cannabinoid receptor system identified.
- 1992-Anandamide isolated.
- Endocannabinoids/Phytocannabinoids

Pharmacology


Brain's Chemical



Anandamide

endocannabinoid

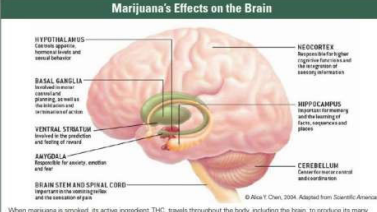
Drug



THC

phytocannabinoid

Marijuana's Effects on the Brain



© Alan F. Clark, 2006. Adapted from Scientific American 295, 10, 104-110.

When marijuana is smoked, its active ingredient, THC, travels throughout the body, including the brain, to produce its many effects. THC attaches to sites called cannabinoid receptors on nerve cells in the brain, affecting the way those cells work. Cannabinoid receptors are abundant in parts of the brain that regulate movement, coordination, learning and memory, higher cognitive functions such as judgment, and pleasure.

Source: NIH/NIDA website

Endocannabinoid system

- N-arachidonylethanolamine (anandamide).
- 2-arachidonoylglycerol (2-AG).
- Fatty acid amidohydrolase (FAAH).

Endocannabinoid system

- **CB1 receptor** primarily presynaptic in brain and peripheral neurons. Inhibits neurotransmitter release. Psychoactive. Cognition and memory, reward sensation, sensory perception, motor control, pain modulation, appetite, and emotional response.
- **CB2 receptor** primarily on cell membrane of B cells, T cells, and macrophages. Inhibits immune cell activation and cytokine production. Immunomodulatory and anti-inflammatory effects.

Phytocannabinoids

• Over 100 identified. The two most active are:

• Δ^9 -Tetrahydrocannabinol (THC)

• Cannabidiol (CBD)

The “Entourage Effect” (?)



CBD

CBD acts on cannabinoid (CB) receptors, which are found in numerous areas of the body, including the peripheral and central nervous systems

CB1 receptors are found pre-synaptically within the neural pathways of the brain and spinal cord. CBD prevents metabolism of endocannabinoids and neuromodulation.

CB2 receptors have an effect on immune cells, where CBD may affect anti-inflammatory processes, decreasing the inflammatory response, and inflammatory modulation.

Phytocannabinoids

• Δ^9 -THC most psychoactive. CB1/CB2 receptor agonist. Metabolized by FAAH to 11-OH-THC form (not euphoric).

• CBD not psychoactive. No direct CB1/CB2 binding. Inhibits FAAH, thus increasing levels of the brain's endogenous cannabinoids, ie. [anandamide]. In conjunction with THC admin will increase [delta-9 form].

• Inhibits FAAH inhibits metabolism of Δ^9 -THC.

• COX inhibition, modulates pain.



Cannabinoids-FDA approved

- Dronabinol (THC) for anorexia HIV/AIDS, chemo-related refractory nausea/vomiting. (III)
- Nabilone (THC) for chemo-related nausea and vomiting. (II)
- Epidiolex (CBD) for refractory pediatric seizures. (V)

• In phase 3 trials

- Nabiximols (1:1 CBD:THC) for MS spasticity.

Epidiolex (CBD)

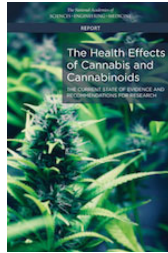


Current legal status of cannabis

- Federal – Schedule I.
- State – Currently **33** states, DC, Guam, PR, have passed legislation legalizing medicinal use of cannabis.
- California first in 1996.
- Wisconsin-limited to CBD oil only, for seizure diagnosis.
- Lack of uniformity/variability among states.
- Rohrabacher-Farr Amendment (2014)
- Compassionate Care Act (NYSPHL, XIII:104)

Clinical Reference

- 2017 National Academies
The Health Effects of
Cannabis and Cannabinoids



<https://www.nap.edu/read/24625>

Approved indications - NYS

- Multiple Sclerosis
- Parkinson's Disease
- Huntington's Disease
- ALS
- Seizures
- Spinal cord injury
- Chronic pain
- Acute pain
- Neuropathy
- Cancer
- HIV
- AIDS
- IBD
- PTSD
- Opioid use disorder

Approved modes of administration - NYS

- **1. Vaporization**
 - Cartridges contain refined oil containing specific ratios of CBD & THC
 - Oil is heated until it vaporizes and is inhaled
 - Immediate onset, duration about 3 hours.
- **2. Tincture/Oral Solution**
 - Administered by sublingual, transmucosal or oral route
 - May be used topically as well
 - Onset of 15 minutes, duration about 6 hours
- **3. Capsule**
 - Oil-filled oral capsules containing specific ratio of CBD:THC
 - May contain proprietary blend of other compounds derived from cannabis plant.
 - Onset of 1-2 hours, duration about 8-12 hours

Case studies

- Ruth B.
- Joanna P.
- Helen W.

Health Affairs, July 6, 2016

- Data source: Medicare Part D enrollees from 2010 to 2013, in District of Columbia and 17 states where medical cannabis laws were enacted.
- Data collected: Total number of prescriptions filled during the study period was measured.

Health Affairs, July 6, 2016

- Findings: Use of prescription drugs for pain, depression, seizures, anxiety, nausea, psychoses, and sleep disorders decreased significantly, once a medical marijuana law was implemented.
- National reductions in Medicare program and enrollee spending when states implemented medical marijuana laws were estimated to be \$165.2 million/year in 2013.
- Conclusions: The availability of medical marijuana has a significant effect on de-prescribing patterns.

European Journal of Internal Medicine,
 March 2018 Volume 49:44-50.

Epidemiological characteristics, safety and efficacy of medical cannabis in the elderly.

- 2736 patients above 65 years of age began cannabis treatment and responded to the questionnaire. Mean age was 74.5 ± 7.5 years. The most common indications for cannabis treatment were pain (66.6%) and cancer (60.8%).

Results:

- After six months of treatment, 93.7% of the respondents reported improvement in their condition and the reported pain level was reduced from a median of 8 on a scale of 0-10 to a median of 4.
- 35% reported decrease in total number of meds or dosage.
- 18.1% stopped using opioid analgesics or reduced their dose.

Adverse effects:

- Falls (21.9%), Dizziness (9.7%), dry mouth (7.1%)

Conclusion:

- Therapeutic use of cannabis may decrease the use of other prescription medicines, including opioids.

Concerns in the elderly

- Cognitive impairment
- Dizziness
- Falls risk
- Coronary ischemia
- Respiratory symptoms (smoking)

Challenges In the Nursing Home

- Federal law – skilled nursing facility.
 Restrictions on possession, administration
- State law – patient.
 Rights of the individual NYS resident

How can we find a safe (and legal) balance?



Conclusions

- Wealth of historical clinical experience.
- Limited high-quality scientific clinical trials.
- Symptom management – pain, spasticity, emesis, seizure.
- Clinical decision-making should always be individualized.
- Age should not be a contraindication to use.

