Marijuana:
Legal History, Neuro-Science & Toxicology

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Judge Mary A. Celeste (Ret.)

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Overview
- Legal History of MJ
- Neuro-Science THC/Cannabis
- MJ Science/Medical Marijuana
- THC Toxicology

Early History
- Early MJ History
- 3000 B.C. Siberia burial grounds
- 3000 B.C. Chinese as Medicine
- Shakespeare’s Pipes
- U.S. Washington Hemp in Mt Vernon
- A Gift from the Good Doctor
  - Dr. William O’Shaughnessy 1839
  - Medicinal Preparations
    - Cannabis became available in American pharmacies in the 1850s
      - 1910-20 USA
      - Marijuana as a Poison
    - 1910 there was a wave of legislation aimed to strengthen requirements for sale
    - Legislation restricted all narcotics, including cannabis, as poisons, limit their sale to pharmacies, and required doctor's prescriptions
    - Under poison laws definitions had to labeled as poison
    - Outright prohibitions began in the 1920s
      - 1930s Cannabis as a Pharmaceutical
    - Parker-Davis and Eli Lily were selling standardized extracts of marijuana for use as an analgesic, an antispasmodic and sedative.
      - Grimault & Company, marketed marijuana cigarettes as a remedy for asthma
        - 1930-40’s
        - 1950s-1970 USA
    - Boggs Act 1952
    - Narcotics Control Act 1956
    - NCA made a first-time possession offense a minimum of two to ten years with a fine up to $20,000
    - 1969 Leary v. U.S
1950s-1970 USA

- **Control Substances Act** as Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970, which repealed the Marijuana Tax Act
- Cannabis became a Schedule I Control along with heroine and LSD
- On December 1, 1975, the Supreme Court ruled that it was "not cruel or unusual" for Ohio to sentence someone to 20 years for having or selling cannabis
- A controlled (scheduled) drug is one whose use and distribution is tightly controlled because of its abuse potential or risk.
- Five categories for drugs Schedule I is reserved for what the DEA considers to be the "most dangerous" drugs without currently accepted medical value.
- Schedule I — drugs with a high abuse risk. These drugs have NO safe, accepted medical use in the United States. Some examples are heroin, marijuana, LSD, PCP, and crack cocaine. {Synthetic Pink}
- Schedule II — drugs with a high abuse risk, but also have safe and accepted medical uses in the United States. These drugs can cause severe psychological or physical dependence. Schedule II drugs include certain narcotic, stimulant, and depressant drugs. Some examples are morphine, cocaine, oxycodone (Percodan®), methylphenidate (Ritalin®), and dextroamphetamine (Dexedrine®).

Cannabis
- Flowering plants that include three putative varieties, sativa, indica, and ruderalis.
- Indigenous to Central and South Asia
- Most used illicit drug in the world
- Active ingredient Delta 9 THC. Resinous substance is known as Hashish
  - MJ & Its Compounds
  - 483 chemical constituents isolated and identified in cannabis to date
  - 60-109 cannabinoids. Some are psychoactive and some are not
  - THC main psychoactive cannabinoid
  - Some 20 Flavonoids
  - 120 Terpenes
The Endocannabinoid System

Cannabinoid Receptors in Brain & Body

Believed to be more numerous than any other receptor system in every living animal on the planet above Hydra and Mollusks 2014 fruit fly

What are Receptors

Receptors are binding sites for chemicals in the brain, chemicals that instruct brain cells to start, stop or otherwise regulate various brain and body functions.

The chemicals which trigger receptors are known as neurotransmitters.

Receptors for Cannabis

There are currently two known subtypes of cannabinoid receptors CB1 and CB2

The CB1 receptor is expressed mainly in the brain (central nervous system or CNS). Also in the lungs, liver and kidneys

Location of Cannabinoid Receptors

Endocannabinoids

Endocannabinoids are the substances our bodies naturally make to stimulate cannabinoid receptors.

Cannabinoid Receptors

Natural transmitter or “endocannabinoid” that fits those receptors: anandamide

More recently an even more important endocannabinoid that normally activates these receptors was discovered 2AG (2 arachidonyl glycerol)

Anandamide

The Bliss Molecule

THC begins this process by binding to the CB1 receptors for anandamide

Anandamide is involved in regulating mood, memory, appetite, pain, cognition, and emotions

Three compounds that strongly resemble anandamide were found in dark chocolate 1996

Corollary

Morphine and Endorphins

Opiate Receptors

In 1972 found that the human brain's neurons had specific receptor sites for opiate drugs: opium, heroin, codeine and morphine

The active ingredient in all these opiates - morphine - had a chemical structure similar to endorphins, a class of chemicals present in the brain

Endorphins are feel-good chemicals naturally-manufactured in the brain when the body experiences pain or stress. They are called the natural opiates of the body

Scheme Endocannabinoid System

IDENTIFICATION

THC Identified - 1964

Opiate Receptors - 1972

Cannabinoid Receptors - 1988

Anandamide Identified - 1992
Brain cells (neurons) communicate with each other and with the rest of the body by sending chemical “messages.” These messages help coordinate and regulate everything we feel, think, and do. Typically, the chemicals (called neurotransmitters) are released from a neuron (a presynaptic cell), travel across a small gap (the synapse), and then attach to specific receptors located on a nearby neuron (postsynaptic cell).

Sativex
Available in the United Kingdom and Canada
Chemically pure mixture of plant-derived THC and Cannabidiol Formulated as a mouth spray
Relieves cancer-associated pain, spasticity and neuropathic pain in multiple sclerosis

DEA Eases Requirements for FDA Approved Clinical Trials on CBD

CBD contains less than 1 percent THC and has shown some potential medicinal value, there is great interest in studying it for medical applications
December 2016 CBD designated as a Schedule I


Cannabinoids
Substantial Evidence: chronic pain in adults; chemotherapy-induced nausea and vomiting; MS spasticity symptom
Moderate Evidence: sleep disturbance associated with obstructive sleep apnea syndrome; fibromyalgia, chronic pain, and MS
Limited Evidence: MS: Tourette syndrome; PTSD; dementia; glaucoma; social anxiety disorders;

Examples of MJ Acute Affects
2016 Independent Predictor of Stress Cardiomyopathy in Younger Men
2016 Heavy cannabis use associated with reduced dopamine release in brain affecting learning behavior
2015 Pot Affects Corpus Callosum
2015 Affects Bipolar
2015 Psychosis
2015 Shorter Boys
2015 Male adolescents at high risk for schizophrenia
2015 Shrinks & Rewires Brain
2014 Reduction in IQ under 21
MJ Toxicology
Toxicology: the study of poisonous chemicals, drugs, etc., and how a person or other living thing reacts to them

Drugs
Route of Administration
Elimination & Detection

Route of administration (injected, inhaled etc.)
Detection time: The length of time that a drug or its metabolite is present in a given biological sample. This may vary depending on the dose (amount)

Elimination rate (how long it takes the body to get rid of the substance)

Manner of Ingestion
Route of Administration

Cigarette -- Dried marijuana buds are rolled into a cigarette, also called a joint.
Cigar -- Slice open a cigar, remove the tobacco and refill it with marijuana. Often called a blunt.
Pipe – Tobacco pipes are also used to smoke marijuana.
Bong -- Water pipes, typically with a long tube rising out of a bowl-shaped base, trap smoke until it's inhaled, raising the amount of THC taken in.
Food -- Marijuana is sometimes baked into foods, such as brownies, or brewed as tea.
Vaporize-Vape heating the cannabis plant/concentrate between approximately 250°F and 400°F

Dabbing the Concentrates
Wax, Budder, Shatter, Honey

Dabbing is the act of consuming the concentrate
A dab is a small amount of a concentrated cannabis extract. “Taking a dab” refers to the process of touching, or “dabbing”, this small amount of extract against a heat source, a titanium nail in most cases (sometimes glass or quartz), in order to vaporize the extract.

Dabbing the Concentrates
Wax, Budder, Shatter, Honey

Marijuana wax (budder) is a cannabis concentrate that has the consistency of ear wax. This is made from a butane extraction — hence the name Butane Hash Oil, or BHO
Shatter behaves like glass in its stable form and can be easily broken apart when poked. Shatter lasts longer and is more stable but is often difficult to handle

MJ Toxicology
Elimination

Active
THC a/k/a delta-9-tetrahydrocannabinol is the main psychoactive substance found in marijuana

Metabolites
11-Hydroxy-THC (aka 11-OH-THC) is the main psychoactive metabolite of THC formed in the body after marijuana consumption
11-nor-9-Carboxy-THC (aka 11-nor-9-carboxy-delta-9-tetrahydrocannabinol, 11-nor-9-carboxy-delta-9-THC, 11-COOH-THC, THC-COOH, and THC-11-oic acid, ) is the main secondary metabolite of THC which is formed in the body after marijuana is consumed. It is NOT active.
Alcohol vs. Drugs
Alcohol is metabolized at a predictable rate
Drugs are not eliminated from the body in a predictable way
Unlike alcohol, there is no retrograde extrapolation for drugs
THC rapidly dissipates 1-2 hours after use/THC levels drops over 80% within first hour of smoking
The time it takes to move through the body can vary from person to person and depends significantly on:
The amount of MJ used
The method and frequency of use
The user's rate of metabolism
The concentration of THC

THC typically reaches the brain seconds after it is inhaled.
The drug and its metabolites are lipophilic (fat soluble), and thus are easily able to pass through the blood-brain barrier
Even antibiotics, or drugs for cancer treatment, do not cross this barrier
Yet, cannabis is able to penetrate the two layers of cells that form the blood-brain barrier.
After metabolism in the lungs and liver, into its metabolites, THC moves rapidly to lipid-rich tissues in the body, including the brain

“The major difference is in the absorption of the [edible] product into the blood stream,”
With smoking, the peak blood levels happen within 3-10 minutes,
With eating, it’s 1-3 hours.
The initial effects created by the THC in MJ wear off after an hour or two, but the chemicals stay in your body for much longer.
THC levels are consistently higher in the brain than they are in the blood. It’s the brain that is impaired, not the blood.

Assumption that cannabinoids will remain detectable in urine for 30 days or longer following the use of marijuana
THC is not found in its active form in urine rather as the metabolite THC-COOH…
For new or infrequent users, the window of time for detection (50ng/ml limit) is believed to last 1 to 2 days
On the other hand, studies have shown that regular users can test positive (20 ng/ml limit) for THC metabolites for up to 46 consecutive days following marijuana usage
In an extreme case, a heavy cannabis user of more than **10 years** was able to test positive (20 ng/ml limit) for up to **67 days** after last being exposed to marijuana.

**Rising & Lowering Concentrations**

**Chronic Users**

- 28 men and women ages 19-38 chronic users sequestered in a closed clinical setting blood and urine samples were collected daily.
- Within 19 hours, 13 people tested negative.
- Of the 15 people who tested positive for THC after the first test, all but 5 had 1 or more blood sample come up negative and then turn positive days later.
- In fact, more people tested positive on day 5 than on day 4.

**Rising & Lowering Concentrations**

**Chronic Users**

- The 5 people whose blood tested THC-positive during the first 7 days were all women
- Urine tested positive 6 days longer in women than in men

**MJ Detection**

**TECHNOLOGY ON THE HORIZON**

- Laser Technology to Detect Drugs
- Fingerprint Technology
- Oral Fluid
- Electronic Sensor
- Drug Breathalyzer