

Marijuana:
Legal History, Neuro-Science
& Toxicology

- ⦿ LifeSavers Conference
- ⦿ Charlotte, North Carolina
 - ⦿ March 28, 2017
- ⦿ Judge Mary A. Celeste (Ret.)

The following presentation may not be copied
in whole or in part without the written permission of the author
© Celeste

- ⦿ 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 be labeled as poison
 - ⦿ Outright prohibitions began in the 1920s
 - ⦿ 1930s Cannabis as a Pharmaceutical
- Parker-Davis and Eli Lilly 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- ⦿ **Control Substances Act** as Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970, which repealed the Marijuana Tax Act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 heroin 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
 - ⦿ Control Substances Act
- ⦿ 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**.
 - ⦿ Control Substances I-V
- ⦿ **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®).
 - ⦿ Reclassifying MJ?
- ⦿ 2015 CARES Act
- ⦿ 2015 *Schweder & 2016 Pickard*
- ⦿ 2016 American College of Physicians, and other professional health-oriented societies
- ⦿ 2016 Utah Legislature
- ⦿ 2016 DEA Denied Reclassification

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
(aka molecules)
- ⦿ **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
1
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 arachido noyl 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

- ⊙ Anandamide

- ⊙ 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

- ⊙ 2AG Identified - 1995
 - ⊙ How Brain Cells Communicate
- ⊙ 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
- ⊙ How Brain Cells Communicate

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)

- ⊙ Cell Communication
- ⊙ Science/Medical Marijuana
- ⊙ 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
 - ⊙ Dec 23, 2015
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

The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence...: Jan., 2017 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
 - ⊙ 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.

⦿ Metabolization

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
- ⦿ How MJ Moves Through the Body
- ⦿ 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

The Blood-Brain Barrier

- ⦿ How MJ Moves Through the Body
- ⦿ 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
- ⦿ How MJ Moves Through the Body
- ⦿ 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
- ⦿ Inhaled v. Eatable
- ⦿ “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.
- ⦿ How MJ Moves Through the Body
- ⦿ 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.

⦿ Metabilization of MJ

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**

⦿ Metabilization of MJ

- ⦿ 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