What’s Medical About Marijuana

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Today

• What we know/what we don’t know
• Pharmacology
• Medical Use
• Addiction
• Utah
What We Know

• There are medically impactful components of Marijuana.
• Of the 400+ components in Marijuana, we know virtually nothing about all but a few
• We will talk about the two we have the most information on:
  – $\Delta^9$ Tetrahydrocannabinol (THC)
  – CBD
Δ⁹ Tetrahydrocannabinol

- Primary psychoactive component of Marijuana (it gets you high).
Cannabidiol (CBD)

• Non-Psychoactive Cannabinoid promoted as therapeutic.
Medical Benefits
What Does Marijuana Cure?

• EVERYTHING!!!
  – Cancer
  – Scoliosis pain
  – Any pain
  – Dietary Problems
  – Cancer (all of it)
  – Headaches
  – Anxiety
  – Depression
  – Epilepsy
  – Crohn’s Disease
  – Multiple Sclerosis
  – Arthritis
  – Anything else you can think of
What is it good for?

It depends on the State Laws but the medical community generally agrees that it has an IMPACT that MAY be beneficial for:

- Muscle spasms caused by multiple sclerosis₁
- Nausea from cancer chemotherapy₁
- Poor appetite and weight loss caused by chronic illness, such as AIDS.
- Nerve pain₁
- Seizure disorders₁
- Crohn's disease₁
- **Marinol and Cesamet (Synthetic medications)₂**
  - **Appetite Stimulation:** The appetite stimulant effect of Marinol Capsules in the treatment of AIDS-related anorexia associated with weight loss was studied in a randomized, double-blind, placebo-controlled study involving 139 patients.
  - **Antiemetic:** Marinol Capsules treatment of chemotherapy-induced emesis was evaluated in 454 patients with cancer
How does it work

• Interacts with the body’s endocannabinoid system.
  – There are approximately 60 cannabinoids in Marijuana and the human body produces about 5 naturally.
  – CB1, CB2 receptors both respond to these and are found throughout the body and with high concentrations in the Nervous system
CB Receptors

- CB1 receptors are concentrated in the brain
- CB2 receptors are concentrated in the spleen and other peripheral tissues
- Both are located throughout the body
Yeah, but how does it work?

“Although the physiological implications of these ligand-receptor interactions are not completely understood, it is suggested to be connected with opioids, GABAergic, dopaminergic, noradrenergic, serotonergic, cholinergic, glucocorticoid and prostaglandin systems (26, 28, 30, 33). The many effects of exogenous cannabinoids derived from cannabis result from perturbation of this complex system, but the exact mechanism is not clear”.

Perturbation - a deviation of a system, moving object, or process from its regular or normal state of path, caused by an outside influence.
Systems thought to be perturbated

- Dopaminergic – the dopamine system
- Endogenous opioid system – Opioid system
- GABAergic - neurotransmitter gamma-aminobutyric acid system (Chief inhibitory neurotransmitter in the CNS of vertebrates)
- Noradrenergic – Norepinephrine System
- Serotonergic – good luck finding a simple and understandable description of this system...it deals with serotonin which impacts inhibition of both sensory input and behavioral output
- Cholinergic – Parasympathetic nervous system responsive to acetylcholine.
- Glucocorticoid – Steroid hormone that impacts metabolism
- Prostaglandin – enzymatic derived from fatty acids and they impact multiple functions...like regulate smooth muscle contraction.
Highest Density of CB Receptors

• Cerebral Cortex
  – Memory, Thinking, Perceptual Awareness, Consciousness
• Hypothalamus
  – Metabolic processes (appetite)
• Brain Stem
  – Basic Functions; Heart Rate, Blood Pressure, Arousal, Pain, etc.
• Hippocampus
  – Memory Storage and Recall
• Cerebellum
  – Coordination and Movement
• Amygdala
  – Emotion Regulation
How Marijuana Affects the Brain

THC, a key ingredient in marijuana, attaches to cannabinoid receptors throughout the body. Several areas of the brain have high densities of these receptors, which helps explain the different effects of the drug.

How the receptors work
Nerve cells communicate by passing chemical messages across contact points called synapses.

The most active ingredient in marijuana, THC, attaches to cannabinoid receptors and modifies nerve action.

Some areas with high concentrations of cannabinoid receptors:

**Cerebral cortex**
Plays a role in memory, thinking, perceptual awareness and consciousness

**Hypothalamus**
Governs metabolic processes such as appetite

**Brain stem**
Controls many basic functions including arousal, the vomiting reflex, blood pressure and heart rate
Also plays a role in pain sensation, muscle tone and movement

**Hippocampus**
Is key to memory storage and recall

**Cerebellum**
Governs coordination and muscle control

**Amygdala**
Plays a role in emotions

Corresponding effects of marijuana:

- Altered consciousness; perceptual distortions; memory impairment; occasional delusions and hallucinations
- Increased appetite
- Nausea relief; rapid heart rate; reduced blood pressure; drowsiness
- Pain reduction; reduced spasticity; reduced tremor
- Impairment in memory
- Reduced spasticity; impaired coordination
- Anxiety and panic in some cases; reduced anxiety and blocking of traumatic memories in other cases; reduced hostility

Sources: Igor Grant, University of California Center for Medicinal Cannabis Research; WSJ research

Maryanne Murray/WSJ
The Entourage Effect

• Theorized by Israeli scientists Shimon Ben-Shabat and Dr. Raphael Mechoulam in 1998
• States that whole plant use is superior to individual component use and/or synthetics
• Highly debated and difficult to find good research on, though there is some that suggests this may be true for certain conditions.
• Vitamin supplement theory.
So We know It Can Be Impactful. What’s the problem?

• What we don’t know
  – Dosing information
  – Quality Control
  – Drug interactions
  – Potency
  – Contaminants
  – Delivery method risks
  – Short term and long term side effects
  – Dr. education and knowledge
  – Addiction risk when using for medical purposes
What’s in your medicine?

**Rx Drugs**
- Know the exact components
- Know most side effects
- Understand most drug interactions
- Have dosing guidelines
- Has approved disorders/diseases they treat
- Overseen by a medical physician AND a pharmacist

**Marijuana**
- Has lots of unknown components
- Dosage? “Doesn’t matter, you can’t die”.
- Not really sure how it interacts with other drugs, though we know it does interact.
- Treats whatever you got
- Overseen by a “bud tender”
Average “Medical” Marijuana Patient

Profile: 32-year old white male with a history of alcohol and substance abuse. No history of life threatening illnesses.

- 94% of reported conditions for “medical” marijuana use is “Severe Pain”. 3% have cancer. Less than 1% have HIV/AIDS.
- 74% are male.
- In California, less than 2% of cardholders have HIV, glaucoma, Multiple sclerosis or cancer.
- 88% tried marijuana before age 19
- 75% of patients had used cocaine in their lifetime
- 50% of patients had used methamphetamine in their

The Four-Prong Case For Addiction
(Yes, both psychological and physical.)

• Neuroscience
• Animal Studies
• Clinical Reports
• Epidemiology
Neuroscience

• Nucleus Accumbens is the reward center of the brain.
• When THC is introduced, increases in dopamine are observed in the Nucleus Accumbens similar to levels seen with other addictive substances
Animal Studies

• Multiple animal studies demonstrate increasing self administration when allowed.
• Antagonist demonstrates immediate adverse reactions in multiple animal models
• Withdrawal symptoms = diarrhea, vomiting, increased aggression, increased restlessness, trembling, head shaking, and sleep disruption
Clinical Reports

• Controlled studies of heavy users report the following upon abstaining:
  – Anxiety, irritability, physical tension, decreased mood and appetite
• Chronic users report:
  – More aggression
• Adolescent treatment seekers:
  – Restlessness, appetite change, cravings, irritability, depression, twitches and shakes, and perspiring.
Epidemiology

• DSM Criteria for abuse and dependence
  – Tolerance/withdrawal
  – Loss of control
  – Preoccupation with the drug
  – Continued use in the face of adverse consequences
  – Cognitive distortion/denial
Addiction Rates

- Initiation Age > 18 = 9%
- Initiation Age < 18 = 17%
- Used at least 5 times = 20% to 30%
- Used almost daily = 35% to 40%
Impacts On Brain

• Reduced receptor numbers, and sensitivity to, naturally occurring cannabinoids throughout the body
• Decreased connectivity between left and right brain (reduced density and size of corpus callosum)
• Decreased size of Amygdala and Hippocampus
Impacts on Schizophrenia

“Our findings suggest that heavy cannabis use in the context of specific CNR1 genotypes may contribute to greater WM volume deficits and cognitive impairment, which could in turn increase schizophrenia risk”\textsuperscript{7}
Harms Brain Development
A variety of brain scans done on college-age marijuana users, showed there were structural abnormalities in gray matter density, volume, and shape in the nucleus accumbens and amygdala parts of the brain—even with occasional use.

(Dr. Jodi Gilman, Journal of Neuroscience, April 16, 2014)

Harms Learning & Memory
“Cannabis use is associated with impairments of cognitive functions, including learning and memory, attention, decision-making, and deficits in time estimation.”

(JAMA. 2002 Mar 6;287)

Increases Risk of Mental Illness
Studies show that young people who use marijuana were twice as likely to develop schizophrenia, a disabling brain disorder, as non-users. They were also twice as likely to develop psychosis (delusional perceptions) over the next 10 years as non-marijuana-users. Use hastened the onset of mental illness by 3 years.

(www.health.harvard.edu/blog/teens-who-smoke-pot-at-risk-for-later-schizophrenia-psychosis-201103071676 )

Weekly cannabis use in teenagers led to a twofold increase in risk for later depression and anxiety.

(Degenhardt, Hall et al. 2001; Patton, Coffey et al. 2002)

Creates Deficits in Social Functioning
“Heavy users of marijuana have persistent decision-making deficits and alterations in brain activity.”

(www.sciencedirect.com/science/article/pii/S105381190500100)

Marijuana use before age 18 resulted in higher rates of addiction—up to 17 percent within 2 years—and disruption to an individual’s life . . . A 21-year study found that regular use was associated with increased rates of illicit drug use, crime, depression and suicidal behaviors.

(Fergusson, Horwood et al. 2002)
More harmful to others than:
- Cocaine
- Amphetamine
- Methamphetamine
- GHB
- Benzodiazepenes
- Ketamine
- Methadone
- Butane
- Qat
- Anabolic Steroids
- Ecstasy
- LSD
- Buprenorphine
- Mushrooms

Reference 8
Criteria For Ranking Drug Harms to Self and Others

Overall harm
- To users
  - Physical
    - Drug-specific mortality
    - Drug-related mortality
    - Drug-specific damage
    - Drug-related damage
    - Dependence
  - Psychological
    - Drug-specific impairment of mental functioning
    - Drug-related impairment of mental functioning
  - Social
    - Loss of tangibles
    - Loss of relationships
- To others
  - Physical and psychological
    - Injury
    - Crime
  - Social
    - Environmental damage
    - Family adversities
    - International damage
    - Economic cost
    - Community

Figure 1: Evaluation criteria organised by harms to users and harms to others, and clustered under physical, psychological, and social effects.
**Panel 1: Evaluation criteria and their definitions**

**Drug-specific mortality**
Intrinsic lethality of the drug expressed as ratio of lethal dose and standard dose (for adults)

**Drug-related mortality**
The extent to which life is shortened by the use of the drug (excludes drug-specific mortality)—eg, road traffic accidents, lung cancers, HIV, suicide

**Drug-specific damage**
Drug-specific damage to physical health—eg, cirrhosis, seizures, strokes, cardiomyopathy, stomach ulcers

**Drug-related damage**
Drug-related damage to physical health, including consequences of, for example, sexual unwanted activities and self-harm, blood-borne viruses, emphysema, and damage from cutting agents

**Dependence**
The extent to which a drug creates a propensity or urge to continue to use despite adverse consequences (ICD 10 or DSM IV)

**Drug-specific impairment of mental functioning**
Drug-specific impairment of mental functioning—eg, amphetamine-induced psychosis, ketamine intoxication

**Drug-related impairment of mental functioning**
Drug-related impairment of mental functioning—eg, mood disorders secondary to drug-user’s lifestyle or drug use

**Loss of tangibles**
Extent of loss of tangible things (eg, income, housing, job, educational achievements, criminal record, imprisonment)

**Loss of relationships**
Extent of loss of relationship with family and friends

**Injury**
Extent to which the use of a drug increases the chance of injuries to others both directly and indirectly—eg, violence (including domestic violence), traffic accident, fetal harm, drug waste, secondary transmission of blood-borne viruses

(Continues from previous column)

**Crime**
Extent to which the use of a drug involves or leads to an increase in volume of acquisitive crime (beyond the use-of-drug act) directly or indirectly (at the population level, not the individual level)

**Environmental damage**
Extent to which the use and production of a drug causes environmental damage locally—eg, toxic waste from amphetamine factories, discarded needles

**Family adversities**
Extent to which the use of a drug causes family adversities—eg, family breakdown, economic wellbeing, emotional wellbeing, future prospects of children, child neglect

**International damage**
Extent to which the use of a drug in the UK contributes to damage internationally—eg, deforestation, destabilisation of countries, international crime, new markets

**Economic cost**
Extent to which the use of a drug causes direct costs to the country (eg, health care, police, prisons, social services, customs, insurance, crime) and indirect costs (eg, loss of productivity, absenteeism)

**Community**
Extent to which the use of a drug creates decline in social cohesion and decline in the reputation of the community

ICD 10—International Classification of Diseases, tenth revision. DSM IV—Diagnostic and Statistical Manual of Mental Disorders, fourth revision.

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final normalisation preserved the ratios of all weights, but ensured that the weights on the criteria summed to 1.0. The weighting process enabled harm scores to be combined within any grouping simply by adding their weighted scores. Dodgson and colleagues\(^1\) provide further guidance on swing weighting. Scores and weights were input to the Hiview computer program, which calculated the weighted scores, provided displays of the results, and enabled sensitivity analyses to be done.
Past Month Marijuana Users Aged 12-17 (Percentage)

Source: National Survey on Drug Use and Health (NSDUH), HHS/SAMHSA (2010-11) and National Conference of State Legislatures (NCSL)
Perception of Harm Compared To 30-day Use (Grades 6, 8, 10 and 12 Combined UT)

% Using MJ past 30 Days

% Believe Marijuana is Harmful

% Believe Marijuana is Harmful

% Using Marijuana in the Last 30 days

UT SHARP Reports
Marijuana Vs. Alcohol Use (UT grades 6, 8, 10 and 12 combined)

% Using Marijuana in the Last 30 days

- 2007: 11.3%
- 2009: 9.3%
- 2011: 8.6%
- 2013: 7%

% Using Alcohol in the Last 30 days

- 2007: 4.1%
- 2009: 4.6%
- 2011: 5.3%
- 2013: 5.8%

UT SHARP Reports
Utah’s Medical Bill

• Failed in the Senate on a 14 yes, 15 no vote.
• Would have allowed access to anyone with a “qualifying Illness” including:
  – AIDS, Alzheimer’s, Lateral Sclerosis, Autoimmune Disorder, Cachexia or Malnutrition associated with chronic disease, Cancer, Crohn’s, Epilepsy, Glaucoma, MS or similar condition that causes persistent and debilitating muscle spasms, PTST, Chronic Pain,
Utah’s Medical Bill Continued

• Card is issued and tied to an account to pay for “medicine” (no cash transactions).
• “Seed to sale” tracking system
• Local jurisdictions must allow at least one of all the “Medical Cannabis Establishments” to be present in their community as long as the application is complete and qualifying.
• Caregiver provision
• Indemnifies physicians
The Utah Survey

- Commissioned by Libertas Institute and the Drug Policy Project of UT and conducted by Y² Analytics.
- 400 phone surveys of likely UT voters
- “72% of likely voters support legal medical cannabis for serious illness”
The Single Question

“Should doctors who specialize in treating serious illnesses like cancer, epilepsy, and Alzheimer’s be allowed to recommend cannabis, sometimes referred to as marijuana, as a treatment for their patients with serious medical conditions, or not?”

• Issues with this question?
• Is any more detail needed to understand individuals beliefs on the issue?
# Substance Use and Perceived Parental Acceptability

## Table 12. Substance Use in Relation to Perceived Parental Acceptability (State 2013)

<table>
<thead>
<tr>
<th>How wrong do your parents feel it would be for YOU to:</th>
<th>Student has used:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alcohol At Least Once in Lifetime</td>
</tr>
<tr>
<td>drink beer, wine, or hard liquor regularly?</td>
<td></td>
</tr>
<tr>
<td>Very Wrong</td>
<td>15.4</td>
</tr>
<tr>
<td>Wrong</td>
<td>64.6</td>
</tr>
<tr>
<td>A Little Bit Wrong</td>
<td>81.4</td>
</tr>
<tr>
<td>Not Wrong At All</td>
<td>65.8</td>
</tr>
<tr>
<td>smoke marijuana?</td>
<td></td>
</tr>
<tr>
<td>Very Wrong</td>
<td>7.7</td>
</tr>
<tr>
<td>Wrong</td>
<td>42.4</td>
</tr>
<tr>
<td>A Little Bit Wrong</td>
<td>68.0</td>
</tr>
<tr>
<td>Not Wrong At All</td>
<td>70.9</td>
</tr>
<tr>
<td>smoke cigarettes?</td>
<td></td>
</tr>
<tr>
<td>Very Wrong</td>
<td>10.0</td>
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<tr>
<td>Wrong</td>
<td>43.9</td>
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<tr>
<td>A Little Bit Wrong</td>
<td>73.3</td>
</tr>
<tr>
<td>Not Wrong At All</td>
<td>47.4</td>
</tr>
<tr>
<td>use prescription drugs not prescribed to you?</td>
<td></td>
</tr>
<tr>
<td>Very Wrong</td>
<td>3.9</td>
</tr>
<tr>
<td>Wrong</td>
<td>19.9</td>
</tr>
<tr>
<td>A Little Bit Wrong</td>
<td>33.5</td>
</tr>
<tr>
<td>Not Wrong At All</td>
<td>26.8</td>
</tr>
</tbody>
</table>
23 States Have Legal Access to Marijuana  
(This does not count the 11 CBD only States)

<table>
<thead>
<tr>
<th>Medical</th>
<th>Recreational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alaska</td>
<td>Colorado</td>
</tr>
<tr>
<td>Arizona</td>
<td>Washington</td>
</tr>
<tr>
<td>California</td>
<td>Alaska</td>
</tr>
<tr>
<td>Connecticut</td>
<td>Oregon</td>
</tr>
<tr>
<td>DC</td>
<td>New Jersey</td>
</tr>
<tr>
<td>Delaware</td>
<td>New Mexico</td>
</tr>
<tr>
<td>Hawaii</td>
<td>New York</td>
</tr>
<tr>
<td>Illinois</td>
<td>Oregon</td>
</tr>
<tr>
<td>Maine</td>
<td>Rhode Island</td>
</tr>
<tr>
<td>Maryland</td>
<td>Vermont</td>
</tr>
<tr>
<td>Massachusetts</td>
<td></td>
</tr>
</tbody>
</table>
Black Market and “Medicine”

- http://www.washingtonpost.com/posttv/national/a-day-in-the-colorado-marijuana-black-market/2014/07/30/a7e89910-17c8-11e4-88f7-96ed767bb747_video.html

- https://www.youtube.com/watch?v=bglEhdmFDXA
7.5%
Current users 12+ years old
3 Early Studies on MJ and Epilepsy

- 1/3 of children reported reductions of 50% or more and this did not correlate with EEGs.
- Families moving to CO for treatment are 3x more likely to report reductions
- Adverse effects = 47% of patients
- 21% = increase or new seizures
- “Substantial gap between clinical observations and various anecdotal reports…”
- Some results are encouraging…but…
- It appears that there are drug interactions that need to be studied.
What do we want Utah to look like in the future?

• This is a politically charged and relevant public health discussion that has many interested parties.

• We may discover that Marijuana is in fact useful in the medical setting.

• How should this look?
• Medicine on display?
• “Bud Tender” with a degree?
• “Donkey D**k” is a choice for medicine?
• Your medicine was regulated by?
• The side effects are?
• The drug interactions are?
• You can get a tee shirt and incense burner with your order.

• Medicine in prescription package.
• Pharmacist and techs both have years of schooling.
• “Fuc**g Incredible” is not an option.
• FDA studied and approved of your medication.
• The side effects are outlined and identified through a rigorous process
• You can get safety information and directions as well as professional advice and consultation with your prescription.
3 Pillars For Talking Points

1. Do not compare to other substances
   – We are talking about what is good for society, not what is the worst.

2. Base your discussion on PEER REVIEWED research that has been published in a REPUTABLE journal

3. Make sure to discuss unintended consequences as well as benefits.
Questions?

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  — http://www.fda.gov/ohrms/dockets/dockets/05n0479/05N-0479-emc0004-04.pdf
  — http://www.accessdata.fda.gov/drugsatfda_docs/label/2006/018677s011lbl.pdf
• 4 - Nutt David J, King Leslie A, D Phillip S Lawrence, (Drug harms in the UK: a multicriteria decision analysis) The Lancet, Volume 376, Issue 9752, 6–12 November 2010, Pages 1558–1565
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• 7 - Beng-Choon Ho , Thomas H. Wassink, Steven Ziebell, Nancy C. Andreasen ; Cannabinoid receptor 1 gene polymorphisms and marijuana misuse interactions on white matter and cognitive deficits in schizophrenia, Schizophrenia Research; Volume 128, Issues 1–3, May 2011, Pages 66–75
• 8 - Drug harms in the UK: a multi-criteria decision analysis", by David Nutt, Leslie King and Lawrence Phillips, on behalf of the Independent Scientific Committee on Drugs. TheLancet.