A DRUG, MEDICINE, OR A DRUG AS MEDICINE?
EDUCATIONAL OBJECTIVES

• Describe the mechanism of action and effects of cannabinoids on the brain.

• Explain the risks with marijuana, particularly among adolescents, and define cannabis use disorder.

• Identify some of ramifications of medicalization of marijuana and how it may impact the educational environment.
FACULTY DISCLOSURE

• No relevant commercial disclosures or conflicts.

• Member of ASAM & Member of ASAM QIC.

• Member of MHA & Governor Baker’s Opioid Task Force, but not involved in MA DPH related work pertaining to marijuana.

• Treat patients for substance use disorders.
CREDIT WHERE IT IS DUE

- National Institutes of Drug Abuse (research, images)
- American Society of Addiction Medicine (research)
- SAM: Smart Approaches to Marijuana (slides, images)
- Centers for Disease Control & Prevention (research)
Marijuana, a.k.a. weed, herb, pot, grass, bud, ganja, Mary Jane, is a plant.

Greenish, gray mixture of dried, shredded leaves and flowers of Cannabis sativa.

Smoked or ingested in a variety of ways, e.g. joints, blunts, brew as tea, and mixed into food.
NOT JUST A PLANT ANYMORE

“Green Crack” wax

“Ear Wax”

Butane Hash Oil (BHO)

Hash Oil Capsules

“Budder”

“Shatter”
NOT JUST A PLANT ANYMORE

Hazelnut spread with Medical Marijuana

Cheeba Chews

DISSIE ELIXIRS

DISSIE ELIXIRS
CANNABIS CANDY STORE
EFFECTS OF MARIJUANA

• **Positive:** pleasant euphoria, sense of relaxation, heightened sensory perception, laughter, altered perception of time, and increased appetite

• **Negative:** anxiety, fear, distrust, panic, acute psychosis, hallucinations, delusions

• **Smoked:** nearly immediate effects, last 1-3 hours

• **Ingested:** delayed onset, 30-60 min, less THC, so may last for many hours or risk for overuse
• Main psychoactive component is delta-9-tetrahydro-cannabinol (THC)

• Resin produced by leaves, buds of female plant

• Contains over 500 chemicals

• > 100 are related to THC = cannabinoids.
ENOCANNABINOID SYSTEM

Delta-9-tetrahydrocannabinol

Delta-9-tetrahydrocannabinol varin

Delta-8-tetrahydrocannabinol

Cannabigerol

Cannabinol

Cannabichromene

Cannabidiol
THC’s chemical structure is similar to the brain chemical anandamide. Similarity in structure allows drugs to be recognized by the body and to alter normal brain communication.
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.
EPIDEMIOLOGY OF USE

• Most commonly used illicit substance in U.S. by both adolescents and adults.

• 22 million over age 12 current use = 8.4%

• Rates in 2014 higher than 2002 – 2013

• Increase in rates highest in ages 26 and over
Daily marijuana use has risen to historic highs

Percentage of people in the United State using marijuana daily
<table>
<thead>
<tr>
<th>Drug</th>
<th>Time Period</th>
<th>8th Graders</th>
<th>10th Graders</th>
<th>12th Graders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana/Hashish</td>
<td>Lifetime</td>
<td>15.50</td>
<td>[31.10]</td>
<td>44.70</td>
</tr>
<tr>
<td></td>
<td>Past Year</td>
<td>11.80</td>
<td>25.40</td>
<td>34.90</td>
</tr>
<tr>
<td></td>
<td>Past Month</td>
<td>6.50</td>
<td>14.80</td>
<td>21.30</td>
</tr>
<tr>
<td></td>
<td>Daily</td>
<td>1.10</td>
<td>3.00</td>
<td>6.00</td>
</tr>
</tbody>
</table>
Long-Term Trends in Annual* Marijuana Use Among 8th-, 10th-, and 12th-Graders

*use in the past 12 months
TEEN PERCEPTION OF HARM
1 in 6 teens become addicted to marijuana

- 1 in 11 adults and 1 in 6 adolescents who try marijuana will become addicted to it
- The adolescent brain is especially susceptible to marijuana use
- When kids use, they have a greater chance of addiction since their brains are being primed

Icon: Connor Shea
<table>
<thead>
<tr>
<th>Criterion</th>
<th>DSM-5 substance use disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolerance</td>
<td>✓</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>✓</td>
</tr>
<tr>
<td>Taken more/longer than intended</td>
<td>✓</td>
</tr>
<tr>
<td>Desire/unsuccesful efforts to quit use</td>
<td>✓</td>
</tr>
<tr>
<td>Great deal of time taken by activities involved in use</td>
<td>✓</td>
</tr>
<tr>
<td>Use despite knowledge of problems associated with use</td>
<td>✓</td>
</tr>
<tr>
<td>Important activities given up because of use</td>
<td>✓</td>
</tr>
<tr>
<td>Recurrent use resulting in a failure to fulfill important role obligations</td>
<td>✓</td>
</tr>
<tr>
<td>Recurrent use resulting in physically hazardous behavior (e.g., driving)</td>
<td>✓</td>
</tr>
<tr>
<td>Continued use despite recurrent social problems associated with use</td>
<td>✓</td>
</tr>
<tr>
<td>Craving for the substance</td>
<td>✓</td>
</tr>
</tbody>
</table>
Marijuana has become significantly more potent since the 1960s

Average THC and CBD levels in the United States

Source: Mehmedic et al., 2010

<table>
<thead>
<tr>
<th>Year</th>
<th>CBD</th>
<th>THC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1960</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>1965</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>1970</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>1975</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>1980</td>
<td>0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>1985</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>1990</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>1995</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>2000</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>2005</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>2010</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>2015</td>
<td>0.5</td>
<td>0.4</td>
</tr>
</tbody>
</table>

THC: Psychoactive Ingredient

CBD: NON-Psychoactive Ingredient
Marijuana-related emergency room visits have risen sharply, both in relative and absolute terms.

Number of Emergency Department Visits Involving Marijuana, Cocaine, or Heroin

Source: Volkow ND et al., NEJM 370(23), June 5, 2014.
Early marijuana use and intensity of use are associated with lower educational attainment.

**High School Completion**
Marijuana users show much higher high school dropout rates than non-users.

- Under 14 years old: -28%* (p<0.01)
- 14 years or older: -11%* (p<0.01)

**University Entrance Score**
Marijuana users that complete high school still do poorly on university entrance tests.

- Under 14 years old: -12%* (p<0.01)
- 14 years or older: -11% (p<0.05)

* p<0.01, ** p<0.05

Legend:
- Low intensity use
- Med/high intensity use

Marijuana use is also associated with lower IQ among adolescents

Change in full-scale IQ (standard deviation units)

1 Diagnosis

2 Diagnoses

3 Diagnoses

Not cannabis dependent before age 18
Cannabis dependent before age 18

$p = .44$

$p = .09$

$p = .02$

Dunedin prospective study of 1037 subjects born in 1972-72
Subjects were tested for IQ at age 13 and 38 years of age. They were also tested for THC use ages 18, 21, 26, 32 and 38 years of age.

Source: Meier MH et al., PNAS Early Edition 2012
Frequent cannabis use by youth correlates with a host of undesirable effects

Adjusted odds ratios

Source: Silins E. et al., *The Lancet*, September 2014
### Adverse Consequences of Marijuana Use

<table>
<thead>
<tr>
<th>Acute (present during intoxication)</th>
<th>Persistent (lasting longer than intoxication, but may not be permanent)</th>
<th>Long-term (cumulative effects of repeated use)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired short-term memory</td>
<td>Impaired learning and coordination</td>
<td>Potential for addiction</td>
</tr>
<tr>
<td>Impaired attention, judgment, and other cognitive functions</td>
<td>Sleep problems</td>
<td>Potential loss of IQ</td>
</tr>
<tr>
<td>Impaired coordination and balance</td>
<td></td>
<td>Increased risk of chronic cough, bronchitis</td>
</tr>
<tr>
<td>Increased heart rate</td>
<td></td>
<td>Increased risk of schizophrenia in vulnerable people*</td>
</tr>
<tr>
<td>Anxiety, paranoia</td>
<td></td>
<td>Potentially increased risk of anxiety, depression, and amotivational syndrome*</td>
</tr>
<tr>
<td>Psychosis (uncommon)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*These are often reported co-occurring symptoms/disorders with chronic marijuana use. However, research has not yet determined whether marijuana is causal or just associated with these mental problems.*
Can the United States afford the risk of further increases in cannabis use?

The U.S. is 30th out of 32 countries in cannabis use w/ 15 & 16-year-old students
Past Month Use, Percentages, 2007 and 2011

The U.S. has fallen behind in educational achievement
(out of 65 jurisdictions, 2012)

Math: 36th
Science: 28th
Reading: 24th

Source: European School Survey Project on Alcohol and Other Drugs (2007 & 2011); Program for International Student Assessment (2012)
Icons: Egon Lastad, Zlatko Najdenovski, Vicons Design
PUBLIC ENEMY NUMBER ONE
in the United States
IS DRUG ABUSE

NIXON
• Used for therapeutic properties since 2737 B.C.

• Introduced into western medicine in 1839

• Extracts marketed in early 20th century, as sedative, analgesic, to improve appetite, etc.

• Prescriptions declined and removed from pharmacopeia in 1942 (opposed by AMA)
• Prohibited with Controlled Substance Act 1970

• Categorized as Schedule 1 substance = highly addictive and devoid of medical value/safety

• Interest in research increased with identification of THC 1964, cannabinoid receptors 70-90s, and few studies and experience showed benefit for chemo-induced nausea and AIDS wasting
1996 California legalized use for medical purpose

Now 23 states and D.C., including MA

States supported by federal statements of cooperative noninterference by Veteran’s Health Administration and US. DOJ in 2009

Research exists, but still needed
EVIDENCE: MARIJUANA AS MEDICINE

- Marijuana is not approved by FDA, but there are pharmaceutical preparations that are (or will be).
  - **Dronabinol**: 1985 chemo-induced nausea, 1992 anorexia/cachexia in AIDS; oral capsule
  - **Nabilone**: 1985 chemo-induced nausea, used off-label for analgesia; oral capsule
  - **Sativex**: Under phase III trials in US for cancer pain; oromucosal spray
• There are only a few RCTs for smoked cannabis

• Limited by small sample sizes, short duration of follow-up and imprecision with dose/potency, crude delivery system (smoking)

• Evidence exists to do more research:
  HIV patients with cachexia, neuropathy, or chronic pain
  Chemotherapy patients with insufficient relief from anti-emetics
  Anti-emetic effect in opioid-based treatment of cancer pain
  Patients with spinal cord injury or neuropathic pain syndromes
  Other patients with chronic pain syndromes
MARIJUANA IS (currently) NOT MEDICINE

• AMA, ANA, ASAM, APA Statements

• Lacks quality control and standardization, not assuring patients of a reproducible dose

• Lack of high-quality evidence base

• No mechanism for collecting data on efficacy or adverse events
An Act for the Humanitarian Medical Use of Marijuana (MA)

- 18 years or older diagnosed by a certifying physician as having debilitating medical condition

- Under age 18 with two certifying physicians (one who is a pediatrician) diagnosed with debilitating, life-limiting illness with prognosis of death <2 yr.

*If not life-limiting, both physicians determine that benefits > risks, written consent with parent.*
• **Medical conditions:** cancer; glaucoma; HIV; AIDS; Hepatitis C; ALS; Crohn’s disease; Parkinson’s Disease; and multiple sclerosis and other conditions as determined by physician in writing.

• **Debilitating:** defined as “causing weakness, cachexia, wasting syndrome, intractable pain, nausea, or impairing strength or ability, and progressing to such an extent that one or more of a patient’s major life activities is substantially limited.”

*An Act for the Humanitarian Medical Use of Marijuana (MA)*
An Act for the Humanitarian Medical Use of Marijuana (MA)

- Amount: 60 day supply = 10 ounces (~500 joints)

- Written certification by physician (benefits > risks for qualifying patient) and registration with the Department of Public Health

- Physicians must take 2 hours of CME
Medical Use of Marijuana Program Update As of Dec 31, 2015:

4 RMDs Open for Sales

18,476 Active Patients & 936 Active Caregivers

129 Certifying Physicians & 23,346 Active Physician Certifications
Medical Use of Marijuana in Schools

• **3 of 23 states** have schools or state officials set up rules (ME, NJ, CO)

  • NJ: schools must adopt policies that allow for children with developmental disabilities to use oil, edibles

  • ME: approved by physician, administered in school by parent or guardian (not staff or a nurse), no smoking

  • CO: parents or professional caregivers can administer if district allows it (not staff or a nurse)
Medical Use of Marijuana in Schools

• Still illegal at federal level

• AAP: The Impact of Marijuana Policies on Youth: Clinical, Research, and Legal Update, Jan 2015 = opposes “medical marijuana” outside the regulatory process of the US Food and Drug Administration.

• Notwithstanding this opposition to use, the AAP recognizes that marijuana may currently be an option for cannabinoid administration for children with life-limiting or severely debilitating conditions and for whom current therapies are inadequate.
Is the true goal of “medical” marijuana compassionate care or increased access to pot?

**THE “AVERAGE” USER ISN’T SICK**

The average “medical” marijuana user is not whom you’d imagine:

- White male
- 32 years old
- No history of life-threatening disease
- History of drug and alcohol abuse

**ILLNESSES USED TO JUSTIFY “MEDICAL” MARIJUANA ARE RARE**

Fewer than 5% of “medical” marijuana card holders are cancer, HIV/AIDS, or glaucoma patients

“Drug use prevention is the best treatment – and it costs less in lives and dollars.”

And good medicine should be driven by good science.