Health Effects of Cannabis

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Learning Objectives

- Identify terminology surrounding cannabis

- Review the medicinal uses of cannabis

- Discuss how cannabis is available

- Review how long cannabis lasts after use

- Identify information on negative effects of cannabis

Same Plant - Different Message

An anti-marijuana movie poster from the 1930s (Getty Images)

172 CONDITIONS THAT MEDICAL MARIJUANA CAN HELP CURE

Marijuana cures cancer
US government has known since 1974
FDA
www.facebook.com/Citizens.Action.Network

Food and Drug Administration and Cannabis

- Has **not** approved cannabis as a safe and effective drug for any indication.
- Has **not** approved a marketing application for cannabis for the treatment of any disease or condition and thus has not determined that cannabis is safe and effective for any particular disease or condition.
- FDA-approved prescription medicines containing synthetic cannabinoids are available
  - Marinol®, Syndros®, Cesamet® (THC)
  - Epidiolex® (CBD)*

*Selling unapproved products with unsubstantiated therapeutic claims is not only a violation of the law, but also can put patients at risk, as these products have not been proven to be safe or effective. This deceptive marketing of unproven treatments also raises significant public health concerns, because patients and other consumers may be influenced not to use approved therapies to treat serious and even fatal diseases.

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Extent of Cannabis Use

- The most widely used illicit substance in the US

- 37.6 million people (13.9%) of US adults reported using cannabis.

- 12% adolescents 12-16 years old

- Highest use among 18-25 year old (33%)

- 68.9% of high school seniors do not view regular marijuana smoking as harmful

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Hemp vs Marijuana

Broad classifications of Cannabis adopted into our culture
Not legitimate scientific nomenclature for Cannabis
Not a physical classification - Can appear identical

Hemp

- Cannabis that contains 0.3% or less THC

- Federally legalized ("2018 Farm Bill")

- Human use for 10,000 years

- Non-intoxicating Cannabis that is harvested for the industrial use of its derived products.

- Only term used to describe cannabis in US pre-1910

Marijuana

- Cannabis that contains more than 0.3% THC

- NOT federally legalized

- Recreational/therapeutic effects derived from THC

- "Evil Weed";

- Term originated during Mexican revolution in early 1900's and expanded during Prohibition/Great Depression

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Cannabis Scientific Classification

- Genus of flowering plants in the *Cannabaceae* family
- Contains three species
  - sativa, indica, ruderalis
- Grows throughout temperate and tropical climates
- Leaves ("flowers") contain over 500 chemical compounds from 18 different classes
  - Over 100 phytocannabinoids
    - Δ^9 tetrahydrocannabinol (THC) (most psychoactive)
    - Cannabidiol (CBD)
- Varying amounts of cannabinoids
  - Different species and strains, soil and climate conditions, and cultivation techniques

Sativa vs Indica

- Different species of genus cannabis
- Differences in appearance and effect
- Determined by amount of myrcene, a terpene that induces sleep
  - Indica = more than 0.5% myrcene
  - Sativa = less than 0.5% myrcene
- Most black market cannabis is indica due to reduced grow time

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Cannabis Strains

INDICA			
9 Pound Hammer	AK-47	Pineapple Chunk	Bay 11
Afghani	Banana OG	Pineapple Express	Chocolope
Afgoo	Blue Dream	Pink Kush	Cinex
Berry White	Cannatonic	Raskal OG	Dirty Girl
Blueberry	Chemdawg	SAGE	Durban Poison
Bubba Kush	Chernobyl	SFV OG	Ghost Train Haze
G13	Cherry Pie	Shiatsu Kush	Grapefruit
Granddaddy Purple	Cinderella 99	Skunk No. 1	Green Crack
Grape Ape	Dancehall	Snoop's Dream	Harlequin
Herijuana	Double Dream	Snowcap	Island Sweet Skunk
Hindu Kush	Dutch Treat	Sour OG	Jack Herer
Ingrid	Ewok	Sour Tsunami	Kali Mist
Kosher Kush	Fruity Pebbles	Space Queen	Lamb's Bread
Lavender	Gelato	Sunset Sherbet	Laughing Buddha
Master Kush	Golden Goat	Tahoe OG	Maui Wowie
Northern Lights	Headband	Tangerine Dream	Panama Red
Obama Kush	Jean Guy	Trainwreck	Purple Haze
Pez	Jillybean	UK Cheese	Red Headed Stranger
Plushberry	Juicy Fruit	White Fire OG	Schrom
Presidential OG	Larry OG	White Widow	Sour Diesel
Purple Urkle	Lemonder	XJ-13	Strawberry Cough
Willy's Wonder	Lodi Dodi		Super Lemon Haze
Zkittlez	Mango Kush	**SATIVA**	Super Silver Haze
	Mendocino Purps	Acapulco Gold	Tangie
HYBRID	Middlefork	Alaskan Thunder Fuck	
ACDC	OG Kush	Allen Wrench	
	Permafrost		

Visit Leafly.com to learn more about these strains and find them nearby.

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THC
Tetrahydrocannabinol

VS
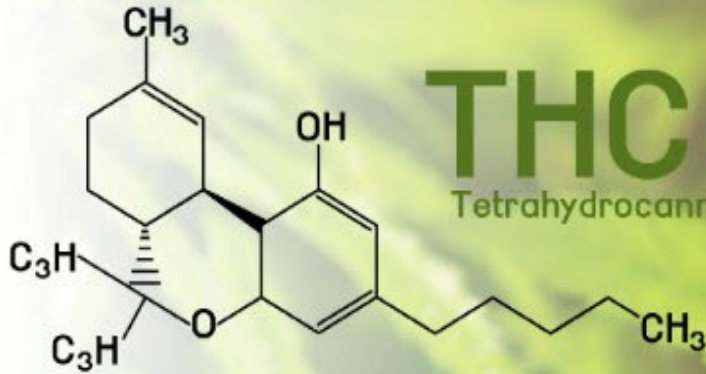
CBD
Cannabidiol
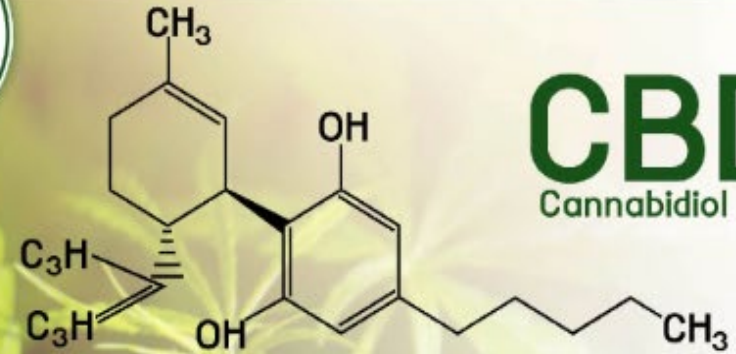
- Psychoactive
- Potent partial agonist of CB1
- Directly binds to CB1 and CB2
- Illegal on a federal level
- Found only in cannabis plants
- Increase appetite
- Can cause anxiety
- Sleep aid

- Non-psychoactive
- Negative allosteric modulator of CB1
- Suppresses CB1 and CB2 receptors
- Legal at Federal level
- Found in cannabis and hemp plants
- Reduce appetite
- Can help reduce anxiety
- Prompt wakefulness

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Cannabidiol and Tetrahydrocannabinol Ratios

How much CBD is right for you?

Which ratio of CBD to THC should you try? Keep in mind, cannabanoids can have varying effects depending on one's tolerance so your mileage may vary.

More CBD

18:1
High CBD, low THC. For novice cannabis users or those who don't want to get high. Rarely psychoactive.

8:1
High CBD, low THC. For novice cannabis users or those who don't want to get high. Rarely psychoactive.

4:1
High CBD, medium THC. Considered mid-range and best for people who have some tolerance for THC.

2:1
More balanced. For people who can tolerate THC. Can be psychoactive at moderate doses.

1:1
More balanced. For people who can tolerate THC. Can be psychoactive at moderate doses.

Less CBD

Source: Care by Design   Mashable

	THC (%)	CBD (%)	CBC (%)	CBN (%)
Marijuana	3.1	0.3	0.2	0.3
Sinsemilla	8.0	0.6	0.2	0.2
Hashish	5.2	4.2	0.4	1.7
Hashish oil	15.0	2.7	1.1	4.1

CBC = cannabichromene; CBD = cannabidiol; CBN = cannabinol; THC = Δ⁹-tetrahydrocannabinol.

Grotenhermen, F. Clin Pharmacokinet (2003) 42: 327.

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Sinsemilla

- "Without seeds"

- Not a different species of cannabis

- Refers to the type of cultivation

- Female plants that are not allowed to produce seeds

- More flowers (i.e. "buds") produced with higher cannabinoid content

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Cannabis Extracts

Plant extract mixture from the leaves and flowers of *Cannabis*.

- ***"Butane hash oil" (BHO), "Propane hash oil" (PHO)*** : Resinous extract made using organic solvents.
- ***"Wax"*** : Extract heated at low temperatures and whipped vigorously to remove solvent. Consistency similar to wax with ranges from a variety of amber shades complete with a milder aroma and flavor profile.
- ***"Budder"*** : Similar to wax but the consistency is oily.
- ***"Live resin"*** : same as wax, but the starting product is fresh frozen cannabis. It is known for its flavor, which resembles the aroma and taste of the cannabis plant.
- ***"Shatter"*** : Shatter refers to a extract collected onto parchment paper and placed in a vacuum oven for 45 min to a full day. It presents a THC content ranging from 20 to 50%.
- ***"Taffy"*** : Similar to *"shatter"* but the solvent of the extract is evaporated. Is closer to *"budder"* in its consistency and stability.
- ***"Pie Crust"*** *or* ***"Honeycomb"****:* Extract obtained by solvent extraction, collected onto parchment paper and placed into a vacuum oven for solvent evaporation. During solvent evaporation, the extracts is pressed to promote faster nucleation, turning the material from a shiny shatter looking substance to more of a cookie crumble, honeycomb look. The final product delivers an amber color with a strong aroma and overall flavor.
- ***"Caviar"*** *:* Soaking cannabis in hash oil. Afterwards, the soaked flower is coated in kif (finely sifted cannabis) and dried.
- ***"Jelly Hash"*** *:* a mixture of kif and hash oil.
- ***"Rosin"*** *:* Rosin is obtained by the use of heat and high pressure to isolate the resinous oils to create a solid form of translucent resin.

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Therapeutic Uses of Cannabis
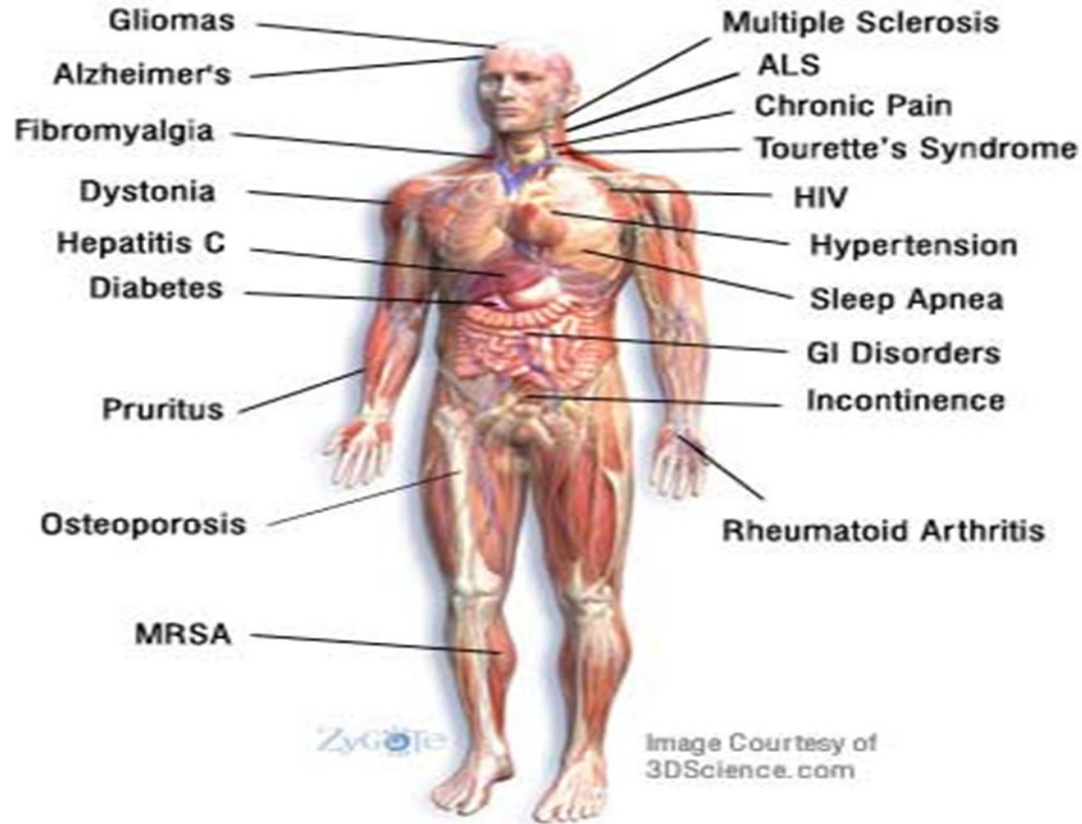
Potential Therapeutic Uses of Medical Marijuana

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Cannabis and Pain Relief

- More evidence for chronic pain relief vs acute

- A systematic review including 2,454 people
  - Moderate quality evidence exists to support the use of cannabinoids to treat chronic pain in individuals already receiving analgesic drugs

- 30% decrease in HIV-associated nerve pain was reported in 52% of cannabis-experienced patients

- Inhalation of 25 mg of cannabis containing 9.4% THC three times per day for five days caused modest decrease in pain intensity

Whiting PF, Wolff RF, Deshpande S, Di Nisio M, Duffy S, Hernandez AV, Keurentjes JC, Lang S, Misso K, Ryder S, et al. Cannabinoids for medical use: A systematic review and meta-analysis. JAMA 2015 Jun 23-30;313(24):2456-73.

Abrams DI, Jay CA, Shade SB, Vizoso H, Reda H, Press S, Kelly ME, Rowbotham MC, Petersen KL. Cannabis in painful HIV-associated sensory neuropathy: A randomized placebo-controlled trial. Neurology 2007 02/13;68

Ware MA, Wang T, Shapiro S, Robinson A, Ducruet T, Huynh T, Gamsa A, Bennett GJ, Collet JP. Smoked cannabis for chronic neuropathic pain: A randomized controlled trial. CMAJ 2010 08/30;182(

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Cannabis Dosing

- Related to the THC content

- Limited clinical studies on minimal and safe dose ranges

- Does not fit well with current drug dosing models
  - Differences in sensitivity and metabolism among people (genetic)
  - Prior exposure (tolerance)
  - Products used and ingestion routes
  - Potency of cannabis plant material (see table below)

Table 3: Relationship between THC Percent in Plant Material and the Available Dose (in mg THC) in an Average Joint

% THC	mg THC per 750 mg dried plant material* ("average joint")
1	7.5
2.5	18.75
5	37.5
10†	75†
15	112.5
20	150
30	225

* WHO average weight

† see text in Section 3.1 for additional details

Carter GT, Weydt P, Kyashna-Tocha M, Abrams DI. Medicinal cannabis: Rational guidelines for dosing. IDrugs. 2004 05;7(1369-7056; 5):464-70.

Cannabis: a health perspective and research agenda [Available at https://apps.who.int/iris/bitstream/handle/10665/63691/WHO_MSA_PSA_97.4.pdf;jsessionid=83E17949A18555849BD76B1903BB3C6A?sequence=1 (accessed 07/30/2019)

Cannabis Dosing

- Dosing is highly individualized and based on titration
  - New patients to start at lowest dose
- Titration
  - Inhaled
    - Waiting a minimum of 10 – 20 minutes between puffs or inhalations
  - Oral
    - Waiting 30 minutes to 3 hours between bites
- If intolerable adverse effects appear without significant benefit, dosing should be tapered and stopped (withdrawal).

Carter GT, Weydt P, Kyashna-Tocha M, Abrams DI. Medicinal cannabis: Rational guidelines for dosing. IDrugs. 2004 05;7(1369-7056; 5):464-70.

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How is Cannabis Consumed?

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Vaping and Dabbing

- "Vaping" is the inhalation of a cannabis-containing aerosol created by a battery-driven, heated atomizer in e-cigarettes or similar devices

- "Dabs" are concentrated doses of cannabis (i.e. extracts)

- "Dabbing" is heating "dabs" on a hot surface or "nail" and inhaling the vapor through a "dab rig"

Varlet V, Concha-Lozano N, Berthlet A, et al. Drug vaping applied to cannabis: is "cannavaping" a therapeutic alternative to marijuana? *Sci Rep*. 2016

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Emerging Routes of Administration

- Oro-mucosal
  - Epidiolex®(CBD) – buccal liquid – for seizures
- Rectal
  - Suppository
  - Beneficial for patients unable to swallow
  - Up to 30-times more THC absorption vs oral
- Topical and Transdermal
  - Patches, creams, ointments
  - No human studies
  - Animal studies demonstrated blood levels up to 48 hours

Mattes RD, Shaw LM, Edling-Owens J, Engelman K, Elsohly MA. Bypassing the first-pass effect for the therapeutic use of cannabinoids. Pharmacol Biochem Behav 1993 03;44(0091-3057; 3):745-7.

Valiveti S, Hammell DC, Earles DC, Stinchcomb AL. Transdermal delivery of the synthetic cannabinoid WIN 55,212-2: In vitro/in vivo correlation. Pharm Res 2004 07;21(0724-8741; 0724-8741; 7):1137-45.

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How Cannabis Works
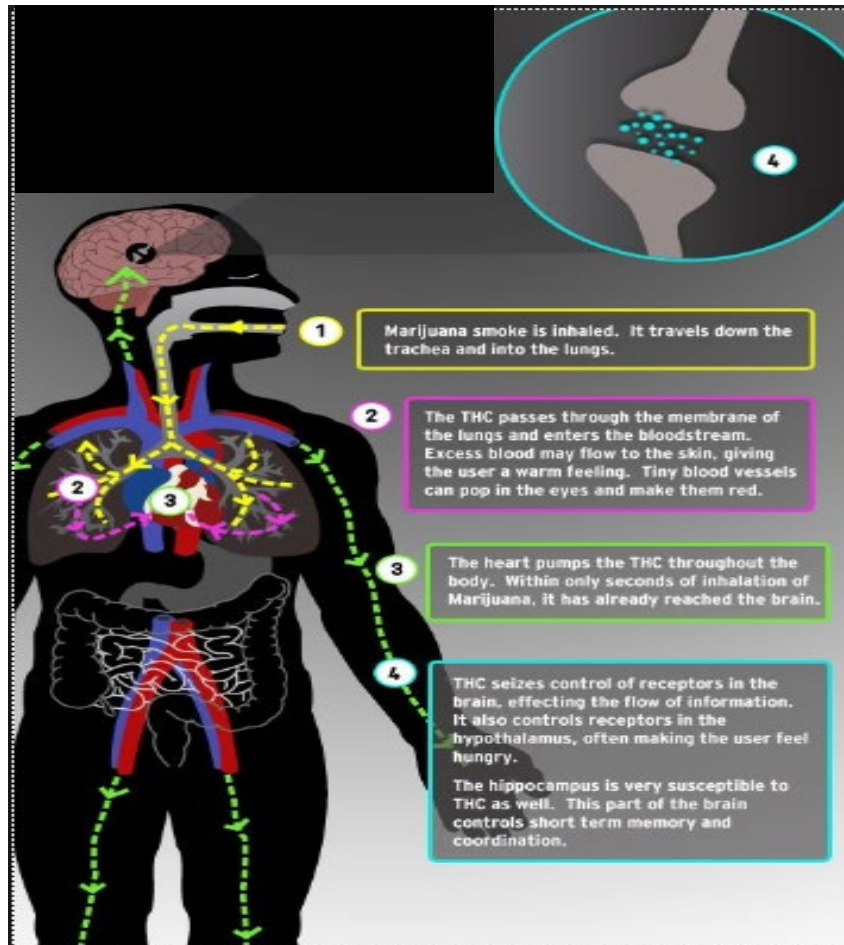
1. Cannabis vapor or smoke is inhaled
2. THC rapidly passes from lungs to blood
3. Blood transports THC to the brain (within seconds)
4. THC works at specific sites ("receptors") in hypothalamus (hunger) and hippocampus (short term memory and coordination)

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Cannabis Effects

Short Term

- Increased heart rate
- Low blood pressure
- Muscle relaxation
- Slowed digestion
- Dizziness
- Distorted perception (sights, sounds, time, touch)
- Difficulty in thinking, memory, and problem solving
- Loss of coordination and motor skills
- Agitation, anxiety, confusion, panic, paranoia
- Increased appetite
- Dry mouth, dry eyes

Long Term

- Anxiety
- Agitation
- Tremulousness
- Insomnia
- Irritability

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Duration of Cannabis Effect
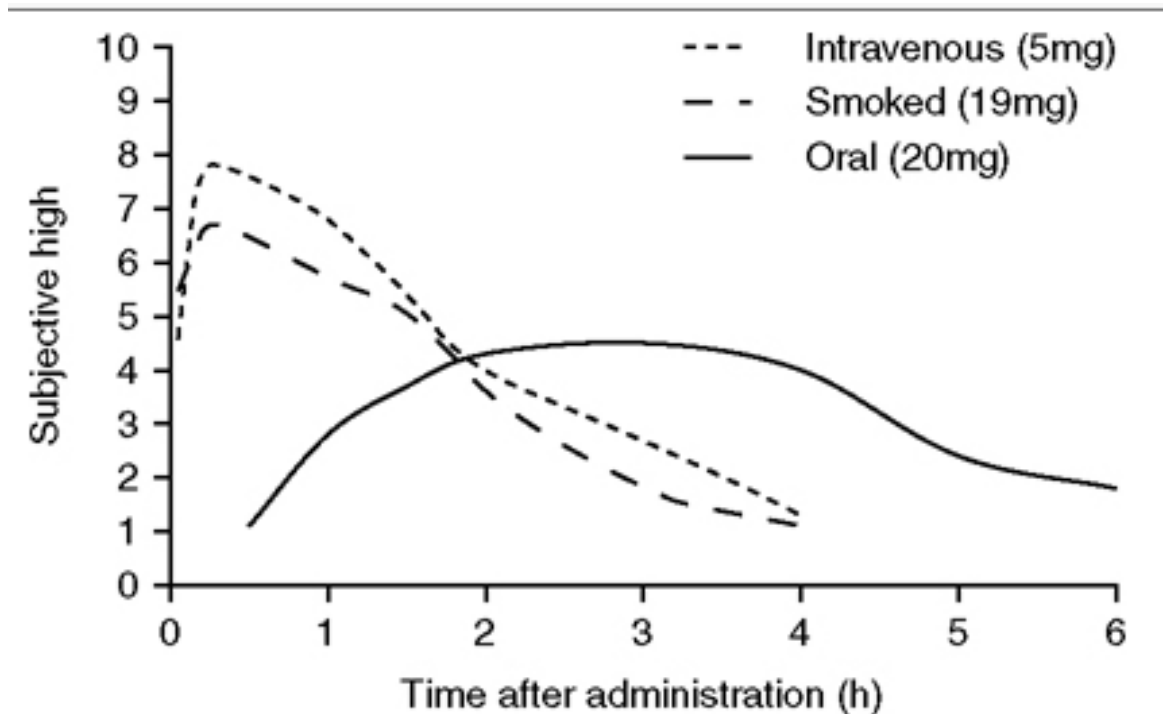
Inhaled – Onset = immediate; Peak = 20 minutes; Duration = 2-3 hours
Oral – Onset = 1 hour; Peak = 3 hours; Duration = 4-5 hours

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Cannabis Detection

Detection Windows of Marijuana Drug Tests
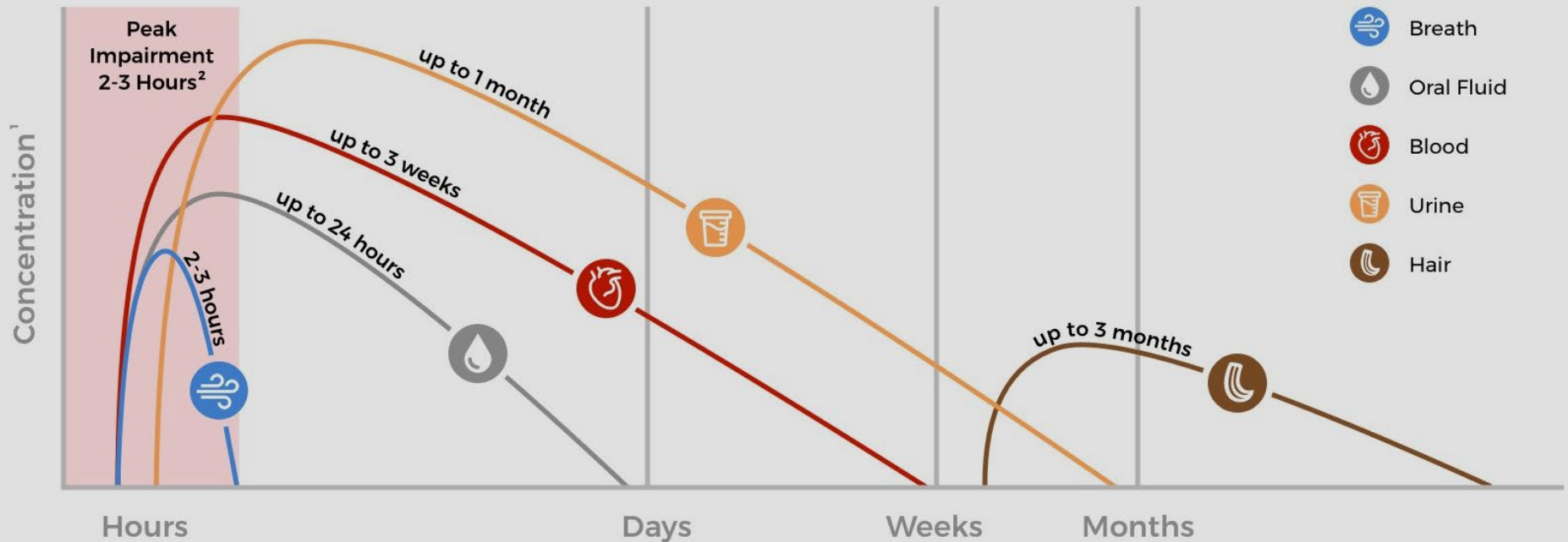
CANNABIS TOLERANCE, DEPENDENCE AND WITHDRAWAL

Cannabis Tolerance

- Tolerance is a "state of adaptation in which exposure to the drug causes changes that result in a diminution of one or more of the drug's effects over time."

- Caused by decreased sensitivity of the body to Cannabis over time

- Can develop to Cannabis after only 4 days
  - Euphoria ("high") reduced by up to 80%
  - Appetite stimulation not effected

Lynch ME, Watson CP. The pharmacotherapy of chronic pain: A review. Pain Res.Manag. 2006;11(1203-6765; 1203-6765;1):11-38.

Jones RT, Benowitz NL, Herning RI. Clinical relevance of cannabis tolerance and dependence. J Clin Pharmacol 1981 Aug- Sep;21(8-9 Suppl):143S-52S.

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Cannabis Withdrawal

- Withdrawal is "abnormal physical or psychological features that follow the abrupt discontinuation of a drug that has the capability of producing **physical dependence**."

- Marijuana withdrawal symptoms
  - Appear within 1-2 days after interrupted use and last for up to 2 weeks
  - Symptoms include
    - irritability, nightmares/strange dreams, insomnia/sleep difficulties, headache, restlessness, and decreased appetite or weight loss

Lee D, Schroeder JR, Karschner EL, Goodwin RS, Hirvonen J, Gorelick DA, Huestis MA. Cannabis withdrawal in chronic, frequent cannabis smokers during sustained abstinence within a closed residential environment. Am J Addict 2014 May- Jun;23(3):234-42.

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Cannabis Addiction

- Psychological dependence (i.e. addiction)
  - impaired control over drug use, compulsive use, continued use despite harm, and craving
    - genetic, psychosocial, and environmental factors
- Cannabis addiction
  - Can develop more quickly than with nicotine or alcohol
  - probability after first year is almost 2%
  - lifetime prevalence is 9%
- Cannabis Use Disorder
  - a problematic pattern of cannabis use leading to clinical significant impairment or distress
  - 12 month (2-8%); lifetime (3-10%)

Lopez-Quintero C, Perez de los Cobos J, Hasin DS, Okuda M, Wang S, Grant BF, Blanco C. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: Results of the national epidemiologic survey on alcohol and related conditions (NESARC). Drug Alcohol Depend 2011 May 1;115(1-2):120-30.

Hasin DS, Saha TD, Kerridge BT, Goldstein RB, Chou SP, Zhang H, Jung J, Pickering RP, Ruan WJ, Smith SM, et al. Prevalence of marijuana use disorders in the united states between 2001-2002 and 2012-2013. JAMA Psychiatry 2015 Dec;72(12):1235-42.

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Gateway or Exit

Cannabis as a gateway drug

- Cannabis use precedes other substance use

- Adults using marijuana more likely to develop an alcohol use disorder within 3 years

- In animal studies, THC caused enhanced responses to other drugs

Cannabis as an exit drug

- Opioid use decreased by 40–60% when cannabis used for pain

- Patients in detox reported using cannabis to prevent withdrawal and cravings but with mixed results

- Low-dose dronabinol improved insomnia, reduced appetite, and reduced energy during detox

Secades-Villa R, Garcia-Rodríguez O, Jin CJ, Wang S, Blanco C. Probability and predictors of the cannabis gateway effect: a national study. *Int J Drug Policy*. 2015;26(2):135-142

Weinberger AH, Platt J, Goodwin RD. Is cannabis use associated with an increased risk of onset and persistence of alcohol use disorders? A three-year prospective study among adults in the United States. *Drug Alcohol Depend*. February 2016

Gossop M, Battersby M, Strang J. Self-detoxification by opiate addicts: a preliminary investigation. Br J Psychiatry. 1991;159:208–212

Heikman PK, Muhonen LH, Ojanperä IA. Polydrug abuse among opioid maintenance treatment patients is related to inadequate dose of maintenance treatment medicine. BMC Psychiatry.

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General Adverse Effects

- Allergy symptoms
  - Sore throat, nasal congestion, food allergy, eczema, hives, anaphylaxis, swelling of mouth and tongue
- Pregnancy
  - Heavy cannabis use during pregnancy is associated with reduced neonatal birth weight.
- Vascular Health
  - Conflicting data suggesting increased risk of heart attack and strokes, especially in middle-aged (and older) users**.**
- Cannabis Hyperemesis Syndrome (CHS)
  - people chronically using cannabis on a daily basis, often for years,
  - episodes of severe nausea and vomiting
  - relieved by compulsive hot water bathing or showering
- Brain Health
  - heavy, chronic cannabis use early-onset use can lead to long term brain structural changes and cognitive impairment.
- Behavioral Health
  - low doses of THC appear to have an anti-anxiety and mood-elevating effect
  - high doses of THC can produce anxiety and lower mood.
  - chronic, heavy use - depressive and bipolar disorders,
  - Worsening of psychotic disorders such as schizophrenia

Abramovici H, Lamour S. INFORMATION FOR HEALTH CARE PROFESSIONALS: Cannabis (marihuana, marijuana) and the cannabinoids); October, 2018

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Smoking Cannabis
Health Effects

- Lung Health
  - Chronic cough/sputum
  - Wheezing/shortness of breath
  - Increased clinic visits for respiratory illness
- Cancer
  - Pre-clinical (i.e. non-human)
    - Cannabis smoke contains many of the same carcinogens as tobacco smoke and that cannabis smoke is as cytotoxic as tobacco smoke.
  - Clinical (i.e. human)
    - Limited and conflicting evidence
    - Epidemiological studies
    - No robust and consistent association between cannabis use and various types of cancer, with the possible exception of a link between cannabis use and testicular cancer.

Tashkin DP. Effects of marijuana smoking on the lung. Ann Am Thorac Soc 2013 Jun;10(3):239-47.

Abramovici H, Lamour S. INFORMATION FOR HEALTH CARE PROFESSIONALS: Cannabis (marihuana, marijuana) and the cannabinoids); October, 2018

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Cannabis and Driving

- There is an increased risk of motor vehicle accidents among persons who drive when intoxicated with cannabis.
- Impairment of various performance measures related to driving skills has been demonstrated immediately following cannabis use and up to 24 hours thereafter
- 7 to 10 % of blood samples of persons involved in traffic accidents were positive for cannabis.
- Young male MVA fatalities in California
  - 37 % samples positive for cannabis.
  - 80 % , when cannabis was present, alcohol was also present in the samples.
- This risk is magnified when cannabis is combined with alcohol.

Smiley AM, Moskowitz H, Zeidman K. Driving simulator studies of marijuana alone and in combination with alcohol. *Proceedings of the 25th Conference on the American Association for Automotive Medicine*, 1981, 107-116.

Smiley AM. Marijuana: on-road and driving simulator studies. *Alcohol, Drugs and Driving*, 1986, 2:121-134.

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Occupational Hazards

- Impairment of mental alertness and physical coordination resulting from the use of cannabis or cannabinoids may significantly decrease the ability to perform operation of heavy machinery and driving

- Depends on the
  - Dose;
  - Route of administration; and
  - Frequency of use

- Impairment can last up to 24 hours after last use

Ramaekers JG, Moeller MR, van RP, Theunissen EL, Schneider E, Kauert G. Cognition and motor control as a function of Delta9-THC concentration in serum and oral fluid: Limits of impairment. Drug Alcohol Depend 2006 11/08;85(0376- 8716; 0376-8716; 2):114-22.

O'Kane CJ, Tutt DC, Bauer LA. Cannabis and driving: A new perspective. Emerg.Med.(Fremantle.) 2002 09;14(1035-6851; 3):296-303.

Desrosiers NA, Ramaekers JG, Chauchard E, Gorelick DA, Huestis MA. Smoked cannabis' psychomotor and neurocognitive effects in occasional and frequent smokers. J Anal Toxicol 2015 May;39(4):251-61.

Haney M, Rabkin J, Gunderson E, Foltin RW. Dronabinol and marijuana in HIV(+) marijuana smokers: Acute effects on caloric intake and mood. Psychopharmacology (Berl) 2005 08;181(0033-3158; 1):170-8.

Karschner EL, Swortwood MJ, Hirvonen J, Goodwin RS, Bosker WM, Ramaekers JG, Huestis MA. Extended plasma cannabinoid excretion in chronic frequent cannabis smokers during sustained abstinence and correlation with psychomotor performance. Drug Test Anal 2015 Jun 11.

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