• Cannabinoids
  • Natural and synthetic compounds resembling delta-9-THC

• Forms Available & “Concentration*
  (amt & % of resin depends on growing conditions)
  • Marijuana, bhang - leaves, fine stems, some flowers/seeds (~4-9 THC%, but some far more potent)(1-2% was the norm in 60’s-80’s)
  • Sinsemilla, ganja - leaves & flowers from unpollinated female plants (~8-15% or more)
  • Hashish, charas - dried resin (10-24% or more) from female flowers of Cannabis indica mostly
  • Hash oil – a solvent is used to extract THC from from hashish, then strained to remove plant material (~15-60%)
  *Remember relative potency of forms; precise numbers change with year & source

• Active Ingredient(s)
  • Major psychoactive ingredient: delta 9 tetrahydrocannabinol (THC) (~50-75 mg/joint or more now vs 20 mg 20 yrs ago). How much is absorbed depends on how one smokes.
  • As with tobacco/nicotine, only a fraction of the available active ingredient is absorbed by user
  • Many, many related cannabinoids in pot – several are psychoactive, others may modulate action of THC, others have non-psychoactive actions, others are created when the liver transforms some of these
  • Peak blood levels reached in 10 min, perceived high lasts a couple hrs, but actual effects last much longer

• Cannabinoid Receptors
  • 1990 - Found THC binds to specific very widespread receptors (CB1) in limbic system, cortex, motor system, spinal cord, but not much of brainstem.
  • Other receptors (CB2) widespread in immune system
  • 1992 Discovered 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-arachidonoylglycerol)
  • Researchers have developed compounds to both stimulate or block CB receptors to study how they function.

• Endocannabinoids work very differently than other neurotransmitters we’ve discussed
  • Released by the post-synaptic neuron
  • Bind to pre-synaptic receptors
  • This “backwards” transmission is called retrograde transmission, providing feedback to pre-synaptic neuron and inhibits the release of whatever transmitter the presynaptic neuron is using. They also affect glial cells.
  • THC mimics this effect
• Oral Route vs Smoking
  • slower, less complete absorption - harder to "titrate" dose because of 2-3 hr delay in action
  • other compounds likely to be absorbed as well - more chance of nausea or "hangover"

• Common Body Effects
  • red eyes
  • droopy eyelids
  • dry mouth & throat
  • increased pulse, BP
  • muscle relaxation & impaired coordination
  • mixed bronchial effects (dilation but irritation)
  • decreased reflexes
  • dose & expectancy-dependent effect on appetite
  • dose & expectancy-dependent effect on sexual behavior
  • decreased sex hormones and sperm count/ovulation
  • decreased body temp
  • decreased body temp

• Common Psychological Effects
  • Relaxation, sedation
  • Euphoria, irritability but stable mood changes
  • Sensory enhancement
  • Impaired short-term memory & learning
  • Impaired attention
  • Longer reaction time
  • Impaired visual tracking & spatial processing
  • Impaired temporal ordering of behavior
  • Decreased problem solving & judgment
  • Altered time perception
  • Decreased motivation
  • Altered cognition
  • Impairments outlast high - up to 3 days
  • half-life = ~30 hrs, but variable
  • Regular users may test positive for as much as 30 days

The Leary Biscuit
• Cannabis Impairs Driving
  • 40% of those under 30 in accidents have cannabis in their system
  • Cannabis users are about twice as likely to be ticketed or have an accident than non-users
  • Even greater impairment when combined with alcohol; affects perception, judgment, vigilance, reaction time, steering
  • About 300,000 ER visits/yr in DAWN hospitals associated with cannabis use

• MJ Smoke vs Tobacco Smoke
  • similar levels of carbon monoxide & other gases, ~50% more tars & carcinogens in MJ smoke; unfiltered
  • pattern of smoking different (less often but deeper) - NOT risk-free
  • decrease in ciliated cells that cleanse lungs leading to joint cough and bronchitis
  • lung studies suggest damage from 1-3 joints = that of 5-15 cigarettes
  • sometimes cannabis contains contaminants

• Other Risks
  • Depends on pattern of use
  • Short-term: lengthy impairment of driving & perform.; affects memory, attention, and, importantly, motivation. Increased pulse risky to some; increased risk of ischemic stroke in some.
  • Long-term: risk to lungs; lowered fertility; adverse effects on fetus & production of breast milk; suppresses immune system (but thus far no clinically significant effects demonstrated); risk of dependency as use increases
  • Heavier use/higher potency likely to have more adverse behavioral effects
  • In those predisposed to mental illness, heavy use is associated with 5-10 fold increase in risk of schizophrenia

Comparison of Rate of Dependency
• Marijuana 9%
  • Alcohol 13%
  • Cocaine 17%
  • Heroin 23%
  • Nicotine 32%
  • But for those who do become dependent on MJ & seek treatment, 41% relapse within 6 months.
  • http://www.scientificamerican.com/article.cfm?id=the-truth-about-pot

• Dependency
  • Occasional use-no physical dependency - may develop a psychological dependency
  • Higher dose regular use can produce tolerance, dependence & a delayed withdrawal syndrome (restlessness, irritability, craving, insomnia, aches, sweating, anxiety, depression, nausea, cramping)
  • This syndrome is now being studied with newly discovered anandamide antagonists which can immediately trigger the withdrawal.
  • Many users find quitting difficult & seek substance abuse treatment

• Possible Medical Uses
  • Anti-nausea and appetite-stimulant
  • Analgesic, treat chronic pain, euphoric to ease suffering
  • Relax muscles/decrease muscle tension in
  • MS, Tourette’s and spastic disorders
  • Reduced intraocular pressure of glaucoma, but other drugs available
  • Occasionally used for acute bronchodilation, but smoking harms lungs in other ways
  • http://www.youtube.com/watch?v=hIIR2g3HAE8
  • (curb your enthusiasm)
Controversy Over Medical Marijuana Continues

- Decriminalization of the medical use of marijuana in 19 states (4 more in works) but Feds crack down periodically since Federal laws have not changed
- State laws vary substantially
- Continued controversy even in those states that have legalized medical marijuana
  - http://www.youtube.com/watch?v=an7neQrpc94
  - http://www.youtube.com/watch?v=c1USWdiJnc&feature=related
- But……
  - http://www.npr.org/2012/02/13/146826169/mendocino-ending-its-medical-marijuana-experiment
  - http://www.npr.org/2012/04/03/149937087/federal-agents-bust-marijuana-school-oaksterdam

Legal Prescription Cannabinoids

- Marinol (dronabinol) 2.5 mg capsules Cessamet (nabilone)
- Most patients prefer marijuana however- faster effects via smoking, able to titrate dose, perceived as more effective
- New in Canada: Sativex – a marijuana extract in an oral spray seeking approval for…. potential use
- Also doing research on cannabinoid antagonists as potentially useful medicines.
- http://www.youtube.com/watch?v=1USWdiJnc&feature=related

What change, if any, should be made in marijuana’s legal status?

- Greater availability for medical use?
- If it is “medicine”, should it be held to FDA standards like other drugs?
- Greater availability for personal use?
- Will we be seeing a repeat of current tobacco related health problems? Or alcohol problems?
- How should sale/supply be handled?

“Spice”, K2, Mojo, Herbal Incense, Smoke, Herbal Smoking Blend, “Legal Weed”

- Marketed as a legal herbal but the “herbs” are generally non- or weakly active & synthetic “designer drug” cannabinoids have been added
- As of March 2011 those synthetic cannabinoids are illegal Schedule 1 drugs and states are enacting their own laws (Iowa’s was passed by the Senate after death of an Iowa teen on spice)
- Some batches have contained toxic contaminants
- Adverse effects range from catatonia & inability to speak to agitation, aggression