Marijuana, Compassionate Care Act and Review of Recent Drug Trends

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November 10, 2014
AITCOY
Springfield, Illinois



Disclosures

- No conflict of interest with this content
- Potential perception of conflict:
 - * Collaborator: Caron Foundation
 - Consultant: Alvee Laboratories, Braeburn Pharmaceuticals, Millennium Laboratories
 - Founder: The Parents Academy (supported, in part, by Caron Foundation)
 - Managing Partner: Treatment Partners LLC (Two Dreams Outer Banks)
 - Medical Director: Encounter Medical Group, P.C.
 - * Partner: EMGlobal LLC
 - Former Consultant: GW Pharmaceuticals

Objectives: Following this presentation the participant will be able to:

- Discuss the physiological and psychological effects of marijuana on the body
- Use information to engage a young person in a discussion about common myths of marijuana use
- * Express common concerns and possible solutions the Compassionate Care Act may have on the fields of education, healthcare and behavioral health
- Create process to follow and understand prescription drug use and local heroin use



My Opinions

- Extensive review of scientific literature
- Personal communications with scientists in the area
- * Physician in addiction medicine
- Former member of FDA advisory board
- Former policy advisor to President Bush





Pharmacology

- The scientific study of the actions of drugs and their effects on a living organism and the effect of the living organism on the way the drug exerts its effects
- The classes of drugs causing substance-related disorders are not fully distinct
- All drugs that are taken in excess have in common direct activation of the brain reward system, involved in reinforcement of behaviors and production of memories
- Activation of reward system so intense that normal activities may be forgotten



Basic Principles

Pharmacokinetics- what the drug does to your body



- Pharmacodynamics- what your body does to the drug
- Absorption- getting in
- Metabolism- getting changed
- Action- receptor interaction- getting busy
- Excretion- getting out



Psychotropic Substance

- Chemical substance that crosses the blood-brain barrier and acts primarily upon the central nervous system where it affects brain function, resulting in alterations in perception, mood, consciousness, cognition, and behavior
- Used to purposefully alter one's consciousness, or as entheogens, for ritual, spiritual, and/or shamanic purposes, as a tool for studying or augmenting the mind
- Have therapeutic utility, e.g., as anesthetics, analgesics, or for the treatment of psychiatric disorders.



Substance-Related Disorders

- Substance use disorders
- Substance induced disorders
 - Intoxication
 - * Withdrawal
 - Other substance/mediation induced mental disorders
 - Psychotic, bipolar and related, depressive, anxiety, obsessive-compulsive and related, sleep, sexual dysfunctions, delirium, and neurocognitive disorders
 - Class specific





The Lure and the Trap

- Start to use drugs
- Pleasure experienced





Path to Addiction



- Innocent beginning
 - Minor effects
 - * Pleasurable effects
 - Cannot "unlearn"
- Continued social use
 - Unpleasant effects diminish
 - Economic costs minimal
 - No interference with activities

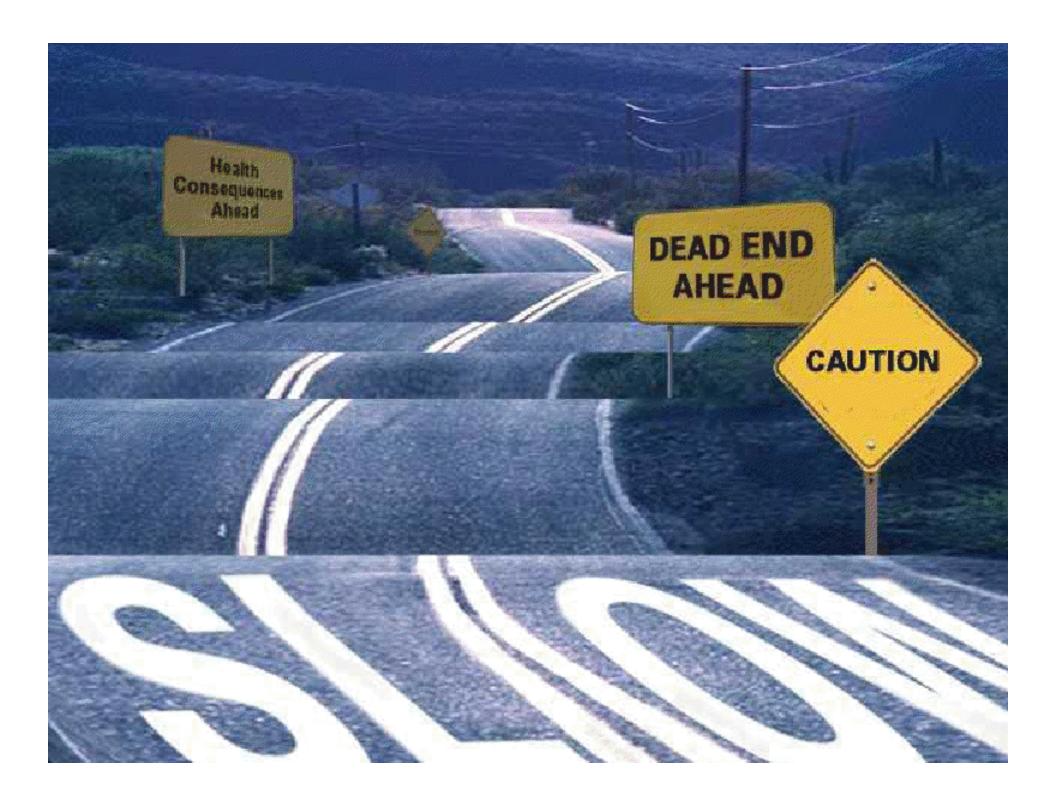




Path to Addiction

- * Line crossed
 - Consequences increase
 - Use to feel normal
 - Hard to connect experience to drugs
- Majority of students, no observable major consequences





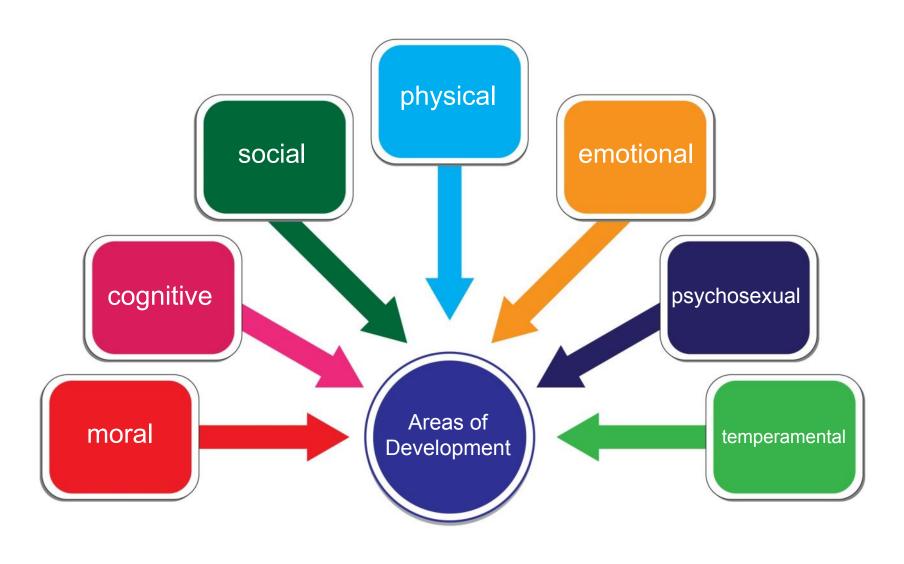
Why Use a Developmental Model?



- To assess
- * To encourage and promote growth
- * To understand



Seven Areas of Development





Four Tasks of Adolescence

Seven areas translate into four major areas where major developmental tasks are defined as:



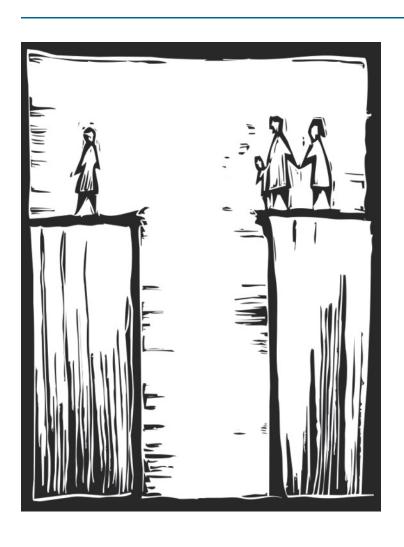
Goals of Development are Balanced by Preoccupations of Adolescence

- Sexual identity
 - Body image (fertility)
- Self identity
 - Friends
- Separation
 - Independence (family)
- Vocational selection
 - Value clarification (future)





Early Adolescence



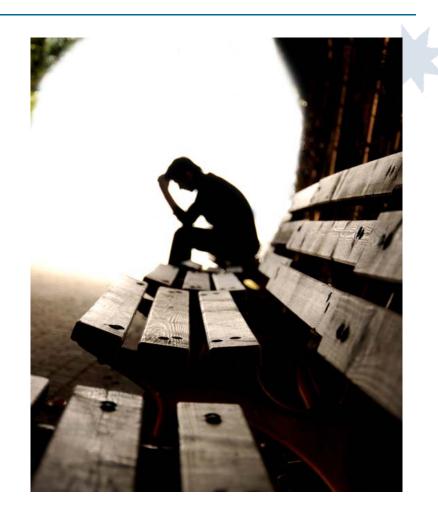
- First efforts at separation
- Recognition of non-perfect parent and rebellion against them
- Strong identification with peers





Early, continued

- Abstract thinking
- Verbalization of values
- Mood swings
- Difficulty with impulse control
- Insecurity about body changes





Middle Adolescence

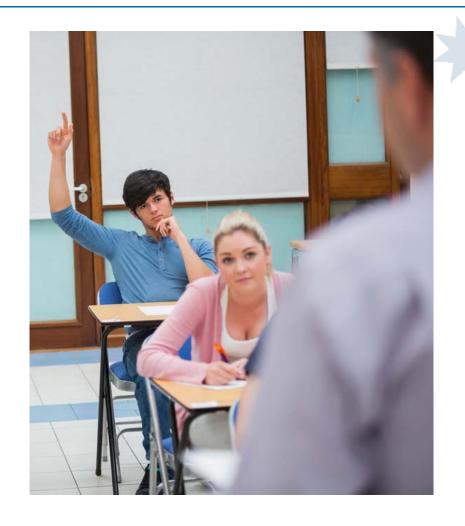


- * Peak of rebellion
- Transition from parental to peer direction
- Increased sexual interest



Middle, continued

- Difficulty with postponement of gratification
- Increased cognitive abilities
- * Values clarification





Late Adolescence



- Firmer identity
- Increased ability to express emotions
- Increased ability to postpone gratification



Late, continued

- Resolution of relationship with authority figure
- Increased emotional stability
- Increased self reliance



Why Use a Developmental Model?



- To assess
- * To encourage and promote growth
- * To understand





Discipline and Independence



- Description
- Security v. Freedom
- * Limits
 - * Clear
 - Age Appropriate
 - * Earned
 - Growth Oriented



- * Related
- * Reasonable
- * Timely
- * Escalate
- Consistently applied
- Calmly applied





Bad Consequences



- * Revengeful
- Self-punishing
- * Empty
- * Shaming



Why Kids Use: Contrasting Views



Parents

- * School
- * Parents
- * Peers
- * Pushers
- Media
- * Police
- * Role Models

Adolescents

- Feelings
- * Fun
- * Risk Taking
- * Thrill Seeking
- * Autonomy
- * Experimentation
- New Identity





Variables to Experimentation

Availability

* Access

★ Perceived Risk

* Prior Use

* Peer Use

* Respect Norms





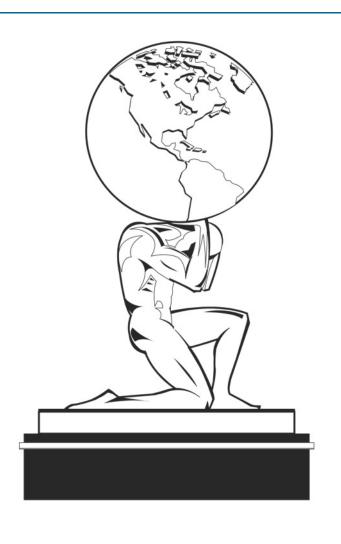
Enabling: Feelings

- Protective instinct
- * Self-doubt
- * Fear
- Performance anxiety
- * Anger





Enabling: Beliefs



- Pressures are too great
- * I am not relevant
- * All kids do it
- I love, therefore,I trust





Enabling: Behaviors

- Keeping secrets
- * Avoiding conflict
- * Shielding from consequences
- Doing their work





Adolescents' Responsibilities

- * Feelings
- * Behaviors
- * Performance
- * Social life
- * Outside life
- * Future





Teaching Adolescents



- * Modeling
- * Reinforcement
- Consistency
- * Encouraging
- * Patience
- Allowing mistakes



Consequences Early

- Ambivalence about separation
- Persistent anger
- Self harming behaviors
- Rebellious peers/subculture
- * Doubts





Early, continued



- Frustration and isolation
- Inability to deal with the abstract
- * Confusion
- Inability to learn from experiences



Consequences, Middle



- Struggles with parents
- * Self involvement
- Peer approval seeking
- Active sexual fantasy life



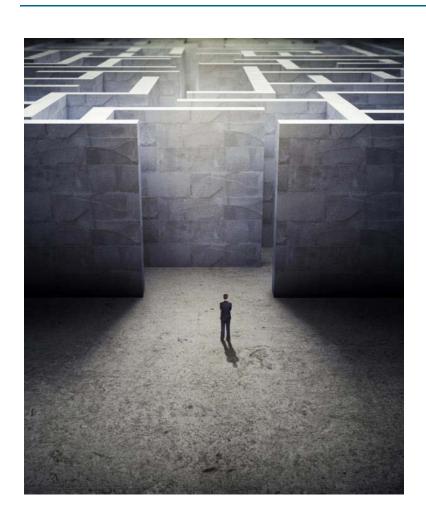
Middle, continued

- Inability to postpone gratification
- Unable to abstract
- Poorly defined moral values
- Inability to use wisdom and to evaluate situations according to appropriate values





Consequences, Late



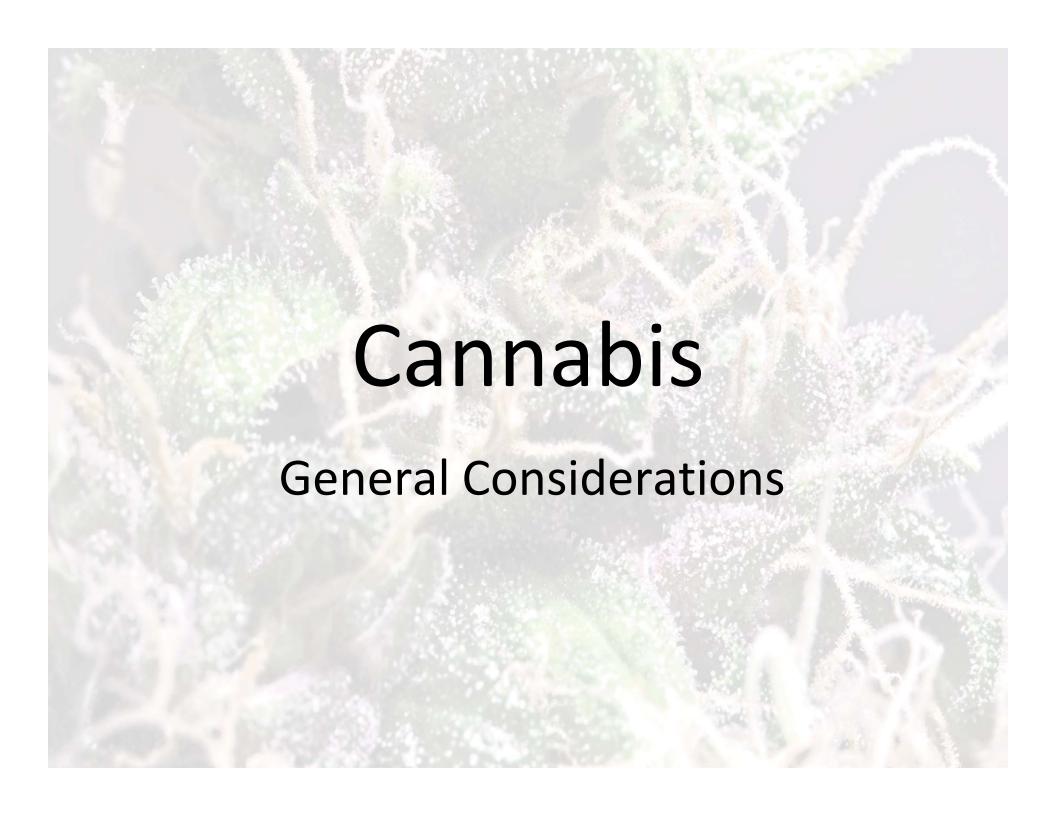
- Minor adult disturbances
 - Unresolved relationship and identity issues
 - Expression stunted
 - Unable to postpone gratification
 - Persistent emotional instability
 - Personal responsibility lags
 - Ability to make choices confused



Late, continued

- Mood swings
- Difficulty in defining vocational goals
- Deficits in formulation of moral, religious, and sexual values



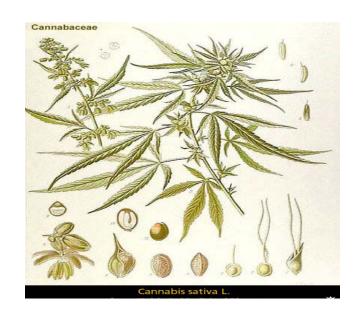




Understanding the Plant

- Composition of herbal cannabis varies significantly
 - Rich source of variety of compounds
 - Cannabinoids
 - * Terpenoids
 - * Flavonoids
- Exact content of chemical composition varies
 - Plant genetics
 - Growth conditions
 - * Time of harvest
 - Drying conditions





- Many species exist: Cannabis Sativa (Europe), Cannabis Indica (India) and Cannabis ruderalis (Siberia and central Asia)
- * 460 known chemical constituents of cannabis
- * 66 constituents have a cannabinoid structure
- * Δ^9 -Tetrahydrocannabinol (Δ^9 -THC or THC) most important constituent
- * Δ^9 -THC is the principal psychoactive component of cannabis
- * Delivery systems do not deliver standardized dose
- * Smoking to de-carboxylate delivers harmful pyrolytic products



The Plant

* Plant Tissue	%THC
* Seeds	0.0
* Roots	0.0
* Stem	0.3
* Leaves	0.8
Seeded Female Inflorescence	6.3
Unseeded Female Inflorescence	15.2

Inflorescence





- During the 1800s, the active ingredient in opium—
 morphine—was identified and isolated.
- Other opiates and synthetic medicines rapidly followed
- Opium was not smoked for medical purposes
- The paths of medicinal opioid development and recreational use of smoked herbal opium became clearly distinct



Different Paths continued

- By contrast, the active ingredients in cannabis remained unknown
- Preparations lacked standardizations
- * Clinical response varied
- Conditions were numerous
- Better, targeted medications developed
- Fell out of favor with the medical profession





Cannabis: Street Names

- * Pot
- * Reefer
- * Buds
- Grass
- weed
- * Dope
- * Ganja
- Kilobricks
- * Thai sticks
- ★ Marinol®

- Herb
- Boom
- Gangster
- Mary Jane
- Sinsemilla
- Joint
- Hash, hash oil
- Blow
- Blunt
- Green



Cannabis: How Taken

- Average THC concentration in marijuana is 1-5%, hashish 5-15%, and hashish oil 20%
- Sinsemilla derived from the unpollinated female cannabis plant, up to 17% THC
- Single intake called a hit, approximately 1/20th of a gram
 - 1-3 hits of high potency Sinsemilla average
 - Calculate hits for "ditch weed"
 - drop or two of hash oil equal to a "joint"
 - Initial starting dose of Marinol® is 2.5 mg, twice daily

Cannabis: Pharmacological Properties

- Duration: smoked 1-3 hours, oral 4-10 hours, 30 metabolites
- Tolerance: rapidly develops
- Physical Dependence: yes
- Psychological Dependence: yes
- ★ Onset: smoked 15 sec to 1 minute, oral- ½ to 1 hour
- Pattern of Use: smoking, daily. Joint delivers 10 mg THC; average dose 20-30 mg/day
- * LD 50 1270 mg/kg in male rat, 730 mg/kg in female rat.
- * TI 40,000



Cannabis: Distribution

- THC acts on cannabinoid receptors in the brain, higher than any other receptor, naturally occurringanandamide
- Cannabinoid receptors are part of the ECS
 - CB1 receptors concentrated in the hippocampus, amygdala, basal ganglia, cerebellum, nucleus accumbens and cortex
 - CB2 receptors are peripheral
- * Functions: relax, eat, sleep, forget, and protect (DiMarzo et al 1998)



Cannabinoid: Therapeutic Uses

- Nausea and Vomiting
- HIV Wasting



Cannabis: Intoxication and Overdose

- Continued use causes reverse tolerance
 - User becomes more sensitive to small amounts of substance
- Below 10 mg/person/day unlikely to experience tolerance
- Psychological dependence more likely to develop than physical dependence
 - Stereotypical abstinence syndrome described
- Acute intoxication increases HR and conjunctival reddening
- * Fingertip titration of dose mediates risk of OD, more likely with oral consumption



Cannabis: Treatment

- * Standard CD treatment
- Challenge- belief that it is not dependence producing
- Challenge- difficulty in creating acceptance for patient in milieu



Outline

- Debunking the myths
- Prevention works



The Marijuana Problem

Bigger Than Previously Recognized



The Marijuana Problem

Most widely used illicit drug in America



- Of 5.6 million suffering, 62% are using marijuana
- Young people represent 23% of the suffering population



Problem, Continued

Average age of initiation decreasing



- Marijuana's potency is increasing
- With increasing potency and earlier use, marijuana poses significant threat



Problem, Continued

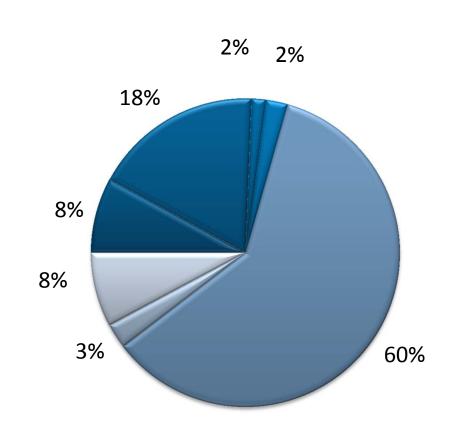
- Of all teens in drug treatment, 62% had primary marijuana diagnosis
- More young people in treatment than for alcohol
- * Almost equal numbers from criminal justice and other sources



Treatment Admissions (Ages 12 – 17) Primary Diagnosis



- Alcohol w/drug
- Opiates
- Cocaine
- Marijuana
- **■** Stimulants
- Other/None



SOURCE: SAMHSA, Treatment Episode Data Set, 1999



Debunking the Myths

- Marijuana is harmless
- Marijuana is not addictive
- Youth experimentation is inevitable
- * The criminalization of marijuana use is what leads to crime, not the drug itself



Myth 1: Marijuana Is Harmless

- Health consequences
- Social consequences
- * Economic consequences



Health Consequences Defined

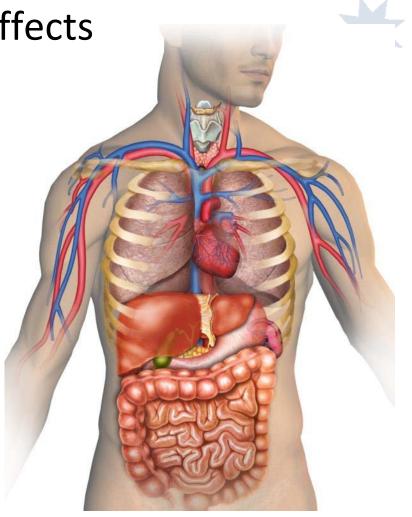
- Acute Effects
 - while intoxicated
- Post acute withdrawal
 - abstinent state in the regular, dependent user



Persistent and Chronic Effects

impairments developed as a result prolonged use, endure beyond the period of intoxication

 impairments due to use, structural and functional changes to major organs







- Time sense alterations
- Short term memory loss
- * Attention skills
- General difficulty expressing simple thoughts in words





- * Motor skills
- Increase in hunger
- * Nausea
- Dizziness







- * Alter mood
- *

- * Euphoria
- State of relaxation
- * Panic

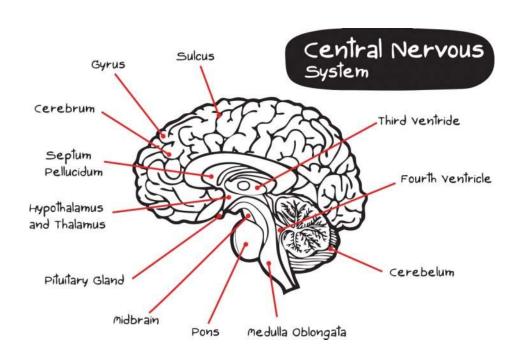


- Anxiety
- Tension and anger
- * Confusion
- Depersonalization and other behavioral effects





Areas of Harm



- Need for acute care
- Central NervousSystem Changes

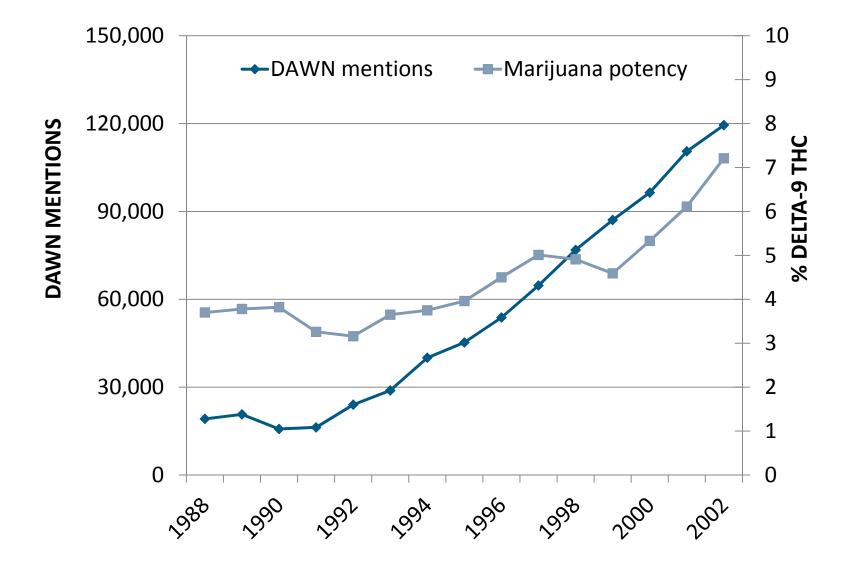


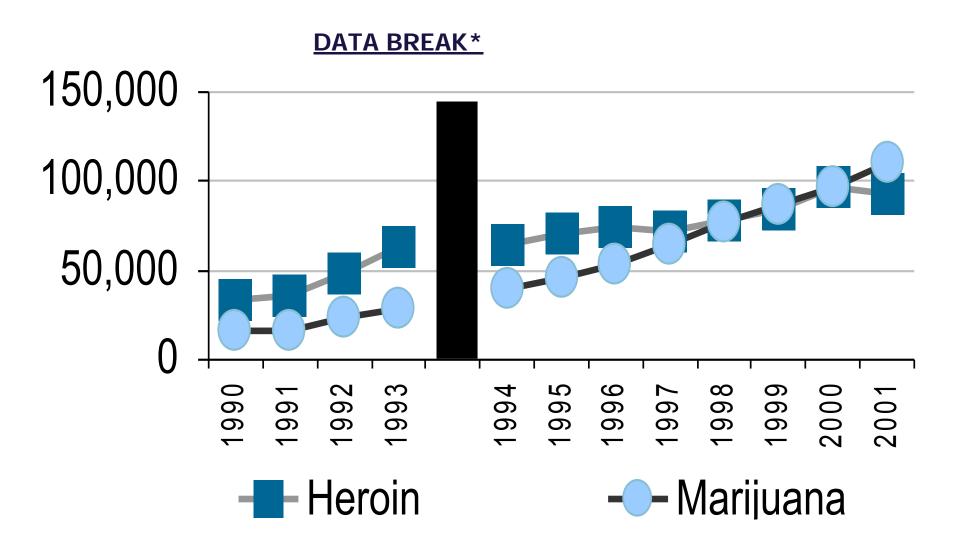
Need for Acute Care

Relationship to acute need for medical assistance



Rising faster than heroin caused need for medical assistance



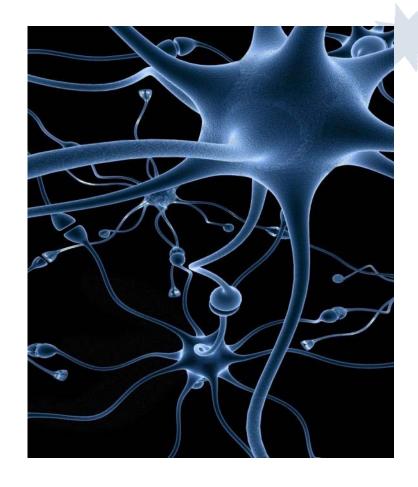


Source: SAMHSA, Drug Abuse Warning Network



Central Nervous System

- * Sites of action
- Memory
- Psychological vulnerability





Mechanisms of Action

 Produces anticipated and unanticipated effects binding with receptors



- High-affinity sites specific for Cannabinoids
- Two receptors CB1 And CB2



Human Memory

Most profound effect on recent memory



- Long term memories not affected
- * Incapable of functioning on the basis of knowledge regarding his personal life



More on Memory

- Hippocampus has receptors for endogenous "marijuana" (anandamide)
- Hippocampal damage is associated with failure to make new memories
- If stimulate receptor, hippocampus activity decreases



More on Memory

With repeated use, tolerance to loss of memory develops



- * With repeated use, tolerance to drug develops and user uses more drug
- * You do the math



Post Acute Effects

- Human aggressive responding
- * Conditions
 - Provoke subjects coming off drug
 - Provide opportunity to retaliate
 - Measure amount of retaliation
- * Acute Marijuana, Ss with ASPD
 - Increased aggressive responding





Persistent and Chronic Effects

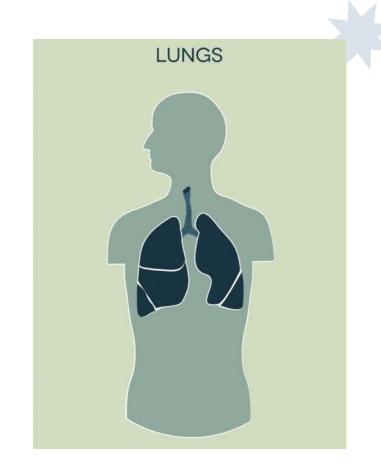
- * Physical
- Psychological



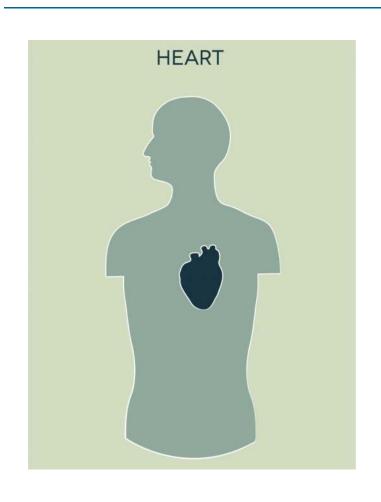


Respiratory

- * Carcinogenic components
- * Air obstruction
- Decreased exercise tolerance
- Chronic cough
- * Bronchitis
- Decreased pulmonary function
- Cancer







* Cardiovascular

- Increases in heart rate
- Can aggravate existing cardiac conditions or hypertension
- Reversed with abstinence



* Reproductive

- Inhibitory effects on pituitary leutenizing hormone, prolactin, and growth hormone
- Decreases plasma testosterone, sperm count and motility
- Marijuana is antiandrogenic with decreased libido or impaired fertility
- Disrupts female reproductive system
- Impacts pregnancy in adverse ways



Immune impairment

- Contradictory in human studies
- * Animal models show impairment
- Decreases signals to T helper cells
- Interferes with macrophage antigen processing
- May increase the risk of cancer (cancer surveillance system)



Psychological

- Psychiatric illness- no specific syndromes, however, may precipitate an illness
- Visual distortions
- Decrease in color discrimination
- Decrease in ocular tracking
- Decreased detection, recognition and analysis of peripheral visual field



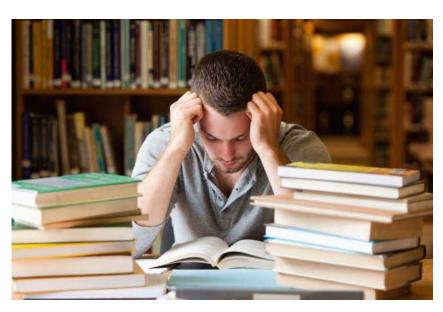
Psychological- Cognitive

- Impairment in ability to learn
- Listening and repetition learning compromised
- Heavy use associated with deficits in mathematical skill and verbal expression



Social Consequences

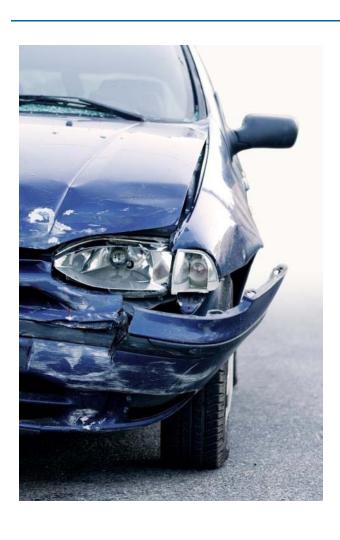
- Marijuana changes the way sensory information is processed
- Poor performance in school
- Increased delinquency







Economic Consequences:



- Lost employee productivity
- * Public health care costs
- * Accidents and crashes
- Americans spend close to \$11 billion annually on marijuana purchases

MYTH 2: Marijuana Is Not Addictive



Science of dependence and addiction



Syndrome described



Laboratory Evidence

- Marijuana is much more powerful today than it was 30 years ago
- Marijuana addicts experience withdrawal
- * There is an animal model for dependence



Absorption and Metabolism

- Self administration is by smoking and inhalation
- Can be taken orally





Absorption and Metabolism

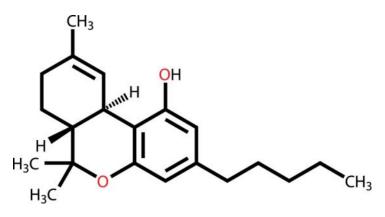
- Smoke contains more than 150 compounds
- Many of the Cannabinoids have psychoactive properties





Pharmacology Is Complex

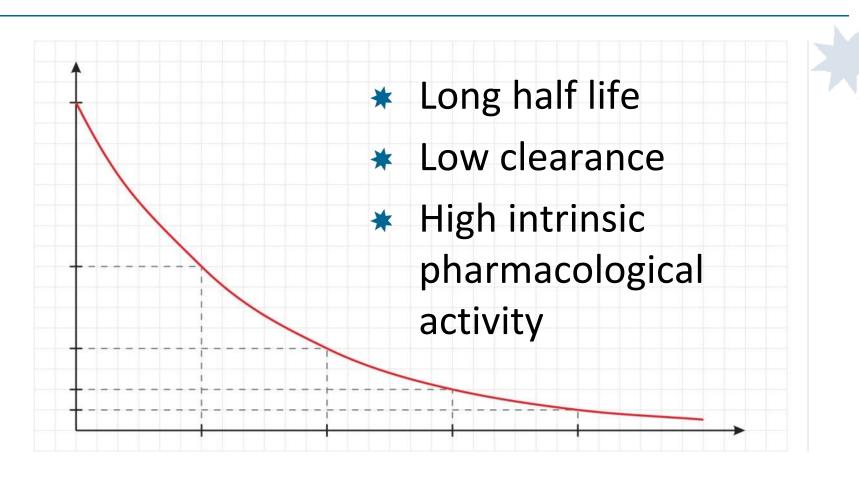
- Volatilized THC
- Deep inhalation
- Rapid absorption from the lungs
- THC and major metabolites traced throughout body and brain





Physical Dependence Producing Properties







Reinforcing Properties

- Rapid absorption
- High intrinsic pharmacological activity
- * Rapid entry into specific regions of brain



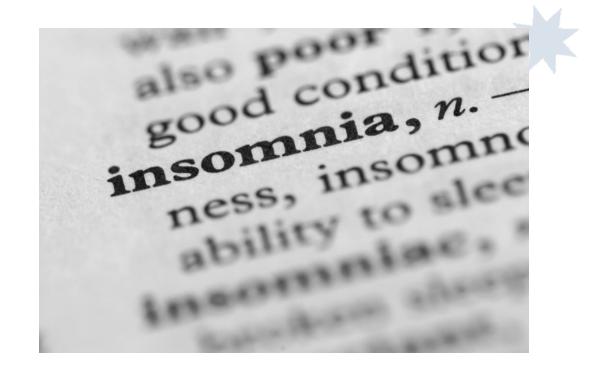
Tolerance

 Tolerance develops quickly and continues for a long time after stopping



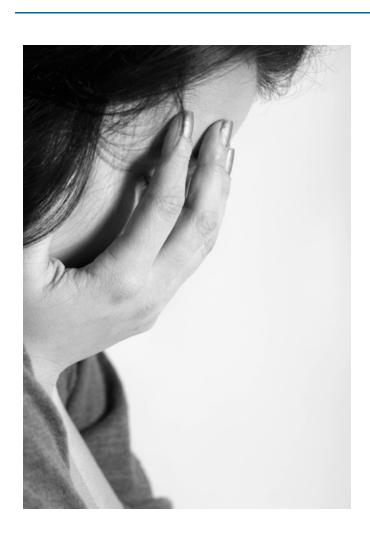
Syndrome Described

- * Insomnia
- * Abstinence
- * Nausea
- * Anorexia





Syndrome Described



- * Agitation
- * Restlessness
- * Irritability
- * Depression
- * Tremor





Syndrome Described

- * After 21 days of heavy use
 - Onset 10 hours of cessation
 - Peaks within 48 hours
 - Terminates by fifth day of abstinence





Clinical Observations

 Antisocial problems associated with progression



One in ten who try develop dependence





- Peer to peer spread has been misunderstood
- * The majority of young people do not use
- Recent decreases belie the belief that "nothing works"

MYTH 4: Criminalization Leads to Crime, Not the Drug



Non-dependent use is harmful



When controls are lifted, harms are increased



Research Links

- Marijuana use and violence
- Availability increases use
- The Dutch experience
- * Prison data
 - <0.5% of prisoners</p>
 - Tonnage of supply





Responsible Public Policy

- Stopping Initiation
- Brief and Early Interventions
- Treatment Improvement
 - Denial Gap
 - Motivation Gap
 - Treatment Gap
 - Recovery Gap





When Controls Are Lifted



- Drug CultureMessages
 - Drugs can't hurt you
 - Drugs are fun
 - You can use responsibly
- * 1970s experience



During the 1970s

- * 11 states decriminalized marijuana
- * 30,000 head shops
- * "Responsible-use" messages
- Drinking age of 18
- Sale of cigarettes, alcohol to teens







By 1979, % Users

* 35% of adolescents



* 65% of young adults had tried an illicit drug



Prevention Messages

- Drugs can hurt you
- Drugs cause addiction and death
- Drugs are not healthy
- Breaking the law is not responsible



Parent Movement

- * Formed 3,000 parent groups
- Stopped decriminalization
- Banned head shops





Parent Movement

- "No-use" messages
- Drinking age of 21
- Worked to stop sale of cigarettes, alcohol to adolescents





Results From 1979 to 1992...

Drug use drops by 2/3 among adolescents, young adults

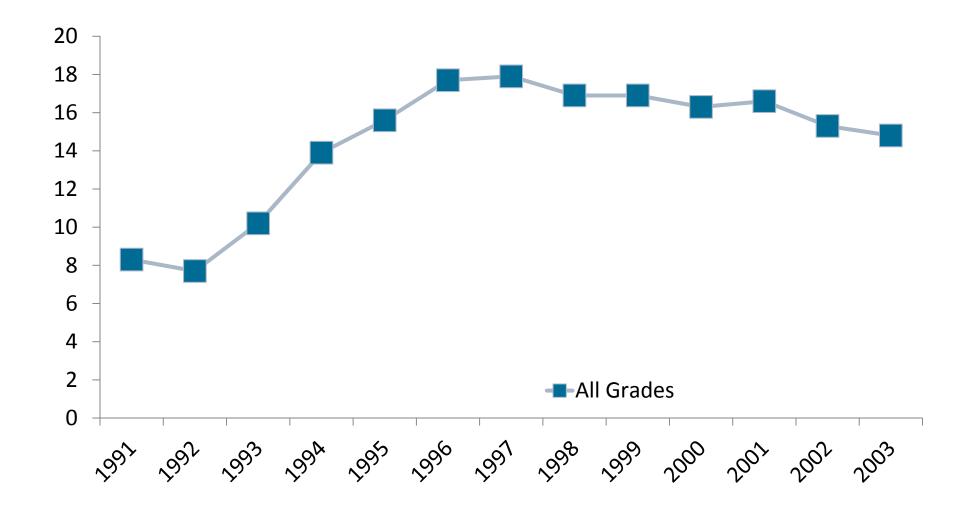


Daily marijuana use drops 500 percent



Fact: We Can Make A Difference

- When communities come together, the drug problem recedes
- Proven techniques can halt marijuana use:
 - Student drug testing
 - Parent involvement
 - Respect for community norms and laws
 - Science-based drug prevention







Major Forms of Drug Use

- Alcohol Use
- * Cocaine Use
- * Hallucinogen Use
- * Heroin Use
- Inhalant Use
- Marijuana Use
- Methamphetamine Use
- Sedative-Hypnotics Anxiolytics Use
- Nicotine Use





Classes of Prescription Drugs

- I- High potential for abuse, no accepted medical use in U.S., lack of accepted safety under medical supervision
- II- High potential for abuse, current accepted use with severe restrictions, may lead to dependence
- III- Potential for abuse, currently accepted use, low or moderate physical dependence and high psychological dependence



Classes of Drugs, continued

- IV-Low potential for abuse, accepted use, limited dependence
- V- Low potential for abuse, accepted use, narrow scope for physical and psychological dependence

What is Prescription Drug Abuse?

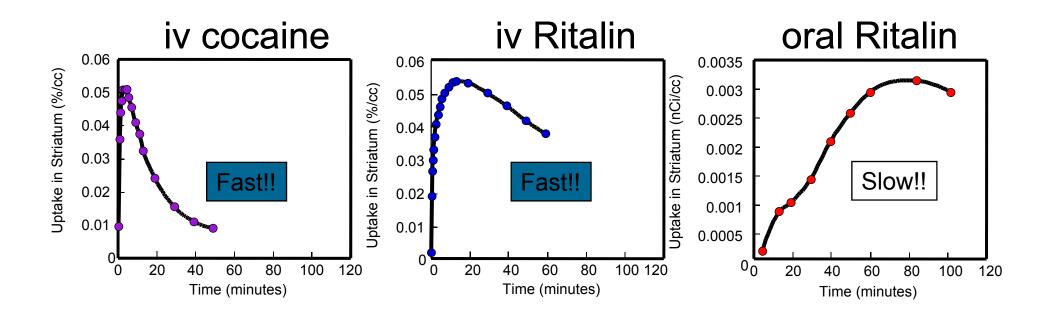
- Misuse: use of a medication (for a medical purpose) other than as directed or as indicated, whether intentional or unintentional" (Katz et al 2007)
- * Abuse: the intentional self-administration of a medication for a nonmedical purpose such as alerting one's state of consciousness, e.g., getting high (Katz et al 2007)

What is the Difference Between Therapeutic Use and Abuse



- Dose and frequency of dosing
 - Lower, fixed regimes vs. escalating use
- Route of administration
 - Oral vs. snorting vs. smoking vs. injecting
- Expectation of durg effects
 - Expectation of clinical benefit vs euphoria, "high"
- Context of administration
 - * Home or hospital vs school, disco, bar, party, etc.

Rate of Drug Uptake Into the Brain



Cocaine (iv) and Ritalin (iv) produce a "high" but Ritalin (oral) does not.

The slow brain uptake of oral Ritalin permits effective treatment without a "high."

Fastest Growing Drug Trend in the US:

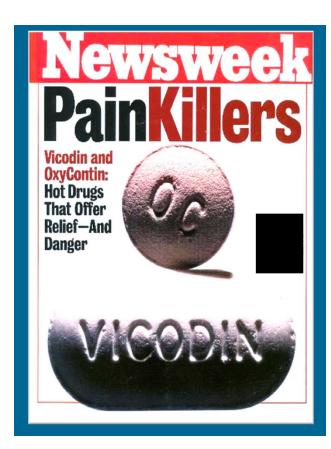
- New users aged 12 and older of prescription drugs outnumber new users aged 12 and older of marijuana (SAMHSA 2004)
- * 48 million people have used a prescription drugs for nonmedical reasons (NIDA, 2005)
- More than 3 million teenagers abuse prescription drugs (2007 NSDUH)

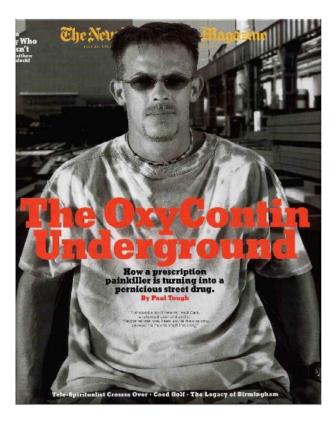
Why has prescription drug abuse been increasing?



Increased Media Attention







Why are These Drugs Abused?

Self-medicating:

- some people use medications prescribed to them in ways other than those described by the prescriber (dosage, frequency)
- Some people use medications prescribed to someone else to treat themselves (taking a family member's pain reliever for your pain)



Why Abused, continued

To get "high":

 Some people use medications to achieve an altered state of consciousness

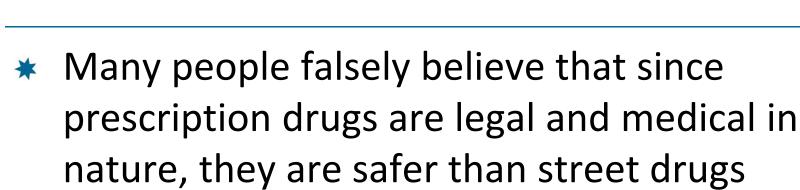
* To perform:

 Some people use stimulants to concentrate, increase alertness

* Other:

Weight management (stimulants)

Just Because It's Prescription Does Not Mean It's Safe



(Partnership for Drug Free America, 2005)



- * One third of teens believe that it is OK to use a prescription medication with a prescription once and a while (Partnership for Drug Free America 2006)
- ★ 29 percent of teens believe that prescription pain relieves are not addictive (Partnership for a Drug Free America 2006)

Non-Therapeutic Use of Prescription Drugs



- Non-medical use of prescription drugs represents a relatively small percentage of all use of these medications, but it is a problem that requires attention
- * A variety of adverse health and social consequences arise from the interactions of multiple drugs (prescribed or illicit) used concurrently
 - * 62% of treatment admissions with opiates (other than heroin) as primary substance of abuse reported abuse of other substances.
 - * The most commonly reported secondary substances of abuse were alcohol (21%) and marijuana (20%), as well as tranquilizers and non-smoked cocaine (10% each)



Age

- Teenagers, young adults, and those over 60 account for the majority of abusers:
- More young people are experimenting with prescription drugs than are experimenting with marijuana (SAMHSA 2004)
- 9 percent of adolescents used prescription medication for nonmedical reasons in 2004 (NSDUH 2004)
- 17 percent of those over 60 abuse or misuse prescription drugs (SAMHSA 2003)



College Students

- The median age of new users is 23 (NSDUH)
 - The majority obtained from a peer
- * Those who abuse pain relievers are:
 - 8 times more likely to use marijuana
 - 4 times more likely to binge drink
- * Those who abuse stimulants are:
 - * 24 times more likely to use marijuana
 - 7 times more likely to binge drink (McCabe, Boyd 2005)



Gender

- * Among college students, both men and women are more likely to abuse opioids than stimulants, but men are more likely than women to abuse either (McCabe et al, 2005)
- Teenage girls are more likely than teenage boys to abuse prescription drugs (ONDCP 2007)

Nonmedical Prescription Drug Use

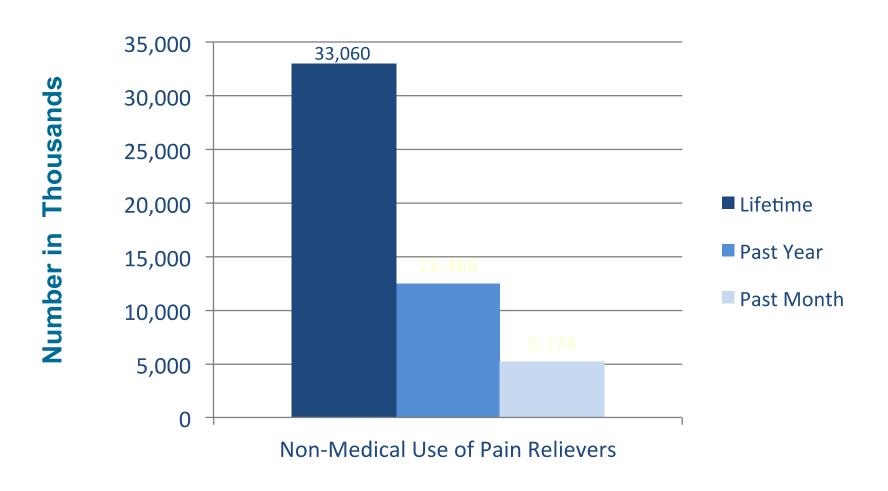
"Not prescribed for you

or

"You took the drug only for the experience or feeling it caused"

(Excludes OTC)

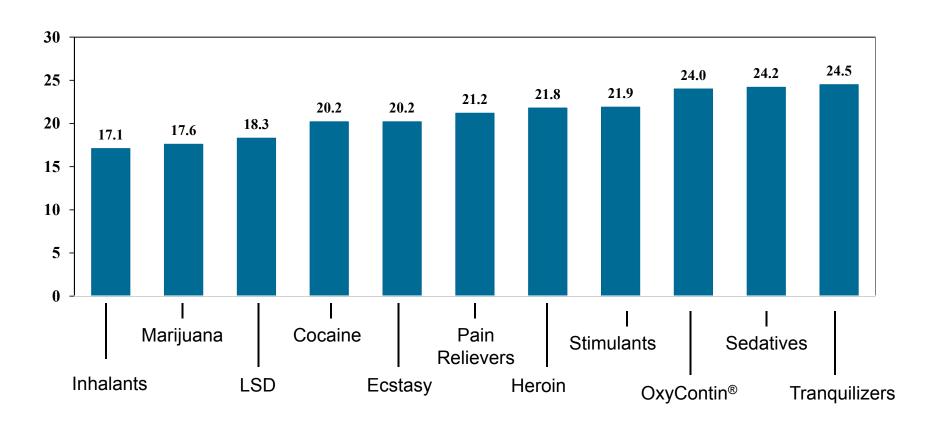
Nonmedical Use of Pain Relievers in Lifetime, Past Year, and Past Month 2007



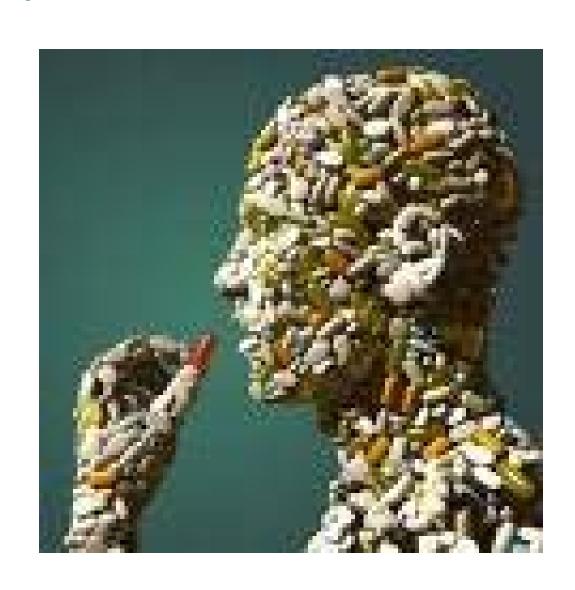
Source: NSDUH 2007

Mean Age at First Use for Specific Illicit Drugs among Past Year Initiates Aged 12 to 49: 2007

Age in Years



Why is This Such a Problem?



Michael Jackson is *Not* the First Victim



- Admissions to treatment centers for prescription pain relievers increased 300 percent from 1995 to 2005 (ONDCP 2008)
 - Admissions to hospitals for overdoes of prescription pain relievers increased a similar amount in the same time period (ONDCP 2008)
- There is evidence that abusers of OxyCotin® graduate to heroin (Educating Voices)

Model Treatment Programs

- Bio-behavioral assessment
- Detoxification considerations
- Counseling
- Medical treatment
- Psychiatric care
- Referral to wrap around services
- Long term follow-up





ASAM Guidelines

- * Literature review
- Consensus discussion
- * Field and Peer review
- * Conclusions and recommendations regarding the therapeutic value of smoked marijuana and the role of the physician



Why President's Action?

- Research in therapeutic potential lags behind other modern medications
- Recent discoveries and elucidation of endocannabinoid receptor system coupled with new research tools facilitates analytical, pharmacological, and other preclinical research
- Liberal cannabis distribution puts patients with medical conditions and others at risk in setting of little scientific evidence to guide rational/ethical action



ASAM Paper Outline

- Modern History
- Basis for Cannabinoid Therapeutics
- "Medical Marijuana" in the U.S.
- Reports from Expert Bodies
- Professional Organizations
- The Federal Position
- Federal Departments and Agencies



Outline Continued

- Modern Medications and the FDA
- "Medical Marijuana" and the Modern Medication Model
- Other Countries
- Existing Research
- Oral Cannabinoid Preparations
- * Are There Principled Reasons to Exempt Cannabis?



Outline Continued

- Could a Cannabis Preparation Achieve FDA Approval?
- The Significance of Scheduling
- * Conclusion
- * Recommendations
- * <u>WWW.ASAM.ORG</u> publications: policy statements: featured policy statements: Medical Marijuana



Pharmacological Strategy

Exploit properties of the cannabinoid system while minimizing the psychotropic effects of the molecule(s) used



Significance of Findings

- Cloning of CB1 and CB2 enabled discovery of endogenous agonists and enzymes that catalyze endocannabinoid inactivation
- Endocannabinoids that are produced endogenously following onset of pathology may act in site- and time- specific manner to minimize consequences of condition



Significance, continued

- * The endogenous endocannabinoids may differ significantly from THC and synthetic CB1 and CB2 agonists in their ability to limit extension of insult, injury
 - Preclinical data supports this view: animal benefit in neuropathic pain, anxiety, irritable bowel syndrome, proliferation and migration of CA cells
- Clinical target at degrading enzymes to prolong pro-homeostatic actions



- Endocannabinoids are neurotransmitters, may have protective function in response to injury/insult
- Cannabinoids (e.g., THC) modulate neural activity
- Endocannabinoids are involved in synaptic remodeling
- Cannabinoids (e.g., THC) can modulate synaptic remodeling
- Depending upon the specific CNS circuits involved, cannabinoids can have a host of actions on brain, cognition, and behavior (some beneficial, some not)



What WE Know

* Unimpeachable Preclinical Research Indicates That There Are Many Diseases (Some Currently Totally Untreatable) That Can Be Successfully Treated By Cannabinoid Agonists or Antagonists



What We Know

* Unimpeachable Preclinical Research Indicates That There Are Many Ways In Which The Endocannabinoid System of The Body Can Be Manipulated to Produce Either Cannabinoid Agonist or Antagonist Actions



Potential Cannabinoid Therapies

- Diseases of Energy Metabolism
 - Appetite Dysregulation
 - Obesity
 - Dyslipidemia
 - Peripheral Energy Metabolism Dysregulation
 - Cachexia
 - * Anorexia
 - Type II Diabetes



- Pain
 - Somatosensory Pain
 - Neuropathic Pain
- * CNS Disorders
 - Closed Head Brain Trauma
 - Spinal Cord Injury
 - Multiple Sclerosis
 - * Tourette's Syndrome
 - Parkinson's Disease



- CNS Continued
 - Alzheimer's Disease
 - Epilepsy
 - Anxiety
 - Depression
 - * Insomnia
 - Post-Traumatic Stress Disorder
 - * Schizophrenia





- Cardiovascular & Respiratory
 - Hypertension
 - * Hypotension
 - Circulatory Shock
 - Myocardial Reperfusion Injury
 - * Atherosclerosis
 - Cardiopathies
 - * Asthma
- Inflammation





- * Eye Disorders
 - * Glaucoma
 - * Retinopathy
 - * Intraocular Pressure
- Reproductive Disorders
- Musculoskeletal Disorders
 - * Arthritis
 - Osteoporosis
 - Post-Fracture Bone Healing



* GI and Liver Disorders

- Inflammatory Bowel Disease
- Ulcerative Colitis
- Hepatitis
- Cirrhosis Encephalopathy
- * Cirrhosis Liver Fibrosis
- Cirrhosis Vasodilatation

* Cancer

- Cancer Cell Proliferation
- Colorectal Cancer

Why Do We Care About the FDA Process?

- Protect patient health and safety
 - promote quality, safety and efficacy of medications
- Testing for body of risk/benefit and pharmacological data
- Registration/inspection ensures manufacturing quality control tools
- Promotional activities of manufacturers limited
- Products prescribed/dispensed under the supervision of licensed health providers

Modern Regulatory Approval Requirements



- Quality
- Safety
- * Efficacy





Quality

- Product Composition
- * Characterization
- Quantification of components
- Standardization / Consistency
- Stability / Storage





Safety

* Animal data, including:

- Carcinogenicity
- Reproductive and chronic toxicology
- Genotoxicology
- Safety pharmacology

Clinical data

- Several hundred patient-years of data required
- Reports of all adverse events (mild/moderate/severe related and unrelated)
- Immediate regulatory notification of serious adverse events



Efficacy

Multiple Phase II & Phase III placebocontrolled clinical trials for each target clinical indication

Hazards of Marijuana contrasted with Pharmaceutical Product

- Harmful constituents of smoked marijuana
 - Bronchial irritation and pyrolytic compounds in a bad delivery system
- Potential for abuse
 - Reward
- * Recreational users seek the "high"
 - Manage therapeutic window
- Lack standardization with contamination
 - * Fungi, heavy metals, variance



Contrasts, continued

- No regulation of sources of manufacture and distribution
 - Distribution chain monitoring
- Lack of patient information and support
 - Unable to study in RCTs, lack information to advise
- * Liability
 - Insurance does not cover recommendation of illegal product, patients are on their own



Contrasts, continued

Stigma

 Illegality of product, not covered by heath care insurance, stress/anxiety/inconvenience associated with illegal product

Access

- Not contained within health care environments
- Public health considerations
 - Undermines prevention- perception of risk

Giving Cannabis a Free Pass = ?

- By creating an exception for cannabis, we are preventing the development of Q, S &E data that would allow it to become broadly accepted as a true medication
- The vast majority of patients want a product that is standardized by composition and dose and about which their physicians can offer meaningful advice



There's More Than THC!

Cannabis used centuries ago would have involved a 1:1
 CBD:THC ratio



- THC (tetrahydrocannabinol):
 - is analgesic, anti-spasmodic, anti-tremor, anti-inflammatory, appetite stimulant, anti-emetic
- CBD (cannabidiol):
 - does not bind to CB1 cannabinoid receptor, but does bind to other receptors in the body;
 - is anti-inflammatory, analgesic, anti-convulsant, anti-psychotic, anti-oxidant, neuroprotective;
 - reduces the negative effects of THC
 - has been bred out of modern herbal cannabis!



What's Coming?

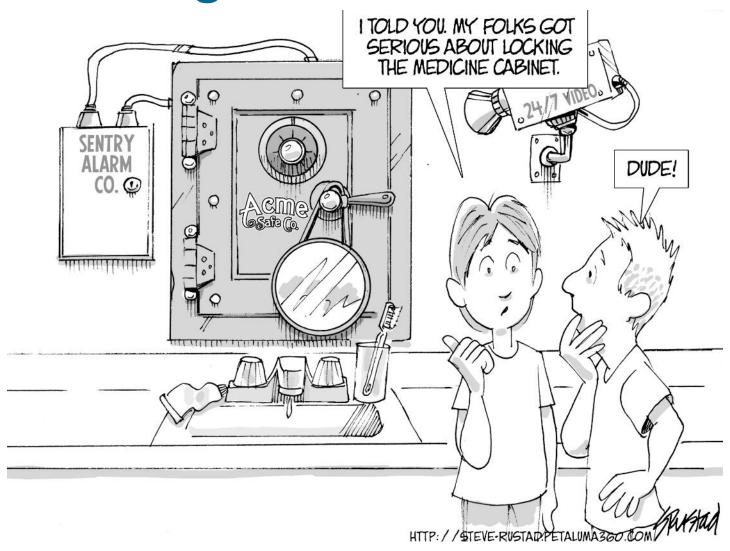
- Generic versions of Synthetic THC, including hard or room temperature capsules
- Cannabis-derived pharmaceutical products
- CB2 agonists
- * THC-precursor suppositories
- Transdermal THC delivery
- Inhaled THC



What's Coming?

- THC tablets
- * THC syrup
- ★ 50 states with "medical marijuana" laws?
- State level "legal" marijuana
- Federal laws decriminalizing medical use (or any use) of marijuana?
- All of it?

Safe Storage





Lock Your Meds

The National Family Partnership and the Center for Lawful Access and Abuse Deterrence

- Public education campaign
- Developed innovative lockbox to store medications safely
- Home inventory checklist
- Facts on abuse



Resources

- ASAM website for PPC (http://www.asam.org/publications/patient-placement-criteria/ppc-2r)
- NIDA (<u>http://drugabuse.gov/)</u>
- * Two Dreams (http://www.twodreams.com)
- Dr. AGB (https://twitter.com/dragb)
- Dr. AGB Goes to Back Rehab (http://drbarthwell.wordpress.com/)
- The Challenge in Higher Education: Confronting and Reducing Substance Abuse on Campus (https://www.ncjrs.gov/ondcppubs/publications/pdf/challenge_higher_ed.pdf/)
- ★ Teenage Drug Use Checklist (http://timetoact.drugfree.org/know-get-focused.html)
- Parents Toll-Free Helpline (http://timetogethelp.drugfree.org/learn/helpline)
- ASAM website for Policy Statements (http://www.asam.org)
- CLAAD for Citizen's Petition, membership, news (http://claad.org)
- * Two Dreams for clinical information (http://www.twodreams.com)

Thank You!

Questions?