

Evidence Regarding Relationship between Marijuana Use and Psychosis



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Question 1

1. The long-term health effects of marijuana use in children and adolescents include:
 - a. Cognitive dysfunction
 - b. Respiratory illnesses
 - c. Psychiatric disorders
 - d. a. and c.
 - e. All of the above

Question 2

There is no evidence associating psychosis with marijuana use in adolescence.

- a. T
- b. F

Question 3

Evidence regarding marijuana usage and its connection to psychotic disorders indicates:

- a. Increase evidence for psychotic disorders in adolescents who are heavy marijuana users
- b. Percentage of grey matter less for chronic marijuana users in adolescence than for for chronic marijuana users in early twenties
- c. Only a.
- d. Both a. and b.

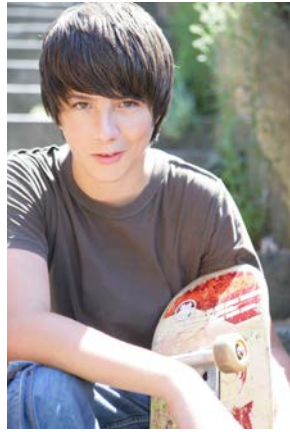
Disclosure

- The presenter has no financial relationship to this program.

OBJECTIVES

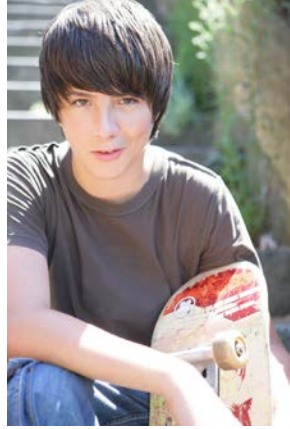
1. Summarize **two studies** regarding **marijuana usage** and its **connection to psychotic disorders.**
2. Evaluate the **long-term health effects of marijuana use** in children and adolescents.
3. Assess the effects of marijuana use on the **incidence of psychotic symptoms.**

Case Study:



- **ID:** 16 year old Hispanic male, slim, tall, neatly groomed and dressed, very cautious initially, then relaxed as interview progressed
- **Family and Relationships:** has single mother, one younger brother, father from Mexico, never in child's life; loving son and brother, verbalizes his love for both, obeys mother, watches after and is protective and kind of brother when mother at work; school counselor connected
- **Education:** Junior in high school, history of being a motivated student and liking school, making A's and B's, wanted to go to college, now failing school, and does not seem to care
- **Social:** used to have a lot of friends, now isolates; reports lots of gf but mother never sees them; loves to skateboard, particularly at night

Case Study:

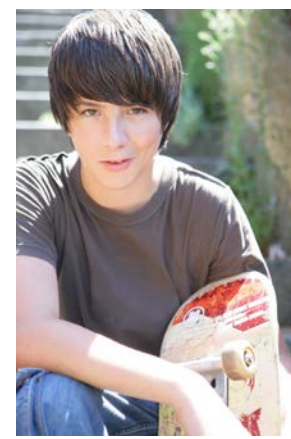


- **Presenting Complaint**: change in behavior; staying out late at night with friends, failing in school, doesn't seem to care; behaving oddly in school- argumentative, takes offense easily, disorganized speech and behavior regarding 'superpowers'; has been expelled twice; not sleeping well; reduced need for sleep, had episodes of being up for two days at a time
 - **Med and Psyche History**: neg
 - **Family Med and Psyche History**: mother reports father used drugs, was intense and violent man, often got into arguments with the law, had been arrested and was deported to Mexico
 - **Sub Abuse Hx**: neg alcohol, hallucinogenics, cocaine, synthetic marijuana
- Pos for smoking marijuana for past 10 months, "as much as I can get"**

Epidemiology

- 2016
 - Past Year Marijuana Use
 - 9.4 % 8th graders
 - 23.9 % 10th graders
 - 35.6 % 12th graders
 - Past Month Current- Marijuana Use
 - 5.4 % 8th graders
 - 14.0 % 10th graders
 - 22.5 % 12th graders and 6% daily or near daily

Case Study: Mental Status Exam



- **AAO x 3**, good grooming, fair to good eye contact, somewhat intense, cooperative
- **Motorically**: calm initially, then more agitated and fidgety
- **Speech**: RRR, languid; demeanor changeable from relaxed and easy to cautious and looking over his shoulder
- **Mood & Affect**: variable from elated, almost silly and easy to laugh, broad and expressive to fearful blunted and closed
- **SI/HI**: denies but very angry at other kids at school and sometimes teacher

Epidemiology

- **Most commonly used illicit drug** in the U.S. (22.2 million use/month)
- **More common among men** than women
- Number of adolescents **who believe marijuana use is risky** is decreasing
- **Legalization of marijuana for medical or adult recreational use** may impact these views
- Marijuana use by 8th, 10th, and 12th graders peaked in the mid-to-late 1990s, **then gradual decline through the mid-2000s before levelling off.**

Case Study:

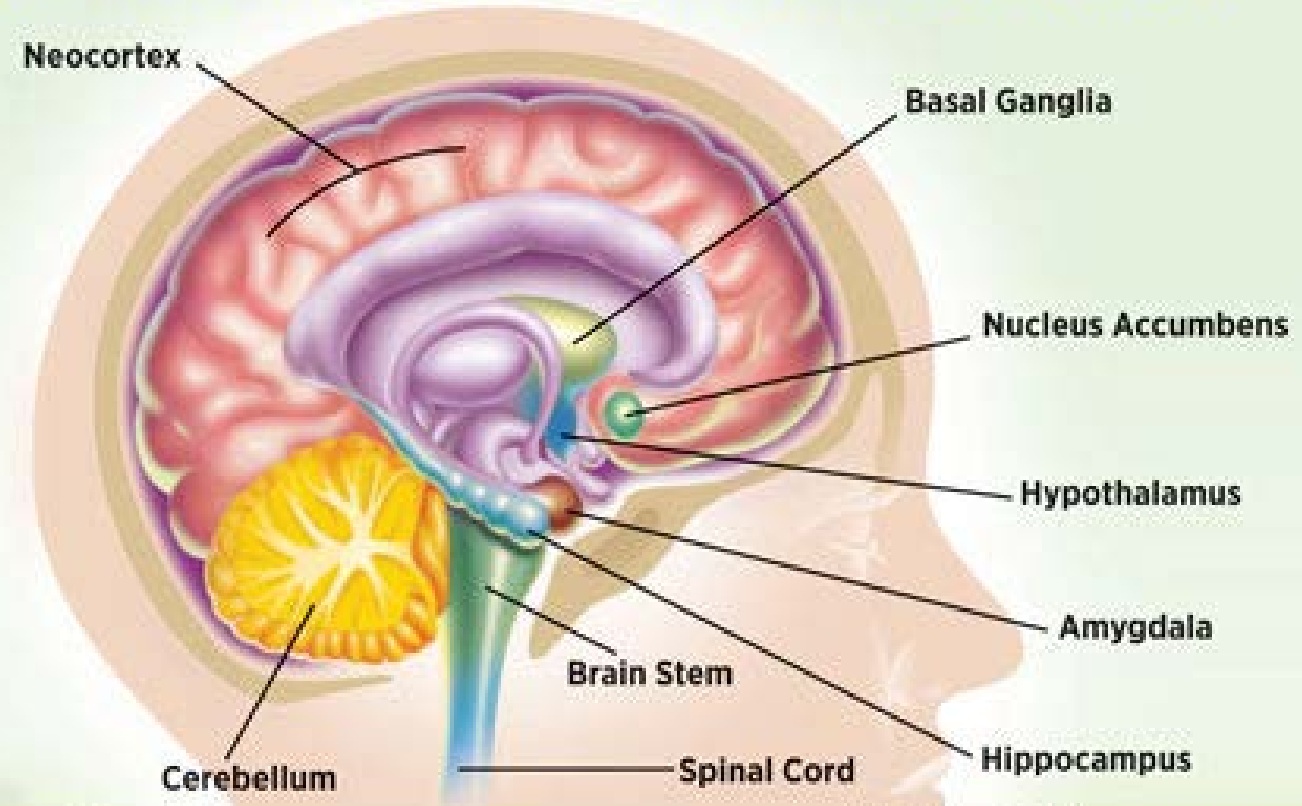


- **Thought Processes & Content**: moderately fast, initially linear but soon derailed, evidence of paranoia and delusions of being super hero; reports at school they “talk behind my back” and he “needs to teach them a lesson”
- **AV Hallucinations**: reports when he walks under street lights at night, they flicker and this is because of his super human powers that draw the power out of the light; believes he is a “babe magnet” and has “dozens of girlfriends”
- **Insight**: poor, does not think current thoughts or behaviors have anything to do with heavy marijuana usage
- **Judgment**: poor

How does THC affect behavior? *It depends on where the CB receptors are in the brain.*

Marijuana- THC's Endocannabinoid System

- Endocannabinoid (EC) system helps to “fine tune” communication between neurons
- THC gets into the brain rapidly attaches to the cannabinoid receptors
- Rapidly overwhelms EC system
- Throws system off balance
- Effects multiple areas of the brain
- Does not impact each brain/person the same

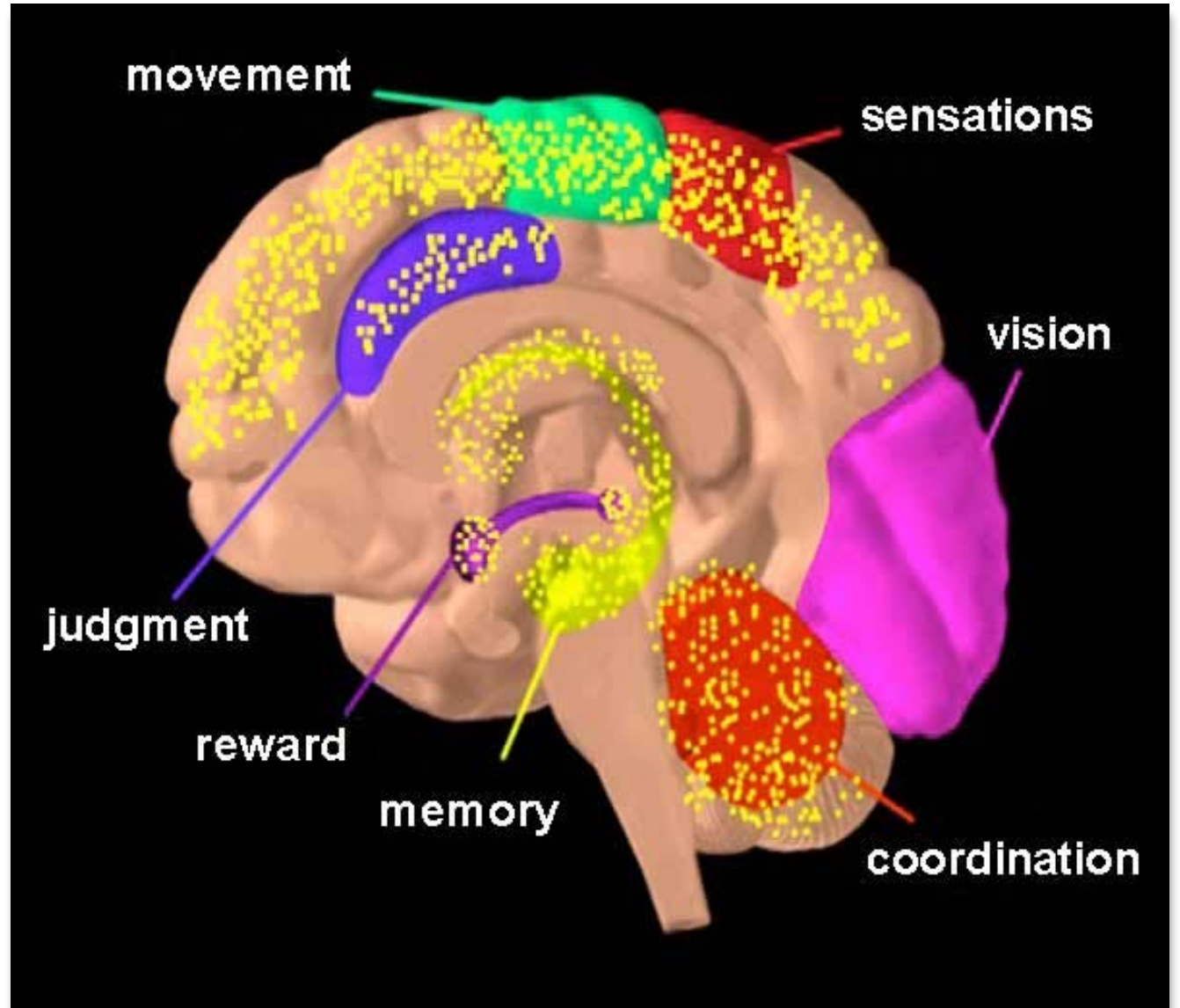


Brain Structure	Regulates	THC Effect on User
Amygdala	emotions, fear, anxiety	panic/paranoia
Basal Ganglia	planning/starting a movement	slowed reaction time
Brain Stem	information between brain and spinal column	antinausea effects
Cerebellum	motor coordination, balance	impaired coordination
Hippocampus	learning new information	impaired memory
Hypothalamus	eating, sexual behavior	increased appetite
Neocortex	complex thinking, feeling, and movement	altered thinking, judgment, and sensation
Nucleus Accumbens	motivation and reward	euphoria (feeling good)
Spinal Cord	transmission of information between body and brain	altered pain sensitivity

The brain structures illustrated above all contain high numbers of CB receptors

Effects on Brain

- Wide ranging
- Slow person's reaction time to impair driving or athletic skills
- Disrupt ability to remember things that just happened
- Cause anxiety
- Affect judgement
- Feel high
- Memory, addiction and mental health



Marijuana (cannabis)

- The illicit drug used most frequently in the United States, may be:
 - smoked in cigarettes (joints, nails, reefers)
 - pipes (bongs, bowls)
 - cigars (blunts)
 - mixed with food
 - brewed as a tea.
 - Hashish (hash) a potent resin of cannabis
 - may be used as a **sticky black liquid** (hash oil)
 - other street terms are pot, herb, weed, grass, widow, and ganja.

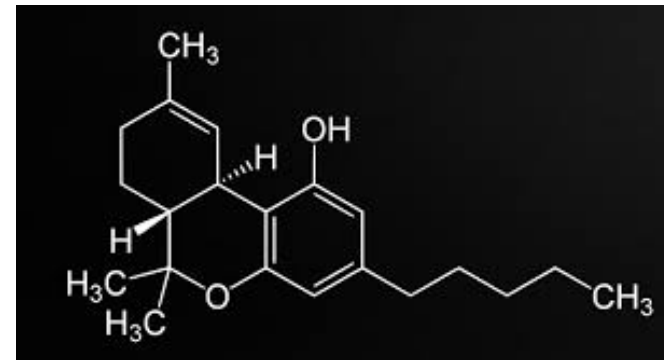


Image source: now.msn.com



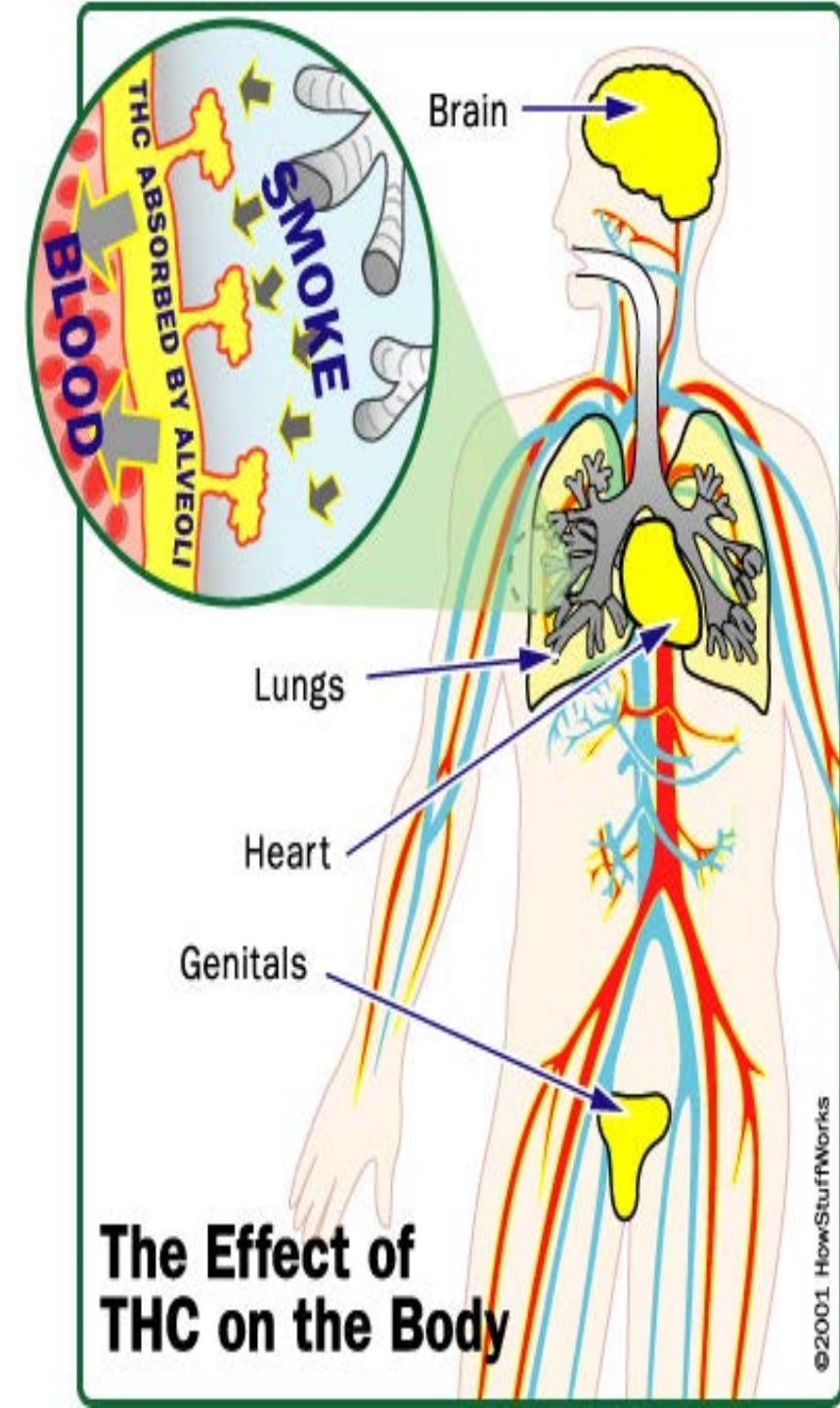
Primary active chemical in marijuana: is delta-9-tetrahydrocannabinol (THC)

- **Increased cultivation** of sinsemilla
- Made from buds of **female cannabis plants**
- Has **raised mean THC content** from **0.7% in the 1970s** to **8.5% in 2008**
- **Wide variability** in dose
- Street marijuana - may be **contaminated** with a variety of other drugs, toxins, and infectious agents



After smoking marijuana...

- THC rapidly passes from the lungs to the bloodstream and brain, where it binds to cannabinoid receptors.
- Euphoria and other brain effects occur within seconds of smoking, peak in 15 to 30 minutes, and taper over 2 to 3 hours.
- Onset of action after oral ingestion is 30 to 90 minutes, with peak effect in 2 to 3 hours and a duration of 4 to 12 hours.
- THC is highly lipid-soluble and has a serum half-life of 19 hours.



Effects of marijuana use on the incidence of psychotic symptoms.

- Past studies did not find increase incidence of psychosis with marijuana use but...
- Recent increase in use began in 90s..
- Recent British and Swiss studies suggest evidence of an increased incidence of psychoses among males in recent birth cohorts with the highest rates of cannabis use in adolescence
- Studies need to be repeated
- Regular cannabis use predicts an *increased risk* of schizophrenia, and the relationship persists after controlling for confounding variables.
- Do not feel related to self-medicating (Hall & Degenhardt, 2008)
- Heavy users are over represented among new cases of schizophrenia

Long-term health effects of marijuana use in children and adolescents.... Chronic, regular use..

- Cognitive Dysfunction-
 - impaired memory
 - amotivational syndrome-
 - reduced ability to establish or attain goals in life=job with low cognitive demands
 - lower % of grey matter than those that start smoking older in life
 - students using marijuana have lower high school grades and graduation rates than do nonusing peers
- Abuse/Dependence-
 - tolerance
 - physiological & psychological dependence
 - withdrawal symptoms if abrupt cessation
- Psychiatric Disorders-
 - increased risk
 - neuronal maturation completed in puberty
 - exacerbate depression
 - anxiety
 - personality disorders
 - sleep disturbance.

Long-term health effects of marijuana use in children and adolescents.... Chronic, regular use.. (cont'd)

- Psychosis-
 - increased risk
 - dose response
- Cancer-
 - marijuana smoke contains 50% to 70% more carcinogenic hydrocarbons than tobacco smoke
 - marijuana users typically **inhale more deeply and longer, increasing carcinogen exposure;**
 - small but consistent risk testicular and penile cancer
- Dental- possible periodontal disease
- Reproductive-
 - lower testosterone, sperm count
 - irregular ovulation has been noted
- Respiratory disease-
 - daily cough
 - more frequent lung infections
 - exacerbation of asthma
 - decreased pulmonary function
 - increased risk of respiratory tract cancer

Table 1 Summary of major adverse health outcomes of recreational cannabis use.

	<i>Evidence</i>	<i>Level of evidence</i>	<i>Strength of effect</i>
<i>Acute effects</i>			
Fatal overdose	+++	No case reports	0
Road traffic crashes	++	Cohort and case control	2-fold
Low birth weight	++	Cohort	
<i>Chronic effects</i>			
Dependence	+++	Cohort studies	1 in 10 among ever users
Educational outcomes	++	Cohort and case control	2-fold in regular users
Cognitive impairment	++	Cohort and case control	Difficult to quantify
Psychosis	++	Cohort studies	2-fold in regular users
Depression	+?	Cohort studies	Probable confounding
Suicide	+?	Cohort studies	2-fold in regular users
Chronic bronchitis	++	Cohort studies	2-fold in regular users
Respiratory impairment	+?	Cohort studies	Mixed
Cardiovascular disease	++	Cohort and case control	3–4-fold for MI
<i>Cancers</i>			
Testicular cancers	++	Case–control	2–3-fold
Respiratory cancers	+?	Case–control	Confounded by smoking

Social and Safety Risks ...

- Increases the risk of:
 - Injury-hurt on job, hit by car, misuse of equipment
 - unwanted and unprotected sex
 - other drug use
- Recreational doses **impair driving as much as blood alcohol concentrations of 0.07% to 0.1%.**
 - MVA- 2 to 3 x more likely if you are under influence of marijuana

Screening

- Part of comprehensive adolescent care.
- Anticipatory guidance - information about marijuana's addictive potential; injury risk; and possible impairment of learning, socialization, and sexual function.
- Parents-encouraged to rehearse strategies to help teenagers avoid drug-using settings.
- Skills-based interventions in schools help increase drug knowledge, decision-making, self-esteem, and peer pressure resistance and have led to reduced marijuana use.
- Interventions in nonschool settings, motivational interviewing, and some family interventions also may help prevent marijuana use.

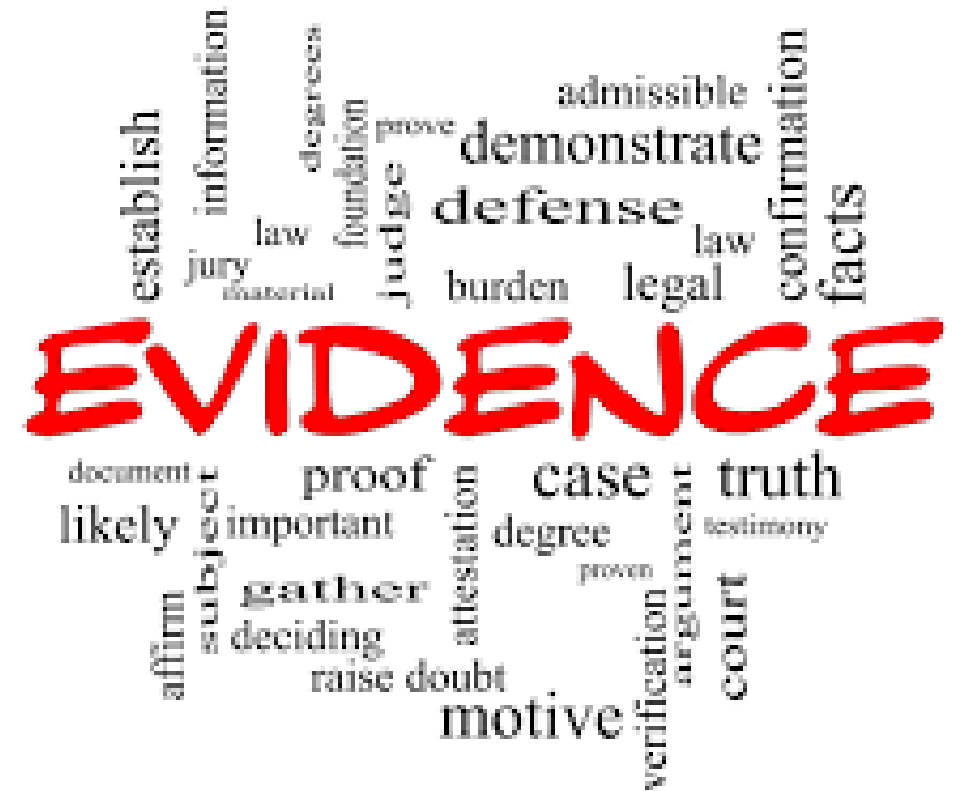
When Marijuana and Metabolites Detected?

- Detectable in urine by enzyme-multiplied immunoassay technique starting **1 hour after smoking.**
- The urine assay usually **remains positive up to 10 days after infrequent use** and up to **30 days in heavy users.**
- Some urine tests **may detect passive inhalation** of second-hand marijuana smoke.
- False-positive results may occur from ingestion of **nonsteroidal anti-inflammatory drugs**; false-negative results may follow urine dilution or adulteration.

Testing adolescents requires their consent, unless... (American Association of Pediatrics)

- (1) a patient lacks decision making capacity; or
- (2) there are strong medical indications or legal requirements to do so.
- Recent court decisions allow schools to perform random drug tests on middle and high school students participating in extracurricular activities, the AAP has opposed school-based testing unless part of a funded, comprehensive approach to addressing substance abuse.
- Positive results should be used as a mechanism to get treatment for the patient, not punishment.

Evidence Regarding Marijuana Use and Symptoms of Psychosis



Meta-analysis

- Statistical procedure for combining ***data from multiple studies***.
- When the ***treatment effect*** (or effect size) is consistent from one study to the next, **meta-analysis** can be used to identify this common effect.

Cannabis use in first episode psychosis: Meta-analysis of prevalence, and the time course of initiation and continued use.

Myles, H., Myles, N., & Large, M. (2016). *Australian & New Zealand Journal of Psychiatry*, 50(3), 208-219.

- Data sources: Search of electronic databases MEDLINE, EMBASE, PsycINFO, Web of Science and CINAHL for English language
- Papers using search terms (psychosis OR schizophrenia) AND (cannabis OR marijuana) IN (title OR keyword OR abstract), current to October 2014.
- Study selection: Studies were included if they reported on prevalence of current cannabis use in first episode psychosis cohorts. A total of 37 samples were included for meta-analysis.

Conclusions

- Cannabis use predates and is prevalent in early psychosis with significant rates of cessation at follow-up.
- **Approximately a third of people who present with first episode psychosis have clinically significant cannabis use**
- Prevalence of cannabis use varies according to region with Australia having rates approaching double that of the United Kingdom and North America.

Twin Studies

- Allow researchers to examine the overall role of genes in the development of a trait or disorder.
- Comparisons between monozygotic (MZ or identical) **twins** and dizygotic (DZ or fraternal) **twins** are conducted to evaluate the degree of genetic and environmental influence on a specific trait.
- Removes confounding issue of genetics

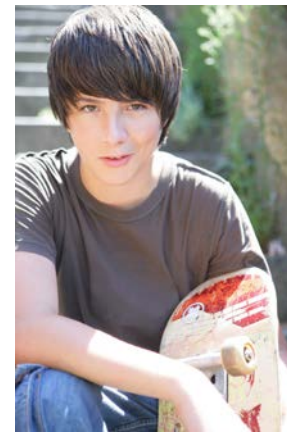
Association between cannabis use and psychosis-related outcomes using sibling pair analysis in a cohort of young adults. McGrath et al. (2010). *Archives of General Psychiatry*, 67(5), 440-447.

- **Context:** Prospective cohort studies have identified an association between cannabis use and later psychosis related outcomes, but concerns remain about unmeasured confounding variables. The use of sibling pair analysis reduces the influence of unmeasured residual confounding.
- **Objective:** To explore the association between cannabis use and psychosis-related outcomes.
- **Design:** A sibling pair analysis nested within a prospective birth cohort.
- **Setting:** Births at a Brisbane, Australia, hospital.
- **Participants:** Three thousand eight hundred one young adults born between 1981 and 1984

Conclusions

- Early cannabis use is associated with psychosis-related outcomes in young adults.
- The use of sibling pairs reduces the likelihood that unmeasured confounding explains these findings.
- This study provides further support for the hypothesis that early cannabis use is a risk-modifying factor for psychosis-related outcomes in young adults.

And now the rest of the story....



Diagnosis: *Cannabis-induced psychotic disorder 292.9*

- Presence of one or both of the following symptoms:
 - Delusions
 - Hallucinations
- Evidence from the history, physical examination, or laboratory findings of either one of the following:
- The symptoms in the first criterion **developed during or soon after substance intoxication or withdrawal.**
- The **involved substance is capable of producing these symptoms.**
- The disturbance is **not better accounted for by a psychotic disorder that is not substance induced.**
- The symptoms **persist for a substantial period (eg, about a month)** after the cessation of acute withdrawal or severe intoxication or are substantially in excess of what would be expected given the type or amount of the substance used or the duration of use.
- Other **evidence suggests the existence of an independent non–substance–induced psychotic disorder** (eg, a history of recurrent non–substance–related episodes).
- The disturbance does **not occur exclusively during the course of a delirium.**
- The disturbance causes **clinically significant distress or impairment in social, occupational, or other important areas of functioning.**

The rest of the story....

- Engagement critical, spoke to him with respect as someone who was interested in his well being and his being able to meet goals he had set for self.... college
- Began risperidone 0.5mg bid targeting hallucinations, delusions, agitation
- Still smoked marijuana
- Risperidone caused sedation and weight gain
- Switched to aripiprazole
- Diagnosis eventually changed to Psychotic Disorder, NOS
- After 9 months decided he did not need the medication, stopped and although still had odd behaviors, no frank psychosis

Summary

- Evidence clear that early marijuana use makes youth at risk for psychosis
- Dose dependent- more use, more risk
- THC concentrations higher
- Health risks evident
- Talk to your kids
- Help parents talk to their kids

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