Facts about Cannabis and "Medical Marijuana" for Youth

Pamela K. Gonzalez MD MS FAAP

Progress in Pediatrics Meeting 21 April 2017



University of Minnesota

Disclosure Information

I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider of commercial services discussed in this CME activity

I will mention clinical trials involving the following:

- Cannabidiol (Epidiolex)
- Nabiximols (Sativex)



University of Minnesota

Objectives

- Name key adverse effects of cannabis use by youth
- Enhanced ability to provide psychoeducation to parents regarding cannabis
- Increased ability and comfort with providing psychoeducation and anticipatory guidance to teens about cannabis
- Be able to explain physician role and responsibilities in "medical marijuana" programs



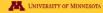
What does one mean by "Marijuana"?

- · Marijuana: non-scientific name for Cannabis sativa
- Cannabis: more scientific, clinical/research term used for C sativa
- Delta-9-tetrahydrocannabinol (THC): the main psychoactive component of C sativa
- THC is a Cannabinoid
- Synthetic cannabinoid analog: JWH-018, dronabinol



What does one mean by "Marijuana"?

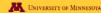
- Cannabis ≠ THC
- Cannabinoid ≠ Marijuana
- Dronabinol & Nabilone ≠ "Medical marijuana"
- Nabiximols ≠ "medical marijuana"
- Cannabidiol ≠ "cannabis oil"
- Endocannabinoid system ≠ endo-THC system



How many?

- Over 60 cannabinoids in cannabis sativa plant
- Most of which have not been characterized, let alone effects of combination

Brenneisen R (2007) Chemistry and Analysis of Phytocannabinoids and Other Cannabis Constituents in Forensic Science and Medicine: Marijuana and the Cannabinoids M. A. ElSohly ed., Humana Press, Totowa, New Jersey



Cannabis IS addictive

8000 subjects, age 15-64 years

Of those who endorsed at least one time cannabis use, about 9 percent eventually developed dependence

Compared to

alcohol 15 percent cocaine 17 percent heroin 23 percent

Anthony JC, Warner LA, and Kessler RC (1994). Comparative Epidemiology of Dependence on Tobacco, Alcohol, Controlled Substances, and Inhalants: Basic Findings from the National Comorbidity Survey. Exp. and Clin. Psychop



UNIVERSITY OF MINNESOTA

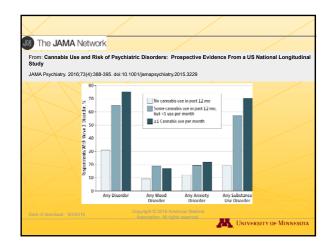
Cannabis IS Addictive Prevalence of Lifetime Diagnosis of Alcohol or Marijuana Dependence by Age of Use Initiation Hope RV as a Not Palat About the 2001/05/10/10 Sales as the of the Sales in the College Annual Sales (2001) Sales to the Sales of the Sales Sales (2001) Sales to the Sales of the Sales Sales (2001) Sales (2001) Sales (2001) UNIVERSITY OF MINNESOTA

Cannabis: Changes in Potency

- Tested product seized by DEA from 1995 to 2014
- 2010-2014: Shift from marijuana to more sinsemilla
- THC potency tripled from ~4 to ~12 %
- CBD content halved (~.28% to <.15%)
- THC:CBD increased from 14 to 80

ElSohly MA, Mehmedic Z, Foster S, Gon C, Chandra S, and Church JC (2016). Changes in Cannabis Potency Over the Last 2 Decades (1995-2014): Analysis of Current Data in the United States. Biol Psychiatry 79(7): 613-9.





Cannabis Use Increases the Risk of Substance Use Disorder

Past year cannabis use associated with:

Dx	Prevalence OR	Incidence OR
alcohol use disorder	2.5	2.7
cannabis use disorder	12.4	9.5
other drug use disorder	r 3.1	2.6
nicotine dependence	1.5	1.7

Blanco et al. (2016) Cannabis Use and Risk of Psychiatric Disorders. JAMA Psychiatry 73(4): 388-395.

Cannabis and Psychosis: How Much Proof Do We Need?

"It has been almost 30 years since Andreasson...demonstrated an association between cannabis use and subsequent onset of schizophrenia."

Gage SH, Hickman M, Zammi S (2015). Association Between Cannabis and Psychosis: Epidemiologic Evidence. <u>Biol. Psychiatr. 9:</u> 549-556



Cannabis Use IS Marker of Other Substance Use

Kids who report past year cannabis use need to be screened for all other substance use

JAMA Pediatr, 2014 Sep;168(9):822-8. doi: 10.1001/jamapediatrics.2014.774.

An electronic screen for triaging adolescent substance use by risk levels. Levy S1, Weiss R2, Sherritt L3, Ziemnik R4, Spalding A5, Van Hook S6, Shrier LA7.

UNIVERSITY OF MINNESOTA

Cannabis and Other Substance Use

- · Child/adolescent cannabis use is a marker for other substance use. Period.
- Child/adolescent cannabis use is neither normal nor normative. Period.
- · There is no "healthy use" in children/teens. Period.

LINIVERSITY OF MINNESOTA

Cannabis and Cars Don't Mix

- Cannabis intoxication impairs driving
 - Reaction time, attention, lane tracking
- Driving under the influence of cannabis doubles MVC risk

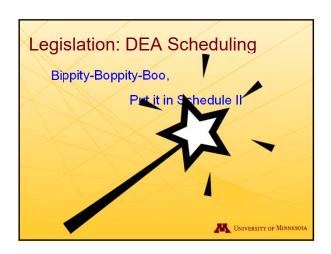
R.L. Hartman, M.A. Huestis, (2013), Cannabis effects on driving skills. Clinical Chemistry, 59 (3) pp. 478–

- R.L. Hartman, M.A. Huestis, (2013), Cannabis effects on driving skills. Clinical Chemistry, 59 (3) pp. 478–492
 G. Battistella, E. Fornari, A. Thomas, J.F. Mall, H. Chtloui, M. Appenzeller, J.M. Annoni, B. Favrat, P. Maeder, C. Giroud (2013) Weed or wheelf fMRI, behavioral and toxicological investigations of how cannabis smoking affects skills necessary for driving PLoS ONE 8(1): e52545
 Ramaekers, J.G., Moeller, M., van Ruitenbeek, P., Theurinssen, E., Schneider, E., & Kauert, G. (2006). Cognition and motor control as a function of Detla sup-9-THC concentration in serum and oral fluid: Limits of impairment. Drug and Alcohol Dependence 85, 114-122.
 LI, M.C., Brady, J.E., DiMaggio, C.J. et al. (2012) Marijuana use and motor vehicle crashes. Epidemiologic Reviews, 34, 65–72.



"Weed" Does Make You Dumber: How would you like to shave off 6 IQ points? **Corrent Issue > vol. 109 no. 40 > Madeline H. Meier, E2657-E2664, doi: 10.1073/pnas.1206620109 **CrossMark* Persistent cannabis users show neuropsychological decline from childhood to midlife Madeline H. Meier **P, **I, Avahalom Caspi**, P,C,G,e**, Antony Ambler **I, Honal-ee Harrington **P,C,d**, Renate Houts **P,C,d**, Richard S. E. Keefe**, Kay McDonald*, Aimee Ward*, Richie Poulton**, and Terrie E. Moffitt** **LINEWEITTY OF MINNESUTA**





FDA Approved Medications

- Nabilone (synthetic delta-9-THC)
 - Indication:
 - N/V associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments (adult)
- Dronabinol (synthetic delta-9-THC analog)
 - Indications:
 - anorexia associated with weight loss in patients with AIDS (adults); and
 - N/V associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments (adult).

FDA Investigational Medications

- Epidiolex plant-derived cannabidiol [CBD]
- Sativex nabiximols; plant-derived CBD+THC

(GW Pharmaceuticals)

University of Minnesota

Variable "Programs" and Products

- Raw plant, <u>smokeable</u> product for "medicinal" use (CA, IL) +/- <u>retail</u> recreational market, including edibles (CO, WA)
- Oral "Cannabis Oil" only (AL*, GA, IA*)
- Non-smokeable C. sativa plant extracts (MN)

University of Alabama at Birmingham Cannabidiol Highlights Must be Alabama resident Specific and complex medical record

requirements
• Neurologist referral



Nttp://www.uab.edu/medicine/neurology/research/uab-cannabidiol-program

UAB CBD Preliminary

- "...many patients do have a reduction in seizure activity, and we hope our efforts will further define how to best utilize CBD oil for maximum benefit to the appropriate patient population."
 - Martina Bebin, M.D., professor of neurology and principal investigator for the pediatric study



Variable Compound Source and Scrutiny

- GW Pharmaceuticals ≠ "Medical Marijuana"
- GW FDA scrutinized trials and regulation
 - Orphan Drug status for CBD in Dravet, Lennox-Gastaut, neonatal HIE
- "Medical Marijuana" no current GMP, or surveillance



UNIVERSITY OF MINNESOTA

How is a plant to be "dosed"?

Example: Trimethoprim/Sulfamethoxazole

- We dose TMP/SMX in mg amounts of TMP component
- · When "dosing" cannabis, milligrams of what?
- · What about the hundreds of other potentially active compounds?
- · How is a pharmacist to check our Rx?
- · How is a nurse to check dose accuracy before administering?



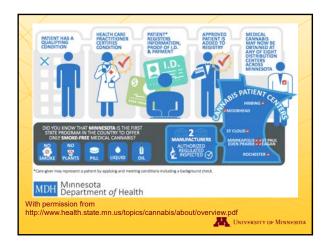
UNIVERSITY OF MINNESOTA

I'll just leave these here ...

Geffrey AL, Pollack SF, Bruno PL, and Thiele EA (2015). Drug-drug interaction between clobazam and cannabidiol in children with refractory epilepsy. Epilepsia 56(8): 1246-51.

Freisthler B, Gruenewald PJ, Wolf JP (2015). Examining the relationship between marijuana use, medical marijuana dispensaries, and abusive and neglectful parenting. Child Abuse Negl 48: 170-8.





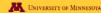
Qualifying Conditions

- Cancer associated with severe/chronic pain, nausea or severe vomiting, or cachexia or severe wasting
- Glaucoma
- HIV/AIDS
- Tourette Syndrome
- Amyotrophic Lateral Sclerosis (ALS)
- Seizures, including those characteristic of Epilepsy



Qualifying Conditions

- Severe and persistent muscle spasms, including
 - those characteristic of Multiple Sclerosis
- Inflammatory bowel disease, including Crohn's disease
- Terminal illness, with a probable life expectancy of less than one year
- · "Intractable" pain
- · Posttraumatic stress disorder



Practitioner Experience So Far: Seizures

- Cost and no reduction in seizures
- Unwillingness to try other proven therapies
- Some seizures improved and others worsened
- Diazepam has been lowered due to somnolence
- We did see some AED level changes
- Has had just 1 follow up appointment with me since starting cannabis



Practitioner Experience So Far: Seizures

 Neurologist who has prescribed anti-seizure medications has threatened to discontinue prescribing due to use of medical marijuana because of concerns for interactions



Minnesota Possession Laws Offense Penalty Incarceration Max. Fine Possession 23 9 of Hear More than 425 9 - Yeas than 10 kg Fetony 0 years 100,000 10 - Heas than 100 kg Fetony 20 years \$200,000 90 - Heas than 100 kg Fetony 25 years \$500,000 100 kg or more Fetony 30 years \$1,000,000 More than 14, grama inside one's vehicle (except the turn) * A conditional discharge is possible for first time offenders. * There is a possible drug education course requirement.

Kansas Possession Laws

It is a crime to possess any amount of marijuana (including small amounts for personal use) in Kansas.

(Kan. Stat. Ann. § 21-5706(b)(3).)



Kansas Proposed Legislation

SB 151, would allow medical professionals to <u>prescribe</u> and <u>dispense</u> "non-intoxicating cannabinoid medicine."



Practitioner Liability

"Policy makers often make decisions based on the majority will of the electorate, but physicians and other healthcare practitioners do not."

http://www.americanbar.org/content/dam/aba/administrative/healt hlaw/health_mo_premium_hl_healthlawyer_v29_2802.authcheck dam.pdf



		_
	Practitioner Liability	
	"The dispositive question in malpractice	
	cases is not whether the physician's	
	actions were legally authorized but whether they were performed in	
	accordance with professional standards	
	of care."	
	http://www.americanbar.org/content/dam/aba/administrative/healt hlaw/health_mo_premium_hl_healthlawyer_v29_2802.authcheck dam.pdf UNIVERSITY OF MINNESOTA	
Į	UNIVERSITY OF MINNESUIA	
		_
	If pediatricians don't initiate the conversation	
	and provide reliable information	
Į	University of Minnesota	
	Someone else will provide propaganda	
	The second secon	
- 1	University of Minnesota	



Quick Facts to Keep Straight

- Cannabis is NOT medication
- Today's marijuana is VERY different from 20 years ago
- Cannabis IS addictive
- Youth cannabis use IS a marker of other substance use



Areas to Cover in Parent Discussion

- Today's marijuana is NOT the same
 - Increasing cannabis THC potency
 - Decreasing cannabis CBD content
- · Cannabis is risk for other substance use
- Routes of use and speed of CNS delivery
- Complicated, real relationship with psychosis
- · High risk sexual activity, injuries, driving
- Most kids AREN'T using it
- Lack of regulation as pharmaceutical

75	UNIVE	RSITY	OF	Min	INESO

Tips for Speaking with Kids

- Speak early and often
- Reminder of confidentiality and its limits
- Make it safe to talk about
- Remember they respect us for being knowledgeable, not cool
- Focus on patient strengths
- Encourage parent/caregiver involvement in discussion



Questions?		
	University of Minneso	ОТЛ