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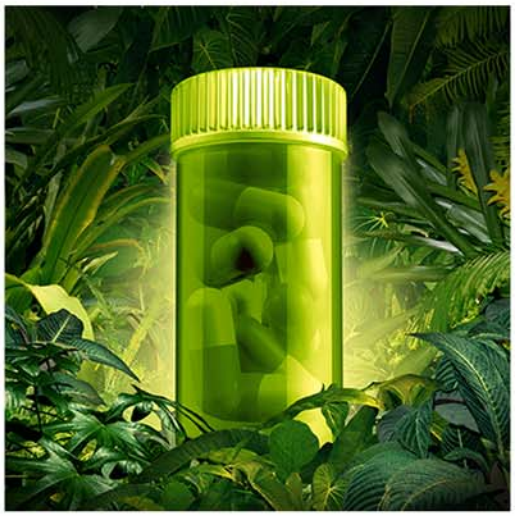

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The Global Climate of Drug Abuse

There are more than 20 states and the District of Columbia that have legalized marijuana under the guise of medicine. Additional states are also considering similar action, either through legislation or ballot initiatives. In this edition of the Journal, a publication entitled, Why Do People Use Medical Marijuana? The Medical Conditions of Users in Seven U.S. States, by Dr. Kevin Sabet and Elyse Grossman explores and quantifies the medical disorders for which people are using marijuana. The paper outlines in detail what states are currently experiencing regarding medical marijuana, along with solutions that can be implemented to curb widespread abuse and diversion of the drug.

Domestic animal poisonings from accidental marijuana ingestion have increased in many states that have legalized marijuana for any purpose. In a reprinted paper entitled, Marijuana Poisoning, Dr. Kevin Fitzgerald, a Colorado Veterinarian, discusses the effects of marijuana toxicosis in dogs along with the treatment, recovery and prognosis of the poisoning.

Our commentary contribution is from the esteemed Harvard Professor of Psychobiology, Dr. Bertha Madras. In her piece, The Medical Marijuana Movement Reflects an Indifference to Public Health, she provides an overview on concerns surrounding the medical efficacy of marijuana

IN THIS ISSUE

COMMENTARY

THE JOURNAL OF
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Why do people use medical marijuana? The medical conditions of users in seven U.S. states

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Abstract

Since 1996, more than 20 states and the District of Columbia have legislated medical marijuana laws. Relatively little is known about the identity of medical marijuana users, and specifically, what medical conditions they claim to have, although the initial campaigns to pass such legislation had been particularly associated with cancer, AIDS, and glaucoma patients. Past studies (most of which are focused on Californian data) find that medical marijuana users identify a diverse variety of medical conditions, and that those with cancer, HIV/AIDS and glaucoma made up only a small percentage of authorized users. This study seeks to contribute to this field of research by taking a more comprehensive approach, by examining the stated medical conditions of marijuana users from every state where the information is available. It records the medical conditions of nearly 230,000 individuals across seven states. The data sets that make up this study were provided by the Health or the Public Health Departments of seven U.S. States: Arizona, Colorado, Montana, Nevada, New Mexico, Oregon and Rhode Island. Our findings suggest that a very small proportion of medical marijuana patients report having serious medical conditions (i.e. HIV/AIDS, glaucoma, cancer, Alzheimer's), while almost all

(91%) of medical marijuana users report using marijuana to alleviate severe or chronic pain. Our results are consistent with past research that found that only a small minority of medical marijuana users report serious, life-threatening illnesses. The implications of these findings are that, although the political campaigns to pass such referenda and legislation often revolved around the needs of the terminally ill, the reality is that most people who utilize such programs do not suffer from serious medical conditions, and that state officials should inform the public about who may utilize such a program if enacted. These findings may indicate the need to develop stricter guidelines to ensure that medical marijuana is not diverted to young people, especially given recent research showing that it is.

Introduction

After delta-9-tetrahydrocannabinol (THC) was identified as the active ingredient in cannabis in 1964, interest in researching cannabinoids piqued, and subsequent studies have identified the benefits of cannabinoids for pain relief, antiemetic therapy, seizures and epilepsy, and other conditions. Generally, however, the medical uses of marijuana do not intend to directly address a particular disease, but rather, to treat the symptoms that can be caused by various diseases and/or their treatments (Institute of Medicine [IOM], 1999).

In 1996, California passed Proposition 215, the Compassionate Use Act, which authorized doctors to recommend medical marijuana use for patients suffering from “cancer, anorexia, AIDS, chronic pain, spasticity, glaucoma, arthritis, migraine or any

other illness for which marijuana provides relief" (Cal. Health & Saf. Code, § 11362.5 (1996). Since then, additional states, including – Arizona, Alaska, Colorado, Connecticut, Delaware, Hawaii, Illinois, Maine, Maryland, Michigan, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, and Washington – as well as the District of Columbia, have enacted similar pieces of legislation, and there are now thousands of medical marijuana dispensaries and hundreds of thousands of medical marijuana users across the United States; in 2012, at least 286,243 people were registered medical marijuana users in the United States (Bowles, 2012). That does not account for the many more who are not registered yet still utilize state medical marijuana laws.

Relatively little is known about the identity of medical marijuana users, and specifically, what medical conditions they claim to have. The campaign in California had been particularly associated with cancer, AIDS, and glaucoma sufferers. However, given that recent studies reveal that the majority of users report pain, not chronic illnesses, it is unclear whether the patients for which such programs were originally promoted (i.e. those suffering from the above-mentioned conditions), are the ones actually utilizing medical marijuana programs. Indeed, recent research has suggested that by 2006, medical marijuana users in California were likely to be identifying a diverse variety of medical conditions, and that overall, those with cancer, HIV/AIDS and glaucoma actually made up only a small percentage of authorized users (Reinarman et al., 2011; Nunberg, Kilmer, Pacula, & Burgdorf, 2011).

Two previous studies have researched the identity of medical marijuana users, but the authors restricted their data to the same sample of around 1,700 such users at nine assessment clinics across California in 2006 (Reinarman et al., 2011; Nunberg et al., 2011). A 2007 study examined characteristics of medical marijuana seekers in California, but restricted their sample to long-term marijuana users who self-selected to participate (O'Connell & Bou-Matar, 2007).

An evaluation of 1,745 medical marijuana patients in California reveals that 82.6 percent self-reported pain relief as their primary use for medical marijuana and that 86.1 percent administer the drug by smoking it (Reinarman et al., 2011), although few studies have been published on the effects and risks of inhaled marijuana. Likewise, the most frequently diagnosed conditions made by MediCann physicians were musculoskeletal and neuropathic chronic pain such as back pain and arthritis (58.2%). HIV/AIDS, cancer, and glaucoma combined comprised of 4.4% of all diagnoses (Nunberg et al., 2011). Other studies reveal similar outcomes. In an examination of Canadian adults in Ontario, Ogborne, Smart, & Adlaf (2000) find that the most commonly cited reason for using medical marijuana was pain or nausea. Moreover, they find that compared with nonusers, self-reported medical marijuana patients tended to be younger and more likely to have used cocaine.

In addition, residents of states with medical marijuana programs have a higher prevalence of marijuana use, abuse, and dependence (Cerdá, M., Wall, M., Keynes, K.M., Galea, S., Hasin, D., 2012). A more recent study of medical marijuana laws across the United States

finds that access to dispensaries and home cultivation increase marijuana consumption, particularly among youth (Pacula, R.L., Powell, D., Heaton, P., & Sevigny, E.L., 2013). While specific reasons for this relationship are not yet known, this concerning evidence points to the need for further understanding of both the characteristics of medical marijuana users, as well as the larger mechanisms at play within states with medical marijuana laws. An analysis of Denver, Colorado adolescents (ages 14-18) in treatment, finds that 73.8% used someone else's medical marijuana and that for each additional year (age) at which the onset of regular marijuana use was delayed, the likelihood of using medical marijuana declines by 21% (Salomonsen-Sautel, S., Sakai, J.T., Thurstone. C., Corley, R., & Hopfer, C., 2012). Likewise, adolescents in states with medical marijuana laws have a higher likelihood of using marijuana and lower perception of its riskiness, compared to adolescents in states without medical marijuana laws (Wall, M.M., Poh, E., Cerdá, M., Keynes, K.M., Galea, S., Hasin, D.S., 2011).

At the federal level, the United States' Controlled Substances Act (CSA) cites cannabis – which contains the psychoactive substance, delta-9-tetrahydrocannabinol (THC) – as a Schedule I controlled substance with a "high potential for abuse" and with no "currently accepted medical use" (CSA, 1970). However, on the state level, marijuana laws vary a great deal and in states where medical marijuana is legally accessible, the guidelines for receiving a license can vary as well. For instance, certain debilitating conditions are approved in some states but not in others. (For example, while Hepatitis C is approved in states such as Arizona, Rhode Island, and New Mexico, it is not an approved debilitating condition in Colorado and Connecticut.) Regulatory inconsistencies between states may pose limitations to the data since a patient in Colorado with, for example, hepatitis C,

might mention another approved condition (such as chronic pain, which can be a symptom of Hepatitis C) in order to obtain a medical marijuana card.

Given that medical marijuana has now become much more widely available to patients in a variety of states, a new study examining the medical conditions of marijuana users across the whole country would be a useful addition to research on the topic. This study seeks to contribute to this field of research by taking a more comprehensive approach, and by examining the stated medical conditions of marijuana users from every state where the information is available. It records the medical conditions of nearly 230,000 individuals across seven states. As far as we know, this is the only study of its kind, which considers multiple states with respect to reasons for medical marijuana use. Moreover, while other studies are confined to California, this is a non-California analysis.

Our findings suggest that a very small proportion of medical marijuana patients report having serious medical conditions (i.e. HIV/AIDS, glaucoma, cancer, Alzheimer's), while most use marijuana to relieve chronic pain, nausea, or muscle spasms. The implications of these findings are that, although the political campaigns to pass such referenda and legislation showcased the terminally ill, the reality is that most people who utilize such programs do not suffer from serious medical conditions.

Methods

The data sets that make up this study were provided by the Health or the Public Health Departments of seven U.S. States: Arizona, Colorado, Montana, Nevada, New Mexico, Oregon and Rhode Island.

Ideally, the results would include data from all 17 jurisdictions where medical marijuana use has been authorized; however, our access to statistics from a number of states was limited. Delaware, the District of Columbia, and New Jersey are either in the process of developing their medical marijuana programs, or have only recently introduced them, and thus do not yet have demographic statistics for users. California, Maine, and Washington do not collect demographic data on users in their medical marijuana programs, while Alaska does not make such data available to the public. Hawaii, Michigan, and Vermont do not publish demographic data on their websites, and when contacted, did not respond to inquiries.

Therefore, we have access to data from seven states. The Health Departments of Arizona, Colorado, Montana, New Mexico, Oregon, and Rhode Island make demographic data on patients enrolled in their medical marijuana programs freely available on their websites (Arizona Department of Health Services, 2011; Colorado Department of Public Health and Environment, 2011; Montana Department of Public Health and Human Services, 2011; New Mexico Department of Health, 2011; Oregon Public Health Authority, 2012; Rhode Island Department of Health, 2011). Furthermore, when contacted, the Public Health Department of Nevada sent their most recent demographic statistics on medical

marijuana users in their program (Nevada Health Division, 2012), although they do not publish this data on their website. The health departments' data are recorded when patients complete the medical marijuana application (either web- or paper-based). Typically, an application form requires general information such as the patient's name and date of birth, as well as information regarding the patient's debilitating medical conditions (often completed by the patient's physician).

Registered users enrolled in each state's medical marijuana programs are required to state their medical condition in order to obtain authorization from a physician. (Age and sex are also recorded, and typically, though not always, also published). In six of the seven states, users can select multiple medical conditions. New Mexico is the exception, as users there can only select one medical condition, which may explain why the findings from that state differ greatly from the other data sets.

These data sets each provide a "snapshot" of medical marijuana users registered in a state at any one time – the date of these data sets range from April 2011 to January 2012. It should be noted, however, that the respective Health Departments might have published more recent demographic statistics since this data was collected.

The data, which was received in Excel spreadsheets, were converted for use in SPSS statistical analysis software. We created several new variables to determine: a) the ages of the individuals using medical marijuana; b) whether they were under or over 50 years of age; c) whether they had a "serious" condition (defined as having reported using

medical marijuana for cancer, HIV, AIDS or Alzheimer's disease); and d) whether they were using medical marijuana for chronic pain and no other condition. We conducted a frequency test to determine the number (and percentages) of people who reported using medical marijuana for any given condition. Next, we conducted a series of frequency tests comparing women versus men, looking at the number (and percentages) who: a) reported using medical marijuana at all; b) reported using medical marijuana for any given condition; c) reported using medical marijuana for a "serious condition"; d) reported using medical marijuana for both a "serious condition" and chronic pain; e) reported using medical marijuana for both cancer and nausea; and f) reported using medical marijuana for only chronic pain and no other condition. We also conducted frequency tests to determine the mean ages (and whether they were older or younger than 50 years) of women and men using medical marijuana for serious conditions. Lastly, we ran a one-sample t-test (a statistical method examining a comparison of the average of the sample and the population with an adjustment for the number of cases in the sample and the standard deviation of the average) to determine whether the mean age of the women using medical marijuana differed from the mean age of the men using medical marijuana.

The first set of analyses uses the data from each of the seven states and examines the total number and percentage of patients reporting each medical condition by state, and overall. The second set of analyses focuses specifically on people in Arizona and Rhode Island – the only states that released more detailed data when approached – and presents more information on the sex and age of medical marijuana users by medical condition listed.

Given this, data from twenty-one people in Rhode Island who did not list a sex were removed from these analyses.

Results

A. *Medical Conditions Cited by Medical Marijuana Users by State*

Overall, 234,075 people from seven different states reported 19 medical conditions for their medical marijuana use (see Table 1). The clearest finding from this set of results is that almost all (91%) of medical marijuana users report using marijuana to alleviate severe or chronic pain. Severe pain was most commonly cited as a medical condition in Colorado, where it was reported by 96% of medical marijuana users. It was least commonly cited in New Mexico, where only 24% of users reported severe pain (however, this may be due to the fact that patients in New Mexico are only able to cite one medical condition – severe pain may often be a secondary symptom of another, primary, medical condition). However, the high level of use of medical marijuana for pain relief is remarkably consistent across the data – reported by over 85% of patients in five of the seven states.

Table 1: Medical Conditions Cited by Medical Marijuana Users Across Seven States

Medical Condition*	AZ	CO	MT	NV	NM	OR	RI	Total
Cancer	859	2828	968	102	562	1837	288	**7444**
% of users	4.40%	2.23%	3.65%	3.01%	10.74%	3.7%	8.20%	**3.18%**
AIDS/HIV	290	678	968	45	236	692	138	**3047**
% of users	1.50%	0.53%	3.65%	1.32%	4.51%	1.41%	3.90%	**1.30%**
Glaucoma	383	1165	968	55	94	655	61	**3381**
% of users	2.00%	0.94%	3.65%	1.62%	1.80%	1.33%	1.70%	**1.44%**

Cachexia	311	1655	947	113	79	1057	204	**4366**
% of users	1.60%	1.31%	3.57%	3.34%	1.51%	2.15%	5.80%	**1.87%**
Seizures	458	1819	577	75	0	1186	75	**4190**
% of users	2.40%	1.43%	2.18%	2.21%	0%	2.41%	2.10%	**1.79%**
Sclerosis	17	0	44	0	194	0	0	**255**
% of users	0.10%	0%	0.17%	0%	3.71%	0%	0%	**0.11%**
Chronic or Severe Pain	16966	120567	24739	3048	1250	44756	2170	**213496**
% of users	87.30%	95.97%	93.38%	89.96%	23.88%	90.93%	62.10%	**91.21%**
Muscle Spasms	2758	24828	4389	1461	0	12170	1076	**46682**
% of users	14.20%	19.58%	16.57%	43.12%	0%	24.73%	30.80%	**19.94%**
Nausea	2377	15503	3365	616	207	6630	603	**29301**
% of users	12.20%	12.22%	12.70%	18.18%	3.95%	13.47%	17.30%	**12.52%**
Epilepsy	0	0	10	0	151	0	0	**161**
% of users	0%	0%	0.04%	0%	2.88%	0%	0%	**0.07%**
Crohn's Disease	253	0	6	0	65	0	0	**324**
% of users	1.30%	0%	0.02%	0%	1.24%	0%	0%	**0.14%**
Hepatitis C	1010	0	0	0	52	0	273	**1335**
% of users	5.20%	0%	0%	0%	0.99%	0%	7.80%	**0.57%**
Painful peripheral neuropathy	0	0	29	0	386	0	0	**415**
% of users	0%	0%	0.11%	0%	7.37%	0%	0%	**0.18%**
Alzheimer's disease	0	0	0	0	0	50	6	**56**
% of users	0%	0%	0%	0%	0%	0.10%	0.2%	**0.02%**
PTSD	0	0	0	0	1688	0	0	**1688**
% of users	0%	0%	0%	0%	32.24%	0%	0%	**0.72%**
Spinal Cord Damage with Intractable Spasticity	0	0	0	0	175	0	0	**175**
% of users	0%	0%	0%	0%	3.34%	0%	0%	**0.07%**
Inflammatory autoimmune-mediated Arthritis	0	0	0	0	73	0	0	**73**
% of users	0%	0%	0%	0%	1.39%	0%	0%	**0.03%**
Hospice Care	0	0	0	0	17	0	0	**17**
% of users	0%	0%	0%	0%	0.32%	0%	0%	**0.01%**
ALS	0	0	0	0	6	0	0	**6**
% of users	0%	0%	0%	0%	0.11%	0%	0%	**0.00%**
Total	**19430**	**126816**	**26492**	**3388**	**5235**	**49220**	**2177**	**234075**

**In New Mexico, patients could only select one medical condition. In all other states, patients could select multiple medical conditions, so percentages do not add up to 100%.*

The second most commonly cited medical condition by medical marijuana users is muscle spasms, reported by 20% of users across the seven states. This rises to 43% in Nevada, and again, New Mexico is the anomaly, where no users cite muscle spasms as their primary medical condition. A further 12.5% of patients report nausea as a contributing factor in their use of medical marijuana. This is also remarkably consistent

across the whole data set – in five of the seven states it accounts for between 12 and 12.5% of cases. The exceptions are New Mexico, where just 4% of patients cite nausea, and Nevada, where 18% cite it. Together, these three conditions account for the vast majority of medical marijuana use – no other medical condition is reported by more than 3.2% of the users.

Indeed, consistent with the Reinarman and Nunberg findings, cancer, HIV/AIDS and glaucoma patients make up a very small percentage of medical marijuana users. Only 3% (rising to 11% in New Mexico) are cancer patients, and less than 1.5% report either of the other two conditions. Patients of other high profile diseases – Alzheimer's, Crohn's disease, Hepatitis C and Lou Gehrig's disease (ALS) – collectively account for less than 1% of the total number of marijuana users. In total, 4.5% of users report cancer, HIV/AIDS, or Alzheimer's, the three conditions that represent the three most common causes of death as reported by the World Health Organization. These results are not consistent with general population prevalence rates for these illnesses - 41% of Americans will have cancer at some point in their lives (United Press International, 2010), while 0.38% currently have HIV/AIDS, and 0.70% have glaucoma. Meanwhile, only 47% of the general population reports chronic pain.

There are several anomalies within the data sets. Almost one third (32%) of medical marijuana patients in New Mexico report posttraumatic stress disorder (PTSD) as their primary medical issue (however, New Mexico is the only state reviewed in this data set that designates PTSD a qualifying condition for medical marijuana). Meanwhile, a third

of users in Rhode Island did not specify a medical condition. However, if we remove New Mexico and Rhode Island from the results, which together only account for fewer than 10,000 patients in a study of 230,000, the findings are extraordinarily consistent.

B. *Medical Conditions of Marijuana Users in Arizona and Rhode Island by Sex and Age*

i. Background on the Arizona and Rhode Island Samples

Arizona's population is around six times that of Rhode Island's and the data reports roughly six times as many medical marijuana users in Arizona (19,430 individuals) than in Rhode Island (3,473). In other words, the proportion of medical marijuana users relative to the general population is roughly equivalent in both states. Moreover, the two states' general demographic profiles with regards to age and sex are comparable. Rhode Island has a slightly (but negligible) higher percentage of residents over the age of 50 years than Arizona (34.7% and 31.6%, respectively) and in both states, there is a larger proportion of women than men over the age of 50 (US Census Bureau, 2012).

Sex and age demographics are also comparable in both samples (see Table 2). Both Arizona and Rhode Island have three times more male than female medical marijuana users (despite women consisting of exactly half of each state's population) and in both states, the mean ages of men are slightly lower than the mean ages of the women (42.4 years old versus 46.0 years old in Arizona; $p < .001$ and 44.7 years old versus 47.7 years

old in Rhode Island; $p < .001$). Further analysis reveals that in both states, a larger percentage of women fall into the older-than-50 group.

Table 2: Demographics of Samples from Arizona and Rhode Island

	Arizona	Rhode Island
Females	4,983 (25.6%)	873 (25.1%)
Mean Age	46.0 years old	47.7 years old
Percentage Over 50	45.7%	46.0%
Males	14,447 (74.4%)	2,600 (74.9%)
Mean Age	42.4 years old	44.7 years old
Percentage Over 50	35.8%	38.2%
TOTAL	19,430 people	3,473 people

ii. Medical Conditions by Sex and Age

Table 3 breaks down reported marijuana usage for each medical condition by sex and age. In both states, significantly more women than men reported using medical marijuana for cancer while significantly more men than women reported using it for Hepatitis C (see Table 3). In addition, significantly more women than men in Arizona reported using medical marijuana for glaucoma, nausea, and Crohn's disease, while more men reported using it for HIV/AIDS. Interestingly, in Arizona, more women than men reported using medical marijuana for muscle spasms; these results are reversed in Rhode Island.

As expected, the mean ages of people reporting certain medical conditions differed depending on the condition reported and the sex of the individual reporting it. Individuals of both sexes who used medical marijuana for cancer, glaucoma, and Hepatitis C were

significantly older than individuals who used medical marijuana for other medical conditions. Individuals of both sexes in Arizona who used medical marijuana for chronic pain or nausea, and individuals in Rhode Island who used medical marijuana for nausea or muscle spasms were significantly younger than individuals who used medical marijuana for other medical conditions.

Table 3: Mean Ages Reported for Different Medical Conditions by Sex in Arizona and Rhode Island

	Arizona			Rhode Island		
Medical Condition	Percentage by Sex	Mean Age for that Condition (vs. Rest of Population)	Percentage Over 50 (vs. Rest of Population)	Percentage by Sex	Mean Age for that Condition (vs. Rest of Population)	Percentage Over 50 (vs. Rest of Population)
Cancer						
Females	5.6%**	53.9 (vs. 45.5)**	66.9 (vs. 44.5)	12.5%**	54.6 (vs. 46.7)**	68.8 (vs. 42.8)
Males	4.0%	54.6 (vs. 41.9)**	72.3 (vs. 34.3)	6.8%	56.4 (vs. 43.9)**	78.5 (vs. 35.2)
AIDS						
Females	0.3%**	44.5 (vs. 46.0)	33.3 (vs. 45.7)	0.6%	50.0 (vs. 47.7)	60.0 (vs. 46.0)
Males	1.3%	46.9 (vs. 42.4)*	39.2 (vs. 35.8)	1.3%	51.6 (vs. 44.6)*	55.9 (vs. 37.9)
HIV						
Females	0.1%**	47.4 (vs. 46.0)	37.5 (vs. 45.7)	1.7%	49.1 (vs. 47.6)	40.0 (vs. 46.2)
Males	0.5%	45.1 (vs. 42.4)	39.7 (vs. 35.7)	3.2%	49.8 (vs. 44.5)**	50.0 (vs. 37.8)
Glaucoma						
Females	2.5%**	58.5 (vs. 45.7)**	80.3 (vs. 44.8)	2.1%	56.7 (vs. 47.5)*	77.8 (vs. 45.4)
Males	1.8%	55.1 (vs. 42.2)**	70.7 (vs. 35.2)	1.6%	55.5 (vs. 44.5)**	78.0 (vs. 37.5)
Cachexia						
Females	1.6%	46.2 (vs. 46.0)	46.3 (vs. 45.7)	7.6%	49.5 (vs. 47.5)	53.0 (vs. 45.5)
Males	1.6%	42.5 (vs. 42.4)	38.0 (vs. 35.8)	5.3%	49.6 (vs. 44.4)**	52.2 (vs. 37.4)
Seizures						
Females	2.7%	43.3 (vs. 46.1)	34.4 (vs. 46.0)	2.9%	38.8 (vs. 47.9)**	20.0 (vs. 46.8)
Males	2.2%	39.8 (vs. 42.5)**	26.2 (vs. 36.0)	1.9%	42.4 (vs. 44.8)	34.7 (vs. 38.2)
Sclerosis						
Females	0.1%	52.5 (vs. 46.0)	75.0 (vs. 45.7)	0.0%	N/A	N/A
Males	0.1%	51.5 (vs. 42.4)	53.8 (vs. 35.8)	0.0%	N/A	N/A
Chronic or Severe Pain						
Females	87.4%	45.6 (vs. 48.9)**	44.4 (vs. 54.6)	65.4%	47.6 (vs. 47.9)	45.0 (vs. 48.0)
Males	87.3%	41.9 (vs. 46.2)**	34.0 (vs. 48.4)	61.2%	44.3 (vs. 45.4)	35.6 (vs. 42.2)
Muscle Spasms						
Females	16.1%**	46.8 (vs. 45.8)	46.4 (vs. 45.6)	25.8%**	44.0 (vs. 48.9)**	38.2 (vs. 48.8)
Males	13.5%	42.7 (vs. 42.4)	36.1 (vs. 35.7)	32.2%	39.6 (vs. 47.1)**	22.3 (vs. 45.7)
Nausea						
Females	15.6%**	43.1 (vs. 46.5)**	34.3 (vs.47.8)	19.1%	42.1 (vs. 49.0)**	32.3 (vs. 49.3)
Males	11.1%	38.9 (vs. 42.9)**	26.8 (vs. 36.9)	16.5%	38.4 (vs. 46.0)**	20.5 (vs. 41.6)
Crohn's Disease						
Females	1.7%*	42.6 (vs. 46.1)	30.6 (vs. 46.0)	0.0%	N/A	N/A
Males	1.2%	40.2 (vs. 42.4)	23.8 (vs. 35.9)	0.0%	N/A	N/A

Hepatitis C						
Females	3.8%**	52.7 (vs. 45.7)**	75.4 (vs. 44.5)	5.6%*	52.8 (vs. 47.4)*	73.5 (vs. 44.4)
Males	5.7%	53.6 (vs. 41.7)**	75.9 (vs. 33.4)	8.6%	53.7 (vs. 43.9)**	72.2 (vs. 35.0)
Alzheimer's disease						
Females	0.1%	75.0 (vs. 46.0)**	100.0 (vs. 45.7)	0.1%	70.0 (vs. 47.7)	100.0 (vs. 46.0)
Males	0.0%	60.2 (vs. 42.4)	60.0 (vs. 35.8)	0.2%	63.4 (vs. 44.7)*	60.0 (vs. 38.1)

** $p < .001$
* $p < .005$

iii. Chronic Pain

As discussed previously, the largest group of medical marijuana patients reported using the drug to address chronic and debilitating pain. A more in-depth analysis of this category finds that only a very small percentage of those people reporting chronic pain also reported a serious underlying medical condition, such as cancer or HIV/AIDS.[*] In Arizona, only 2.9 percent of those with chronic pain also reported a serious condition; in Rhode Island only 3.4 percent. There is no significant difference between the women who reported a serious condition and the men who did so in either Arizona (3.3 percent versus 2.7 percent, respectively) or in Rhode Island (4.9 percent versus 2.8 percent).

Nearly two-thirds of the individuals from Arizona and a little over one-third of the individuals from Rhode Island reported using medical marijuana for chronic pain and no other medical condition. Given that both samples had three times as many men than women in them, it is not surprising that the subsample of those who only used medical marijuana for chronic pain and no other condition was also comprised of three times as many men. However, the percentages of women who only reported chronic pain and no other conditions were similar to the percentages of men who only reported chronic pain

[*]In this case, "serious" conditions refer to those with mortality rates of over 1.0% according to the World Health Organization's 2008 Causes of Death Summary Table. These include malignant neoplasms, HIV/AIDS, and Alzheimer and other dementias. See Table 4.

and no other conditions. For example, in Rhode Island 37.1 percent of all women only reported chronic pain, compared to 34.7 percent of all men.

Interestingly, the mean ages of those who reported using medical marijuana only for chronic pain was significantly lower in Arizona and significantly higher in Rhode Island. However, once again, the differences were small, ranging from one to three years. Therefore, the only noticeable difference between the samples of the two states occurred in the number of people reporting only chronic pain who were over 50. In Arizona, 34.9 percent of people who reported use of medical marijuana only for chronic pain were over 50 compared to 44.3 percent of people who reported using it for other conditions ($p <$ .001). In Rhode Island, there is little difference between those who reported only using it for chronic pain who were over 50 (42.1 percent) and those who reported using it for other conditions and were over 50 (39.1 percent)

iv. Serious vs. Less-Serious Medical Conditions

To help simplify and better understand the data, all of the diseases listed by medical marijuana users are divided into "serious" conditions and "less-serious" conditions using the World Health Organization's 2008 Causes of Death Summary Tables (see Table 4). Of the thirteen diseases in this study, the three with mortality rates of over 1.0% (i.e. Malignant Neoplasms, Alzheimer's Disease and other dementias, and HIV/AIDS) are included in the serious category. The other ten diseases are not listed in the World Health Organization's Causes of Death Summary Tables or had mortality rates of less than 1.0% and thus are labeled as "less serious."

Table 4: Medical Conditions Ranked Using WHO's 2008 Cause of Death Summary Tables

Disease	Number of People	Percentage[i]
Malignant Neoplasms (i.e. Cancer)	1,193,257	19.33%
Alzheimer and Other Dementias	215,890	3.50%
HIV/AIDS	68,605	1.11%
Hepatitis C	10,785	0.17%
Epilepsy	9,675	0.16%
Multiple Sclerosis	5,273	0.09%
Glaucoma	26	0.00%
Cachexia or Wasting Syndrome	N/A	N/A
Muscle Spasms	N/A	N/A
Agitation (related to Alzheimer's)	N/A	N/A
Severe, Dehabilitating Chronic Pain	N/A	N/A
Severe Nausea	N/A	N/A
Crohn's	N/A	N/A

In Arizona, 5.7 percent of the sample report having serious conditions compared to 11.7 percent in Rhode Island. In general, those with serious conditions are significantly more likely to be over 50 than those with a less-serious condition in both Arizona (63.7 percent versus 36.8 percent, $p < .001$) and Rhode Island (67.9 percent versus 36.5 percent, $p < .001$).

In Rhode Island, significantly more women than men report using medical marijuana for serious conditions (see Table 5). In Arizona, there is no significant difference between the number of women who report using medical marijuana and the number of men reporting it. The clearest finding from these results is that medical marijuana users for serious conditions, regardless of sex, are significantly older than those using it for less-serious conditions in both states ($p < .001$); in both states, almost twice as many users

with serious conditions are over the age of 50 when compared to those with less-serious conditions.

Table 5: Serious versus Less-Serious Medical Conditions in Arizona and Rhode Island

	Arizona			Rhode Island		
Medical Condition	Percentage by Sex	Mean Age	Percentage Over 50	Percentage by Sex	Mean Age	Percentage Over 50
Serious						
Females	6.1%	53.8	65.6%	14.5%*	54.0	65.4%
Males	5.6%	52.1	63.0%	10.7%	54.4	69.1%
Less-Serious						
Females	93.9%	45.5	44.4%	85.5%	46.6	42.8%
Males	94.4%	41.8	34.2%	89.3%	43.6	34.5%

Conclusion

Only a very small percentage of all medical marijuana patients in the seven states reported having serious conditions. Even in the two states where patients could indicate multiple conditions (Arizona and Rhode Island), the proportions of serious conditions reported are low (5.7% and 11.7%, respectively). Those with serious conditions were significantly older than those with less serious conditions. These data do not mirror nation-wide disease prevalence rates of the general population.

In the only two states with more detailed data, we also found that men were significantly more likely to use medical marijuana programs for illnesses like pain or nausea, even though men and women in the general population have similar prevalence rates of these two – indicating that men are much more likely to use marijuana as medicine than women.

Lastly, we must acknowledge limits to the data. We do not know exactly how patients reported the reasons for their use of medical marijuana. It is possible they just listed the symptoms that they were treating (i.e. nausea, chronic pain) rather than the underlying medical condition. Also, there are obvious limits to any self-reported data. In addition, states have different procedures for patients to obtain medical marijuana, and some programs are larger than others, making it easier for prospective patients to obtain a medical marijuana card.

Still, our results are consistent with Reinarman et al. (2011) and Nunberg et al. (2011) who found that only a small minority of medical marijuana users report serious, life-threatening illnesses.

Medical marijuana is an ever-growing topic in state governments and has important implications for drug abuse, generally. Particularly in light of recent findings that indicate higher overall marijuana use in states with medical marijuana programs, state officials should inform the public about who may utilize such a program if enacted. For instance, a recent study by Pacula and colleagues (2013) indicates that the existence of home cultivation and large dispensaries are positively associated with marijuana use, while Cedrá, et al.'s (2012) study finds a positive relationship between marijuana programs and marijuana use, abuse, and dependence. In states with current programs in place, these findings should be made widely available to a public who likely believes that medical marijuana is only confined to the seriously ill. Finally, these findings may also indicate

the need to develop stricter guidelines to ensure that medical marijuana is not diverted to young people, especially given recent research showing that it is. (For instance, a 2012 study of Denver-area teens in treatment found that 74% of them got their marijuana from *somebody else*'s medical marijuana an average of 50 times (Salomonsen-Sautel, S., et al., 2012).)

Reference List:

Arizona Department of Health Services. (2011). *Application Monthly Report – Arizona MedicalMarijuana Program*. Retrieved from http://www.azdhs.gov/medicalmarijuana/reports/

Bowles, D. (2012). Persons registered for medical marijuana in the United States. *Journal ofPalliative Medicine 15*(1), 9.

Cal. Health & Saf. Code, § 11362.5 (1996).

Cedrá, M., Wall, M., Keyes, K. M., Galea, S., & Hasin, D. (2012). Medical marijuana laws in 50 states: investigating the relationship between state legalization of medical marijuana and marijuana use, abuse and dependence. *Drug and Alcohol Dependence 120*(1), 22-27.

Centers for Disease Control and Prevention (2012 July). HIV in the United States: At a Glance. Retrieved from: http://owl.english.purdue.edu/owl/resource/560/10/

Colorado Department of Public Health and Environment. (2011). *Medical Marijuana RegistryProgram Update*. Retrieved from: http://www.colorado.gov/cs/Satellite/CDPHE-CHEIS/CBON/1251593016680

Controlled Substances Act § 812 Schedules of controlled substances. (1970).

Glaucoma Research Foundation (2013 April 22). Glaucoma Facts and Stats. Retrieved from: http://www.glaucoma.org/glaucoma/glaucoma-facts-and-stats.php

Institute of Medicine. (1999). *Marijuana and Medicine: Assessing the Science Base*. Retrieved from: http://www.nap.edu/openbook.php?record_id=6376

Kazura, A. (2012). Medical marijuana and teens: Does an adjective make a difference? *Journal of the American Academy of Child and Adolescent Psychiatry 51*(7), 667-669.

Montana Department of Public Health and Human Services. (2011). *Medical Marijuana Program Current Registry*. Retrieved from http://www.dphhs.mt.gov/marijuanaprogram

Nevada Health Division Medical Marijuana Program. (2012). *Medical Marijuana Program Statistics*. Retrieved from http://health.nv.gov/medicalmarijuana.htm

New Mexico Department of Health. (2011). *Medical Cannabis Numbers.* Retrieved from: http://nmhealth.org/mcp

Nunberg, H., Kilmer, B., Pacula, R. L., & Burgdorf, J. R. (2011). An Analysis of Applicants Presenting to a Medical Marijuana Specialty Practice in California. *Journal of Drug Policy Analysis 4*(1), 1-16.

O'Connell, T. J., & Bou-Matar, C. B. (2007). Long term marijuana users seeking medical cannabis in California (2001–2007): demographics, social characteristics, patterns of cannabis and other drug use of 4117 applicants. *Harm Reduction Journal 4*(16), 16-22.

Ogborn, A.C., Smart, A.G., & Adlaf, E.M. (2000). Self-reported medical use of marijuana: a survey of the general population. *Canadian Medical Association Journal 160*(2), 1684-1686.

Oregon Public Health Authority. (2011). *Medical Marijuana Program*. Retrieved from: http://public.health.oregon.gov/DiseasesConditions/ChronicDisease/MedicalMarijuanaProgram/Pages/data.aspx.

Pacula, R.L., Powell, D., Heaton, P., & Sevigny, E.L. (2013). Assessing the affects of medical marijuana laws on marijuana and alcohol use: The devil is in the details. *National Bureau of Economic Research Working Paper 19302.*

Reinarman, C., Nunberg, H., Lanthier, F., & Heddleston, T. (2011). Who Are Medical Marijuana Patients? Population Characteristics from Nine California Assessment Clinics. *Journal of Psychoactive Drugs 43*(2), 128-135.

Rhode Island Department of Health. (2011). *Rhode Island Medical Marijuana Program.* Retrieved from: http://www.health.ri.gov/publications/programreports/MedicalMarijuana2011.pdf

Salomonsen-Sautel, S., Sakai, J.T., Thurstone. C., Corley, R., & Hopfer, C. (2012). Medical Marijuana Use Among Adolescents in Substance Abuse Treatment.

Journal of the American Academy of Child & Adolescent Psychiatry 51(7), 694-702.

Wall, M.M., Poh, E., Cerdá, M., Keynes, K.M., Galea, S., Hasin, D.S. (2011). Adolescent Marijuana Use from 2002 to 2008: Higher in States with Medical Marijuana Laws, Cause Still Unclear. *Annals of Epidemiology 21*(9), 714-716.

United Press International (2010 May 7). 41 percent of Americans will get cancer. *Life Extension Daily News*. Retrieved from: http://www.lef.org/news/LefDailyNews.htm?NewsID=9654&Section=DISEASE

United Press International (30 April 2012). Chronic pain common in American adults. *Personal Liberty Digest*, Retrieved from: http://personalliberty.com/2012/04/30/chronic-pain-common-in-american-adults/

United States Census Bureau. (2012). *Statistical Abstract.* Washington, DC: Government Printing Office. Retrieved from: http://www.census.gov/compendia/statab/2012edition.html

World Health Organization. (2008). *Cause-specific mortality, 2008: WHO region by country* [Data file]. Retrieved from http://apps.who.int/ghodata/?vid=10012

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Kevin A. Sabet, Ph.D. has studied, researched, and written about drug policy, drug markets, drug prevention, drug treatment, criminal justice policy, addiction, and public policy analysis for almost 18 years. In 2000, he served in the Office of National Drug Control Policy in the Clinton Administration and from 2003-2004 he was the senior speechwriter at the Office of National Drug Control Policy in the George W. Bush Administration. From 2009-2011, he was a political appointee and senior drug policy advisor to President Obama's drug control director, R. Gil Kerlikowske. He was the youngest senior staffer in that office and the only one to have ever served as a political appointee in a Democrat and Republican administration.

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He has been featured on the front page of the New York Times and in virtually every top media publication and news channel. He received his doctorate and M.S. from Oxford University as a Marshall Scholar in 2007 and 2002, respectively, and his B.A. in Political Science from the University of California, Berkeley in 2001. He resides in Cambridge, MA.

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Conflict of Interest Statement

I declare that I have no proprietary, financial, professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in, or the review of, the manuscript entitled except for the following: NONE

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THE INSTITUTE ON GLOBAL DRUG POLICY

Topical Review

Marijuana Poisoning

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ABSTRACT

The plant *Cannabis sativa* has been used for centuries for the effects of its psychoactive resins. The term "marijuana" typically refers to tobacco-like preparations of the leaves and flowers. The plant contains more than 400 chemicals but the cannabinoid δ-9-tetrahydrocannabinol (THC) is the major psychoactive constituent. "Hashish" is the resin extracted from the tops of flowering plants and generally has a much higher THC concentration. Marijuana is the most commonly used illicit drug in the United States. Currently, several states have passed legislation to decriminalize possession of small amounts of marijuana for both medical and personal use and several other states have similar legislation under consideration. The most common form of marijuana use in humans is inhalation of the smoke of marijuana cigarettes, followed by ingestion. In animals, although secondhand smoke inhalation is possible, the most common source of exposure is through ingestion of the owner's marijuana supply. The minimum lethal oral dose for dogs for THC is more than 3 g/kg. Although the drug has a high margin of safety, deaths have been seen after ingestion of food products containing the more concentrated medical-grade THC butter. There are two specific cannabinoid receptors in humans and dogs, CB_1 (primarily in central nervous system) and CB_2 (peripheral tissues). In animals, following oral ingestion, clinical effects begin within 60 minutes. All of the neuropharmacologic mechanisms by which cannabinoids produce psychoactive effects have not been identified. However, CB_1 activity is believed to be responsible for the majority of cannabinoid clinical effects. Highly lipid soluble, THC is distributed in fat, liver, brain, and renal tissue. Fifteen percent of THC is excreted into the urine and the rest is eliminated in the feces through biliary excretion. Clinical signs of canine intoxication include depression, hypersalivation, mydriasis, hypermetria, vomiting, urinary incontinence, tremors, hypothermia, and bradycardia. Higher dosages may additionally cause nystagmus, agitation, tachypnea, tachycardia, ataxia, hyperexcitability, and seizures. Treatment of marijuana ingestion in animals is largely supportive. Vital signs including temperature and heart rate and rhythm must be continually monitored. Stomach content and urine can be tested for cannabinoids. Gas chromatography and mass spectrometry can be utilized for THC detection but usually may take several days and are not practical for initiation of therapy. Human urine drug-screening tests can be unreliable for confirmation of marijuana toxicosis in dogs owing to the interference of a large number of the metabolites in canine urine. False negatives may also arise if testing occurs too recently following THC ingestion. Thus, the use of human urine drug-screening tests in dogs remains controversial. No specific antidote presently exists for THC poisoning. Sedation with benzodiazepines may be necessary if dogs are severely agitated. Intravenous fluids may be employed to counter prolonged vomiting and to help control body temperature. Recently, the use of intralipid therapy to bind the highly lipophilic THC has been utilized to help reduce clinical signs. The majority of dogs experiencing intoxication after marijuana ingestion recover completely without sequellae. Differential diagnoses of canine THC toxicosis include human pharmaceuticals with central nervous system stimulatory effects, drugs with central nervous system depressant effects, macrolide parasiticides, xylitol, and hallucinogenic mushrooms.

Introduction

For centuries, marijuana has been used both as a psychoactive intoxicant and for its hemp fiber used in rope.[1] In the United States, mention of the use of marijuana as an intoxicant can be found in the popular literature starting in the 1850s. By the 1930s, the US Federal Bureau of Narcotics began to characterize marijuana as harmful and addictive. Marijuana was listed as a Schedule I drug (high potential for abuse without any recognized medical value or purpose) by the Controlled Substances Act in 1970.[1]

For the last 40 years, the decriminalization and legalization of certain types of marijuana use has been a highly controversial topic. In addition, marijuana has been reported to be effective in the treatment of a variety of medical conditions.[2,3] Despite a nationwide ban on its growth, sale, and utilization, US marijuana consumption has skyrocketed since the 1960s. At present, marijuana is the most commonly used illicit drug in the US.[1,4] In one study, 40% of Americans older than 12 years admitted that they had tried the drug at least once.[1]

During the last 3 decades, public opinion regarding prosecution for possession of small amounts of marijuana for personal use has changed dramatically. Although for most parts of the country, possession of any marijuana is illegal and federal law bans the drug, some states such as Arizona, California, Colorado, and Wisconsin have allowed the medicinal use of marijuana under certain circumstances with more states expected to follow suit. Nevertheless, Arizona, in 1997, passed legislation nullifying a physician's right to prescribe Schedule I substances (such as marijuana) without federal approval. In Colorado, in the general

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election of 2000, an amendment passed legalizing the sale and possession of marijuana for medical use. By 2010, there were 717 licensed medical marijuana dispensaries and 106,000 registered medical marijuana users in the state of Colorado.[5,6] In 2012, legislation passed in Colorado and Washington State decriminalizing the possession of small amounts of marijuana for personal use. Similar legislation in other states is expected. Dogs and cats are very susceptible to marijuana toxicosis but dogs are much more often affected. Marijuana poisoning in dogs results from inhalation of secondhand smoke; ingestion of the seeds, stems, leaves, and flowers; ingestion of products made from marijuana leaves (cookies, suckers, brownies, teas, etc.); and ingestion of products made with concentrated tetrahydrocannabinol (THC) or hashish oil. Because of the changes with regard to the legal status of marijuana making it more readily accessible, an increase in the number of accidental intoxications of pets (especially dogs) can be expected.

Sources

The plant *Cannabis sativa* is the source of marijuana. It has been used historically not only for its psychoactive resin but also for hemp fiber.[1,4] Cannabis was cultivated by the early North American colonists for use in making hemp ropes. "Marijuana" refers to any part of the plant, but generally, it has come to refer to the dried tobacco-like preparations of the leaves and flowers.[1,4,7] Marijuana in its raw form comprises the dried and chopped stems, leaves, and seeds of the plant. *C. sativa* plants produce more than 60 chemical substances called cannabinoids.[8,9] The major psychoactive constituent in the plant is the cannabinoid δ-9-THC.[4] The only other cannabinoids in marijuana shown to produce psychoactive effects are cannabinol and cannabidiol, with less than 10 times the potency of THC.[1,4] The THC content in marijuana can range from 0.4% to almost 20% depending upon the cultivation techniques (amount of light, moisture, soil type, soil pH, nutrients, elements, and fertilizers provided).[1,4,9] Hashish is made from the resin collected from the tops of flowering plants and often has THC levels that exceed 10%.[1,4,9] Hash oil contains much more concentrated THC with values often reaching 20% or even higher. A typical marijuana cigarette (a "joint") generally contains 500-1000 mg of crude plant material and 15-30 mg of THC (with an average 3% THC content).[4,10] Most commonly in humans, exposure occurs through inhalation of marijuana, smoke from cigarettes ("joints") or modified pipes ("bongs"). It may be ingested when present in brownies, cookies, candy, and food products. Many of these food items are now available in the licensed medical marijuana dispensaries and sold to registered medical marijuana patients. Marijuana is known by a variety of street names: "grass," "weed," "hemp," "reefer," "pot," "herb," "MJ," and "Mary Jane." "Sinsemilla" is seedless marijuana with a fairly high THC content. Sinsemilla marijuana accounts for 85% of domestic production in the United States.[11] By 2010, a variety of synthetic cannabinoids had appeared upon the scene. Initially marketed as an herbal incense and sold in gas stations, head shops, and tattoo parlors, these potent synthetic cannabinoids had names like JWH-11 and others, "Spice," "K2," "Skunk," "Wild Greens," "Head Trip," "Purple Haze," and "Zombie Matter."[9] Smoking these incenses produced more severe effects than traditional marijuana although the products were clearly marked "not for human consumption." The paranoia, hallucinations, tremors, seizures, injury, and death caused by these substances resulted in many formulations being banned with the passage of the Synthetic Drug Control Act in 2011.[12]

Although secondhand smoke exposure is possible, the main route of animal marijuana exposure is through ingestion of the owner's supply ("stash").[6,10] Even though smokers of marijuana can control their level of intoxication by how much they smoke and how often they inhale, and because the effects of the active ingredient are more rapidly achieved, oral ingestion of THC is much more insidious. The drug is baked inside food products and ingested, usually knowingly (humans), and for the most part unintentionally (animals). Unlike inhalation, psychoactive effects following ingestion are not immediate.[1,4,6,9] Peak brain levels of THC may not be achieved for a few hours but may last longer than through inhalation.[4] Thus the person or animal ingesting marijuana cannot control the level or length of the intoxication and this makes it difficult for medical providers.

Increasingly, dogs through their ingestions of marijuana products are becoming exposed to baked goods made with medical-grade THC butter. This is made by boiling parts of the plant to extract the highly lipophilic THC.[6,9] Butter is then added to absorb the THC and allow the psychoactive agent to infuse into the butter. Then the butter, sautéed in THC and with the plant material strained out, can be used to make food items free of the crunchy taste of the plant and very high in THC. The butter can achieve THC concentrations higher than in the plant. Although the margin of safety following marijuana ingestion in animals has always been documented to be very high, recently 2 deaths have been reported in dogs after eating foods containing THC butter.[6]

The cannabinoids have been proposed and championed for a variety of medical conditions, most notably glaucoma and arthritis.[2,3] Currently, they are only approved for control of chemotherapy-related vomiting and nausea, appetite stimulation in patients with human immunodeficiency virus who have anorexia-cachexia syndrome, some patients with glaucoma, and for patients with multiple sclerosis. For these conditions, purified THC analogues are available and prescribed.[1,9,11] Dronabinol (Marinol), pure synthetic THC and a Schedule III drug, and Nabilone (Cesamet), a synthetic cannabinoid and a Schedule II drug, are routinely prescribed for certain human medical conditions. Sativex® (not marketed in the US) is a mouth spray for multiple sclerosis (MS) patients used to treat neuropathic pain, spasticity, and overactive bladder that contains tetrahydrocannibol (THC) and cannabidiol. Medical use of marijuana and its constituent real and synthetic cannabinoids remains controversial. The claims of the benefits of THC in the treatment of a wide array of other medical conditions have not been supported by robust clinical evidence.[1] Table 1 shows a list of human conditions proposed to be helped by cannabinoids.

Table 1
Human Medical Conditions Proposed Helped by Cannabindiols

Proposed	Actually Approved for
• Anxiety	• Anorexia-chacexia syndrome (HIV)
• Depression	• Chemotherapy-induced nausea and vomiting
• Insomnia	• Glaucoma
• Epilepsy	• Multiple sclerosis
• Head injury	
• Migraine headaches	
• Arthritis	
• Chronic pain	
• Muscle spasms	
• Parkinson disease	
• Tourette syndrome	

Abbreviation: HIV, human immunodeficiency virus.

Toxic Dose

THC has a wide safety margin in dogs with the minimum lethal oral dose greater than 3 g/kg.[13] This dose is 1000 times the

dosage where behavioral effects are observed. Nevertheless, providing a true toxic dose for THC in mg/kg proves difficult because the degree of purity for marijuana varies so greatly and also depends upon the route of exposure. It should be pointed out that medical-grade THC butter used in baked goods may have a higher concentration of THC than of marijuana alone.[6]

Toxicokinetics and Mechanism of Toxicity

Almost all effects of a single exposure to marijuana (like most animals experience) can be predicted by the dose.[4] THC is absorbed readily when smoked. Oral ingestion produces similar pharmacologic effects, but the absorption after ingestion is slower and more erratic than by smoking.[1,4,6,9] The onset of psychoactive effects following cannabis ingestion is unpredictable when compared with smoking. Oral absorption of THC can be increased with the ingestion of fatty foods.[9] In dogs, following THC ingestion, the onset of effects usually begins within 60 minutes.[6,9]

THC is highly lipid soluble and is distributed into fat, liver, brain, and kidney.[1,4,6,9,14] The majority of THC is metabolized by the liver, with the THC converted to the primary metabolite, 11-hydroxy-Δ-9-THC.[15] THC and its metabolites are excreted in the urine and feces. Enterohepatic recirculation is a prominent feature of marijuana metabolism.[1] Following ingestion, 15% of THC is excreted in the urine and the remainder in feces through biliary excretion.[4] Adipose storage produces a biological half-life for THC of approximately 30 hours.[16] In dogs, 80% of THC is excreted from the body in about 5 days (approximately 5 half-lives).[14]

Two specific cannabinoid receptors have been identified: CB_1 and CB_2.[1,17] CB_1 receptors are distributed throughout the brain, particularly in the basal ganglia, substantia nigra, globus pallidus, hippocampus, cerebellum, and frontal regions of the cerebral cortex. CB_2 receptors are found peripherally and are not detected in the central nervous system (CNS). This may give THC a potentially analgesic effect.[1] The CB_2 receptors are found peripherally in splenic macrophages, peripheral nerve terminals, and the vas deferens. The CB_2 receptors are also found in the tonsils and thymus gland. Peripheral CB_2 receptors may play a role in mediating release of cytokines. In addition, recent studies have identified cannabinoid receptor ligands as well as cannabinoid receptor agonists and antagonists.[18] Both receptors inhibit adenyl cyclase and stimulate potassium channel conductance.[1] CB_1 receptors are found on the presynaptic side of CNS synapses, and once activated, they inhibit acetylcholine, L-glutamate, gamma-aminobutyric acid, noradrenaline, dopamine, and serotonin. CB_2 receptors are believed to be involved in the regulation of immune system responses and inflammation.[1]

The precise effect that THC and the cannabinoids have upon the nervous system causing the well-known marijuana toxidrome, remains unknown. Nonetheless, activity at CB_1 receptors is thought to be the cause of all the clinical effects of THC.[18,19] In humans, these effects are interruption of cognition and memory, disrupted motor activities, and regulation of nociception, nausea, and vomiting.[1,20] In addition to neurologic effects, ingestion of large amounts of plant material may irritate the gastrointestinal tract and cause vomiting. One dog that presented to our practice had swallowed a plastic baggie full of marijuana that caused a gastrointestinal foreign body obstruction requiring surgical intervention.

Clinical Signs

The various effects of THC exposure, including time of onset, duration of effect, and severity of clinical signs, depend upon the dose and the route of administration of the drug. In dogs, clinical signs include ataxia and incoordination, hypersalivation, depression, disorientation, hypothermia, mydriasis, bradycardia, vomiting, and tremors.[6,9,10,14] In one study, nearly half of the dogs displayed urinary incontinence.[6] The authors postulated that dogs exposed to medical-grade marijuana may have a higher incidence of urinary incontinence on account of active THC metabolites. Signs may vary with dosage, size and age of the dog, and underlying medical conditions. Other signs that can be seen with marijuana ingestion in dogs are stupor, nystagmus, apprehension, vocalization, hyperexcitability, tachypnea, tachycardia, and hyperthermia.[14] Occasionally, dogs may present completely obtunded and comatose. In a recent retrospective study, ataxia and depression were the most common clinical findings at presentation for dogs with THC poisoning.[6] In addition, 48% of dogs presented following marijuana ingestion displayed mydriasis.[6] Cardiovascular effects produced by THC exposure have been well documented in humans and in dogs. A sinus tachycardia is often seen in dogs upon an electrocardiographic study following TCH ingestion.[1,4,6,9,14] Higher dosages have been shown to be capable of causing bradycardia and hypotension.[14] No long-term cardiovascular effects have been described following acute cannabis ingestion.[9,14] For dogs, onset of clinical signs usually occurs within 1-2 hours of exposure.[6,9,14] Again, for canines the duration of clinical signs can range from 1-3 days, with 24 hours being the average time for signs to persist.[9,14] Dogs may also show hyperesthesia with heightened sensitivity to motion, light, and sound.[6]

Minimum Database

Although THC intoxication is not reflected in either a complete blood count or a biochemical blood panel, blood should be drawn in marijuana suspects to rule out other causes for the clinical signs or the presence of concurrent medical conditions. Body temperature and heart rate and rhythm must be continually monitored during the course of therapy.[9,14]

Confirmatory Tests and Diagnostics

Taking a medical history is an essential skill. For a variety of reasons, owners may give histories that are inaccurate, unreliable, and sometimes purposely deceitful. Owners may deliberately falsify a history owing to fear of legal repercussions and potential grounds for prosecution.[21] Nowhere is there a greater potential for an untruthful history as in the case of an animal's ingestion of an illicit drug. Veterinary clinicians must gain the confidence of the client quickly so as to obtain a valid history.

Stomach contents can be sampled for cannabinoids.[1,4,14] A relationship with a reliable diagnostic laboratory is encouraged and consultation with a toxicologist or a diagnostic toxicology laboratory is recommended before sample collection and submission of any specimens. Urine can be tested for the presence of cannabinoids.[1,4,9,14] Owing to their lipophilic nature and enterohepatic recirculation, THC can be detected in the urine for several days following acute ingestion.[17] The use of human urine drug-screening test has been brought into serious question by a recent retrospective study of THC toxicosis in dogs.[6] One type of qualitative urine drug-screening test is a 5-channel urine dipstick with a colorimetric bar and a control. It was designed for humans to test for illicit drugs. In the retrospective study, numerous dogs known to have ingested marijuana had negative urine drug screen tests. It was suggested that these false negatives occurred if the testing was too recent after exposure.[6] It was also postulated that these false negatives occurred and the test was

not effective owing to the large number of THC metabolites in dog urine. This altered metabolite in dog urine may produce false negatives when using a human urine drug-screen. Finally, it was pointed out that samples tested for THC must be handled appropriately because THC can bind to rubber stoppers and glass giving false negative results.[1,6,9] The use of human urine drug-screening tests in dogs remains controversial. The findings of the retrospective study suggest that the human urine drug-screen test may be unreliable in dogs and only helpful if the test is positive.[6] Furthermore, various human urine drug-screen tests are available and these may vary in specificity and sensitivity.[6]

Gas chromatography-mass spectrometry is also used in humans to detect marijuana but it may take several days to perform and obtain results.[1] This is not helpful in directing appropriate therapy. In addition, the use of this test in dogs has been reported to be of questionable value. Likewise, invalid results have been obtained using enzyme-linked immunosorbent assay.[6] Currently, there is no single scientific laboratory test (enzyme-linked immunosorbent assay, gas chromatography, liquid chromatography, or mass spectrometry) that reliably detects THC in the urine of dogs.[6,9,14] As a result, interpretation of dipstick human urine drug-screening tests must be made with caution. Until a reproducible and reliable laboratory test is developed that can consistently detect THC in dog urine, no cage-side tests can be validated. Obtaining a urine drug screen is no substitute for a thorough history, physical examination, documentation of minimum database, and establishing a list of differential diagnosis. These components remain essential to confirming a diagnosis of marijuana intoxication.

Treatment

There is no specific antidote for cannabis.[1,4,9,14] Emesis may be unrewarding; THC has been shown to have a significant antiemetic effect.[22] Emesis can be initiated if the ingestion was recent (within the last 2 hours) but should never be employed if signs of CNS stimulation are present, if the animal is severely agitated, or if the animal is severely depressed or unresponsive. Treatment objectives in cases of marijuana toxicosis are prevention of further absorption and supportive care. Activated charcoal may be given to reduce absorption and THC half-life by blocking enterohepatic recirculation.[9,14] Just as emesis must be undertaken judiciously, administration of activated charcoal must be prudent and not given if the animal is somnolent, dramatically agitated, or showing severe anxiety. Charcoal aspiration can turn a minor exposure into severe morbidity or mortality. The risk of aspiration due to emesis or activated charcoal administration must not outweigh the benefit of the intervention. For the majority of cases of marijuana poisonings, even without such gastrointestinal intervention, the toxicosis is not fatal.[9] Treatment must never be more dangerous than the intoxication. Animals not badly agitated may be managed simply by a quiet, supportive, and protective environment.[6,14] Dogs experiencing acute anxiety and severe CNS stimulation can be treated with a benzodiazepine (diazepam 0.25-0.5 mg/kg, intravenously [IV]) to achieve sedation.[14] Chlorpromazine (0.5-1.0 mg/kg IV) has likewise been recommended to counter acute anxiety. Intravenous fluids may be given to counter dehydration in animals that have vomited severely and also to counter hypothermia. Hypothermic animals may require warming fluids until normal temperature has been achieved. Animals whose vomiting becomes persistent or severe may be treated with antiemetics (maropitant at 1 mg/kg, subcutaneously every 24 hours or ondansetron at 0.1-0.2 mg/kg IV every 8-12 hours). While hospitalized, temperature, pulse rate, and respiration should be monitored every 2 hours. In addition to temperature, animals must be observed closely for respiratory depression. Recovery is dependent upon the dose ingested and may take 24-72 hours.[9,14] Longer recoveries of up to 5 days are not uncommon in animals exposed to a very large dose.[14]

Table 2
Treatment of Acute Marijuana Intoxication

- Emesis may be induced if ingestion was within last 2 hours (apomorphine 0.04 mg/kg IV).
- Activated charcoal may interrupt enterohepatic recirculation of THC and reduce its half-life.
- Intravenous fluids can be administered if animal is dehydrated secondary to vomiting and to control body temperature.
- Animals should be closely monitored during hospitalization for body temperature, respiration, and heart rate.
- Sedation may be required for animals with severe CNS stimulation, agitation, and anxiety. (Diazepam 0.25-0.5 mg/kg IV.)
- Antiemetic agents may be given to animals with persistent vomiting.
- In severely poisoned animals, intravenous lipid therapy may be of benefit.

Recently, the use of intralipid therapy in cases of severe THC toxicosis has been employed and reported.[6] Lipid therapy has been shown to be effective in treating other highly lipophilic substances in dogs and cats.[23,24,25] Intravenous lipid given in these instances is a sterile, nonpyogenic fat emulsion which has been used previously in parenteral nutrition. In the past decade, evidence has accumulated supporting the use of intravenous lipids to reverse, or at least lessen, the effects of various lipophilic toxins.[25,26] Exact mechanisms of action of lipid therapy in treating toxins is presently unelucidated, but it may work in several ways.[25] First, the lipid may create a sink for fat-soluble, highly lipophilic drugs. Intravenous lipid added to the serum is thought to "extract" lipophilic molecules from the aqueous serum into a lipid phase. This binding causes a gradient that may also facilitate movement of toxins from the interstitium, thereby decreasing their tissue availability. A recent study of canine ivermectin poisoning showed a rise in serum ivermectin after each administration of intravenous lipid.[23] This finding supports the idea that poisons are moving from the interstitium into the intervascular space. It may be that lipids move directly into the interstitium and further bind with toxins. In addition, intravenous lipid therapy may also be helpful in some poisonings because they have been shown to provide free fatty acids, a major substrate of cardiac and other muscular ATP production.[25] In a negative sense, intravenous lipids may bind with beneficial lipophilic drugs given and take them out of circulation (the lipid sink in reverse). Despite this development, at least theoretically, administration of intravenous lipids could be expected to hasten the resolution of clinical signs, thereby reducing medical costs, and reduce time of hospitalization. Although evidence exists showing few adverse reactions to intralipid therapy, the use of lipids in humans and dogs for marijuana poisoning remains investigational. Further studies are needed to assess the efficacy of lipid therapy in cannabinoid poisoning. In certain of these toxicologic instances, intravenous lipid therapy may prove to be quite useful. A summary of treatment protocol for marijuana toxicosis is included in Table 2.

Prognosis and Prevention

Although recovery in dogs following marijuana toxicosis may be prolonged (up to 5 days), the majority of dogs ingesting THC recover completely with no long-term adverse effects.[9,14] Severity of the poisoning is dose dependent, and animals exposed to higher dosages require longer and more aggressive therapy.[6]

Table 3
Differential Diagnoses for Marijuana Intoxication

- Opioids
- LSD
- Phencyclidine hydrochloride (PCP)
- Ethanol
- Tranquilizers
- Benzodiazepines
- Ethylene glycol
- Propylene glycol
- Hallucinogenic mushrooms
- Amphetamines
- Diethylene glycol
- Methanol
- Isopropanol
- Acetone
- Macrolide parasiticides (ivermectin)
- Xylitol
- Depressants
- Muscle relaxants

Abbreviation: LSD, lysergic acid diethylamide.

Dogs that ingest medical-grade THC butter and food products containing the butter have been shown to be more at risk for serious intoxication and require more involved and prolonged treatment.[6] Recovery time is closely dependent upon the dose ingested. Prevention of marijuana toxicosis in dogs depends upon educating the public about the potentially hazardous effects marijuana can have on pets that ingest it. Marijuana must never be kept in a dog's environment. Extra care must also be afforded to law-enforcement drug-detection dogs that may be overzealous and ingest discovered marijuana products.[27]

Histologic Lesions

For the majority of animals, intoxication with marijuana is an acute, 1-time event. As a result, no long-term histologic lesions have been described in animals poisoned by THC. In humans, where repetitive and chronic marijuana use is common, heavy marijuana smokers show a high prevalence of pulmonary immune cells. In addition, heavy marijuana smokers had a much higher incidence of bronchitis and precancerous cells in the bronchial epithelium.[4] In rats, high doses of THC administered during pregnancy resulted in increased numbers of stillbirths, decreased litter size, decreased birth weight, and increased malformations in the offspring.[4,28] Currently, no such studies have been conducted in dogs or cats.

Differential Diagnoses

A correct diagnosis of marijuana intoxication may be initially missed owing to a purposely misleading history by the owners, the nonspecific clinical signs characteristic of THC toxicosis, and the current paucity of reliable laboratory tests confirming this poisoning. Furthermore, the avenue of exposure in these cases is not always immediately evident. Potential look-alikes for marijuana toxicosis are numerous and differentials must include opioids, lysergic acid diethylamide, phencyclidine hydrochloride (PCP), amphetamine, ethanol, tranquilizers, ethylene glycol, propylene glycol, methanol, benzodiazepines, isopropanol, acetone, macrolide parasiticides (such as ivermectin), xylitol, muscle relaxants, depressants, and hallucinogenic mushrooms.[1,4,9,14] A list of differential diagnoses is included in Table 3.

References

1. McGuigon M. Cannabinoids. In: Goldfrank LR, Flomenbaum NE, Lewin NA, et al.,editors. *Goldfrank's Toxicological Emergencies.* 8th ed. New York: McGraw-Hill; 2006. p. 1212–1220
2. Bagshaw SM, Hagan NA. Medical efficacy of cannabinoids and marijuana: a comprehensive review of the literature. *J Palliat Care* **18:**111–122, 2002
3. Guy GW, Whittle BA, Robson PJ, editors. *The Medicinal Uses of Cannabis and Cannabinoids.* London: Pharmaceutical Press; 2004
4. Martin B, Szara S. Marijuana. In: Haddad LM, Shannon MW, Winchester JF, editors. *Clinical Management of Poisoning and Drug Overdose.* 3rd ed.. Philadelphia: W.B. Saunders; 1998. p. 528–541
5. Warner J: Medical marijuana dispensary applications: 700 plus, earning Colorado 7 Million. *Westword,* 2010
6. Meola SD, Tearney CC, Haas SA, et al. Evaluation of trends in marijuana toxicosis in dogs living in a state with legalized medical marijuana: 125 dogs (2005-2010). *J Vet Emer Crit Care* **22:**690–696, 2012
7. Donalson CW. Marijuana exposure in animals. *Vet Med* **6:**437–439, 2002
8. Voth EA, Schwartz RH. Medicinal applications of delta-9 tetrahydrocannabinol and marijuana. *Ann Intern Med* **126:**791, 1997
9. Volmer PA. "Recreational" drugs. In: Peterson ME, Talcott PA, editors. *Small Animal Toxicology.* 3rd ed.. Philadelphia: W.B. Saunders; 2013. p. 309–334
10. Janczyk P, Donaldson CW, Gwaltney S. Two hundred thirteen cases of marijuana toxicosis in dogs. *Vet Human Toxicol* **46:**19–21, 2004
11. Marijuana and other cannabinoids. In: Ellenhorn MJ, editor. *Ellenhorn's Medical Toxicology.* 2nd ed.
12. *Synthetic Drug Control Act of 2011,* A.R. 1254. http:/www.gpo.gov/fdys/pkg/Bills-112hr/254rh.pdf
13. Thompson GR, Rosenkrantz H, Schaeppi UH, et al. Comparison of acute oral toxicity in rats, dogs, and monkeys. *Toxicol Appl Pharmacol* **25:**363, 1973
14. Klatt C. Marijuana. In: Osweiler GD, Hovda LR, Brutleg AG, Lee JA, editors. *Small Animal Toxicology.* Ames, IA: Wiley-Blackwell; 2011. p. 224–229
15. Agurell S, Halladin M, Lindgren J. Pharmacokinetics and metabolism of delta-9-tetrahydrocannabinol and other cannabinoids with emphasis on man. *Pharmacol Rev* **38:**21–43, 1986
16. Editorial Staff: Marijuana (Kinetics). In: Klasco RK, editor. *POISONDEX System.* Thomson Microdex, Greenwood Village, CO, vol 121, expires Sept 2004
17. Amari A. The effects of cannabinoids on the brain. *Prog Neurobio* **58:**315–348, 1999
18. Sugiura T, Waki K. Cannabinoid receptors and their endogenous ligands. *J Biochem* **132:**7–12, 2002
19. Felder CC, Glass M. Cannabinoid receptors and their endogenous agonists. *Annu Rev Pharmacol Toxicol* **38:**179–200, 1998
20. Green B, Kavanaugh D, Young R. Being stoned: a review of self-reported cannabis effects. *Drug Alcohol Rev* **22:**453–460, 2003
21. Fitzgerald KT. Taking a toxicological history. In: Peterson ME, Talcott PA, editors. *Small Animal Toxicology.* 3rd ed.. Philadelphia: W.B. Saunders; 2013. p. 39–43
22. Chang AE, Shiling DJ, Stillman RC. Delta-9-tetrahydrocannabinol as an antiemetic in cancer patients receiving high dose methotrexate: a prospective randomized evaluation. *Ann Intern Med* **91:**819–824, 1979
23. Crandall DE, Weinberg GC. Moxidectin toxicosis in a puppy successfully treated with intravenous lipids. *J Vet Emerg Crit Care* **19:**181–186, 2009
24. O'Brien TQ, Clark-Brice SC, Evans EE, et al. Infusion of a lipid emulsion to treat lidocaine intoxication in a cat. *J Am Vet Med Assoc* **237:**1455–1458, 2010
25. Haworth MD, Smart L. Use of intravenous lipid therapy in three cases of feline permethrin toxicosis. *J Vet Emerg Crit Care* **22:**697–702, 2012
26. Rosenblatt MA, Abel M, Fischer GW, et al. Successful use of a 20% intralipid emulsion after a presumed bupivacaine related cardiac arrest. *Anesthesiology* **105:**217–218, 2006
27. Llera RM, Volmer PA. Toxicologic hazards for police dogs involved in drug detection. *J Am Vet Med Assoc* **228:**1028–1031, 2006
28. Wenger T, Croix D, Tramu G, Leonardelli J. Effects of delta-9-tetrahydrocannabinol on pregnancy, puberty, and the neuroendocrine system. In: Murphy L, Batke A, editors. *Marijuana/Cannabinoids: Neurobiology and Neurophysiology.* Boca Raton, FL: CRC Press; 1992. p. 539–560

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GLOBAL DRUG POLICY AND PRACTICE

The Medical Marijuana Movement Reflects an Indifference to Public Health

Bertha K. Madras, PhD

In 1996, the stringent procedures that regulate drug safety and the practice of medicine were imperiled in the United States. The California ballot initiative Prop. 215 (and its successor SB420), was passed by voters following an intense and heavily funded campaign to shape their views: a "yes" vote was deemed a vote of compassion, a vote to enable physicians to "recommend" smoking marijuana to end the suffering of debilitating and life-threatening ailments. Smoked marijuana was approved by voters as a valid treatment for serious medical conditions - "AIDS, anorexia, arthritis, cachexia, cancer, chronic pain, glaucoma, migraine, persistent muscle spasms, seizures, epilepsy, severe nausea, and any other chronic or persistent medical symptom that substantially limits the ability of the person to conduct major life activities." Energized by the California decision and empowered by the success of their compassionate care strategy, itinerant, strategic, wealthy ballot backers invested millions of dollars in other states, and succeeded in legitimizing smoked marijuana as a medicine in more than 20 states and the District of Columbia. There are grave implications to a drug approval process by the ballot box or by politicians; neither party is accountable to patients.

Objections to smoking marijuana for medical reasons

1. **Smoking as a delivery system for drugs is objectionable.** Our 50-year national campaign to end smoking has finally succeeded in reducing smoking. Yet, nearly half our states now permit physicians to recommend smoking to their patients as a medical treatment!

2. **The scientific evidence for most medical claims in state medical marijuana laws is of poor quality, or does not exist, or the side effects after long term use are not reported. Access to smokable marijuana is not the reason.** A few years after Prop 215 passed in California, Governor G. Davis funneled millions of dollars into medical marijuana research, to seek validation, *after the fact*, for these "ballot-approved" medical claims. After a decade of funding, this California Center for Medicinal Cannabis Research has a poor track record in validating the majority of medical claims in Prop 215. Intriguingly, even in the strongest case to be made, neuropathic pain, recruited subjects were required to be experienced marijuana smokers and subjects were maintained on other painkillers. Five major clinical trials were discontinued because the investigators could not recruit enough patients, despite extensive advertising, to study marijuana effectiveness for relief of cancer pain, muscle spasticity, multiple sclerosis, severe nausea and vomiting, and neuropathic pain. The intent to investigate was present but candidate patients refused to enroll.

In the majority of observational studies published on the effects of smoked marijuana, there is no reporting of side effects (e.g. intoxication, cognitive impairment, etc), information that the FDA considers essential for FDA approval. These include whether marijuana produced a feeling of “high” (“euphoria”), being impaired, feeling sedated and showing cognitive impairment in objective tests of learning, speed recall, and attention.

3. The vast majority of patients receiving cards of permission to buy or grow marijuana for medical purposes do not suffer life-threatening debilitating disease. They are relatively young males who self-report vague symptoms of pain and anxiety, with a surge of purchases on the weekends.

4. B**allot initiatives circumvent stringent federal FDA standards, a direct threat and challenge to our elaborate, technical- and evidence-based, national drug approval system.** FDA standards have protected Americans from fraudulent, dangerous or ineffective drugs for decades, with an approval system, although imperfect, that is among the most rigorous in the world. Consider the wise FDA response to 17 states that had approved the sham cancer treatment laetrile by ballot, their denial of thalidomide approval and a myriad of other drugs deemed unsafe and unacceptable by rigorous standards. To circumvent the FDA approval by a ballot initiative is a dangerous precedent, a slippery slope that can create chaos in the safety of our drugs.

5. **Who bears responsibility for the patient if smoking marijuana causes harm?** Over the past three years FDA fined pharmaceutical companies over $10 billion for making unproven, off-label claims on their drugs. What is the recourse to a patient, if they suffer serious side effects?

6. **Every drug approved by the FDA and prescribed by a physician requires an insert in the package that provides detailed descriptions of side effects.** Marijuana patients are given no information on the side effect profile of the smokable drug.

7. **Marijuana does not fulfill stringent FDA requirements. The FDA requires that:**

a. **A drug is a pure compound:** Marijuana is not pure but composed of more than 400 compounds of unknown effect, and over 80 cannabinoids

b. **The drug's chemistry, manufacturing, and composition of matter are tightly controlled so that each batch is identical;** marijuana production is unregulated and its contents are unknown

c. **Production methods are validated;** this criteria is not applied to marijuana production

d. **Drug shelf life is known and can be dated to protect patients from a degraded chemical;** marijuana shelf life and products are unknown

e. **The microbiology of a drug is known and batches of chemicals contaminated with bacteria are rejected.** Marijuana production is unregulated and bacterial contents are unknown

f. **Its pharmacology and toxicology in animals is known.** Marijuana production is unregulated and bacterial contents are unknown

g. **Its rate of entry, bioavailability, and toxicology are known.** Marijuana rate of entry bioavailability and toxicology for different batches is unregulated and are unknown.

h. **Its dose response, efficacy, and safety are known.** Most studies do not interrogate marijuana side effects

i. **After approval, case reports and safety updates are required to be submitted to the FDA for ongoing evaluation. There are no requirements for marijuana reporting.**

Ballot initiatives for alleged treatments erode this carefully constructed process and lead to compromised quality of our nation's medications.

The FDA ruling on marijuana as medicine is given below. It has not changed. Marijuana is listed in schedule I of the Controlled Substances Act (CSA), the most restrictive schedule.

• The Drug Enforcement Administration (DEA), which administers the CSA, continues to support that placement and the FDA concurred because marijuana met the three criteria for placement in Schedule I under 21 U.S.C. 812(b)(1).

• Marijuana has a high potential for abuse has no currently accepted medical use in treatment in the United States.

• It lacks accepted safety for use under medical supervision.

• There is sound evidence that smoked marijuana is harmful.

• A past evaluation by HHS agencies, FDA, SAMHSA and NIDA, concluded that no sound scientific studies supported medical use of marijuana for treatment in the United States.

• No animal or human data supported the safety or efficacy of marijuana for general medical use.

• There are alternative FDA-approved medications in existence for treatment of many of the proposed uses of smoked marijuana.

• A growing number of states have passed voter referenda (or legislative actions) making smoked marijuana available for a variety of medical conditions upon a doctor's recommendation.

• These measures are inconsistent with efforts to ensure that medications undergo the rigorous scientific scrutiny of the FDA approval process and are proven safe and effective under the standards of the FD&C Act.

• Accordingly, FDA, as the federal agency responsible for reviewing the safety and efficacy of drugs, DEA as the federal agency charged with enforcing the CSA, and the Office of National Drug Control Policy, as the federal coordinator of drug control policy, do not support the use of smoked marijuana for medical purposes.

8. **The practice of medicine is impacted by marijuana as medicine ballot initiatives.** Medicine increasingly is evidence-based but marijuana has no academic presence in medical training or scholarship.

Contrary to good medical practice, there is no requirement to:

a. Issue a prescription (only a recommendation)

b. Extract medical history

c. Give a detailed medical exam

d. Discuss long term treatment, effects or follow-up

e. Provide informed consent

f. Consult with other physicians

g. Keep proper records that support recommending marijuana instead of safe, approved alternatives

h. Have a good faith relationship with a patient rather than a "marijuana mill"

i. Be able to identify substance abusers or the addicted

j. Forewarn patients on maintaining control of their product

9. **Contrary to regulations governing pharmacies, dispensaries have:**

a. No product liability

b. No product regulation

c. No chain of custody

d. No accountability

e. No pharmacists trained in drug-drug interactions of appropriate dose measures and requirements

Over the past 150 years the US moved rapidly away from plants as medicines to purified products, for obvious reasons: the composition of a plant is unknown, the composition of its thousands of constituents are uncontrolled and the long term effects of each of these chemicals, alone or together on body, brain, behavior are unknown. Marijuana's scientific record is not sufficient to fulfill FDA's rigorous standards of safety, efficacy, consistent dosing and side effect profile. The evidence for smoked marijuana as a safe and effective treatment for over 12 diseases (e.g. glaucoma, Alzheimer's disease), including the myriad forms of chronic pain that respond to different class of drugs does not begin to meet professional and FDA standards.

10. **Restrictive marijuana laws are driven primarily by public health considerations.**

Maintaining restrictions on marijuana are more compelling than ever, as marijuana potency and availability soar, in parallel with escalating scientific evidence of marijuana's adverse consequences.

There are acute effects of marijuana on brain function. Unlike opioids, marijuana is not likely to cause death by overdose but it resides in Schedule I because of its high abuse liability, and no medical indications – essentially because it adversely disturbs brain function and biology. A Saturday night marijuana binge is intoxicating in the short term, but it can also produce residual cognitive deficits (on learning and memory) for several days. (Marijuana research protocols generally wait at least 5-30 days for marijuana to clear, before measuring long term

residual cognitive effects). These deficits are readily quantified, are exaggerated in schizophrenics, and refute advocacy for marijuana treatment of Alzheimer's disease. Who is compromised by marijuana? The student in class who can't focus, the construction worker at risk for injury, the unemployed who is less likely to find work, the poor, the high school drop-out, the criminal. It is unacceptable for soldiers, airline pilots, nuclear power plant operators, federal workers to test positive for marijuana. Should it be acceptable for teachers, day care providers, construction workers, students, machine operators, miners, parents, or drivers? A 2009 National Highway Traffic Safety Administration (NHTSA) report showed that more people are driving on weekend nights under the influence of marijuana (8.3%) than alcohol (2.2%). Emergency department mentions of marijuana in the US have increased from 281,619 to 374,435 during 2004-2008, in parallel with linear increases in marijuana potency and marijuana addiction.

Adverse effects of repeated long term use of marijuana:

a. Brain changes (reduced grey matter)
b. Addiction (9% of users)
c. Cognitive impairment (effects on learning and memory)
d. Reduction in IQ
e. Association with psychosis, schizophrenia
f. Adverse effects on developing fetus
g. Greater effects in adolescent initiators:
    - 2 X more likely to develop a non-mood psychosis
    - 4 X increased risk for schizophrenia
    - 4 X more likely to have high psychiatric scores

- 5-6 times more likely to become addicted
- More likely to develop psychosis
- More likely to display cognitive impairment
- More likely to have compromised school work

11. **What every patient should know if they are recommended medical marijuana**

They may experience:

a. Altered sensations, perceptions, thinking, memory, and/or judgment (impaired ability to safely drive, work, operate machinery for hours to days after last use depending on the type, amount and frequency
b. Risk for falls, accidents or injury due to impairments
c. Anxiety or panic in some persons
d. Dryness of mouth, other mucosal membranes
e. Increased appetite
f. Rapid heart rate, increased blood pressure, increased risk of heart attack
g. Increased risk of stroke (brain injury) due to spasm of brain blood vessels
h. May worsen symptoms of asthma, COPD or other pulmonary conditions

Long term marijuana use may be associated with these risks and side effects:

a. Physical dependency on the marijuana which means withdrawal symptoms if regular use is stopped
b. Addiction, an inability to stop using marijuana despite the fact it is causing ongoing negative effects

c. Academic, social, or work related problems due to delays or challenges in intellectual, psychological or social development

d. Schizophrenia and some other psychiatric disorders appear to be more common and earlier in onset in persons who use marijuana regularly in their teenage years

e. Smoked marijuana may cause bronchitis, increased asthma symptoms and possible increased risk of lung cancer

f. Use by pregnant women is associated with abnormal development of the nervous system in unborn babies and in growth retardation and low birth weights

About the Author

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has given hundreds of presentations worldwide, on how drugs affect the brain and consults to government, organizations and industry. She holds 19 patents, is a recipient of a NIDA Public Service award, a NIH MERIT award, American Academy Addiction Psychiatry Founders' Award, and Marian Fischman Award. A brain imaging agent strategy she developed was cited by The Better World Report, 2006, as one of "25 technology transfer innovations that changed the world". Her experiences in translational neurobiology, government and public service afford her a unique perspective on science and public policy.