THE JOURNAL OF
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

Dr. Bertha K. Madras is Professor of Psychobiology, Department of Psychiatry at Harvard Medical School (HMS), and is cross-appointed at the Massachusetts General Hospital. She served as Deputy Director for Demand Reduction (prevention, intervention, treatment) in the White House Office of National Drug Control Policy (ONDCP), a Presidential appointment confirmed unanimously by the US Senate. At Harvard, her multidisciplinary research focuses on neuropsychiatric diseases and addiction biology, documented in over 150 manuscripts and as co-editor of books “The Cell Biology of Addiction”, “Effects of Drugs in the Human Nervous System”, “Imaging of the Human Brain in Health and Disease”. At ONDCP, she incorporated Screening, Brief Intervention, Referral to Treatment (SBIRT) into the national drug control strategy, spearheaded SBIRT CPT®, other billing code approvals, Medicaid reimbursement, SBIRT adoption by Health Resources and Services Administration, the Veterans Administration, recruitment of Federal healthcare insurers, a UN declaration of endorsement, and other initiatives. In service to the public, she directed creation of a Museum exhibit, a CD (licensed by Disney Corp), “Changing your mind: drugs in the brain” for the Boston Museum of Science. She

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.