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PLEASE RESPOND TO:
☐ 322 EIGHTH AVENUE, SUITE 1700
NEW YORK, NEW YORK 10001
PHONE: (212) 633-8052
FAX: (212) 633-8096

☐ ROOM 711B
LEGISLATIVE OFFICE BLDG
ALBANY, NY 12247
PHONE: (518) 455-2451
FAX: (518) 426-6846

Testimony Before the Committee on Mental Health, Mental Retardation, Alcoholism, Drug Abuse and Disability Services and the Subcommittee on Drug Abuse of the New York City Council

November 18, 2011

My name is Thomas K. Duane and I am the New York State Senate sponsor of S.2774, which would legalize the possession, manufacture, use, delivery, transfer, transport or administration of marijuana by a certified patient or designated caregiver for a certified medical use. Thank you for this opportunity to testify on Proposed Resolution No. 94-A, which calls on the New York State Legislature to pass this legislation. I wish to applaud New York City Councilmember Daniel Dromm for introducing this resolution.

Existing laws that criminalize patients who use medical marijuana are cruel and unjustified by medical science. Medical marijuana's safety and efficacy in treating certain painful, often life-threatening diseases is a well-documented scientific fact. For example, the National Academy of Sciences' Institute of Medicine concluded in a 1999 report that "nausea, appetite loss, pain and anxiety...all can be mitigated by marijuana." Doctors and patients report that marijuana can be an effective treatment—where other medications have failed—for at least some patients who suffer from HIV/AIDS, cancer, epilepsy, multiple sclerosis, Crohn's Disease and other debilitating conditions. There is no reason we cannot establish common sense controls to ensure safe access to this medicine for suffering patients who have their doctors' recommendations while ensuring it does not wind up in the wrong hands. This bill does exactly that and that is why I believe it enjoys broad support among New York lawmakers and constituents of both parties. Indeed, a February 2010 Quinnipiac Poll found that 71% of all New Yorkers—including a majority of Republicans—support the legalization of medical marijuana.

Concerns about this legislation generally relate to an increased risk of abuse of marijuana. However, under the provisions of S.2774, this medicine would be more tightly regulated than a number of other highly intoxicating prescription drugs, including opiates. Patients and their designated caregivers would have to register with the New York State Department of Health (DOH), as would organizations responsible for acquiring, possessing, manufacturing, selling, delivering, transporting or distributing marijuana for certified medical use. Consumption of

marijuana for medical use would be explicitly prohibited in public places, motor vehicles, aircraft, waterborne vessels and any place where tobacco may not be smoked under Article Thirteen-E of the New York State Public Health Law. Licensed practitioners allowed to prescribe medical marijuana would be limited to physicians, physician assistants and nurse practitioners. In addition, unlike certain other states with medical marijuana laws, patients would not be allowed to grow their own marijuana.

This legislation is supported by the Medical Society of the State of New York and the New York State Nurses' Association, as well as thousands of New Yorkers who are desperate for relief from devastating illnesses that they have been unable to attain from existing prescription drugs. During a 2009 press conference called by me and Assembly sponsor Richard Gottfried, self-identified Conservative Party member Joel Peacock spoke compellingly of the chronic pain he has endured since a 2001 car accident. Refusing to break the law, he is forced to suffer, yet he has worked for years to advocate for compassionate medical marijuana laws. Countless others have had to violate the laws of our State to alleviate some of the worst symptoms of their conditions.

It is outrageous that we continue to criminalize the medical use of marijuana. This legislation, which would be among the most restrictive in the nation, achieves the dual goals of providing compassionate relief to suffering patients and protecting the public's interest in regulating a controlled substance. Fifteen states, including the District of Columbia, currently sanction the use of this medicine. While New York delays action, acquiescing to fear-mongering and outdated rhetoric, people are living and dying without the basic palliative care they need and deserve.

I thank the members of the City Council Committee on Mental Health, Mental Retardation, Alcoholism, Drug Abuse and Disability Services and the Subcommittee on Drug Abuse for allowing me to submit this testimony and I urge you to pass Res. No. 94-A.

Testimony
of
Adam Karpati, MD, MPH
Executive Deputy Commissioner for the Division of Mental Hygiene
New York City Department of Health and Mental Hygiene

before the

New York City Council Committee on Mental Health, Mental Retardation, Alcoholism, Drug Abuse and Disability Services

and

Subcommittee on Drug Abuse

regarding

Oversight: Medical Marijuana
November 18, 2011

250 Broadway, Hearing Room, 16th Floor
New York, NY

Good morning Chairperson Koppell, Chairperson Wills and members of the Committee on Mental Health, Mental Retardation, Alcoholism, Drug Abuse and Disability Services. I am Adam Karpati, Executive Deputy Commissioner for the Division of Mental Hygiene at the New York City Department of Health and Mental Hygiene. On behalf of Commissioner Farley, I would like to thank you for the opportunity to testify.

Currently, 16 states and the District of Columbia have legalized possessing and smoking marijuana for medical reasons, with various restrictions. In states where medical marijuana is legal, it is prescribed to treat patients with cancer, HIV/AIDS, multiple sclerosis, chronic pain, severe nausea, and other chronic or debilitating diseases and conditions. Reports suggest that cannabinoid drugs, those containing the same chemical compounds as marijuana, could be beneficial for relief of pain and nausea and for appetite stimulation. Some patients who suffer simultaneously from severe pain, nausea and appetite loss, such as those with AIDS or who are undergoing chemotherapy, believe that cannabinoid drugs offer relief not found in any other single medication. However, based on the lack of clear, scientifically validated medical benefits of smoked marijuana and the known harmful components of marijuana smoke, the Department opposes legalization of marijuana for medical use.

Medical expert bodies say more research is needed on the benefits of the active ingredient in marijuana and the risks of smoking it. The Institute of Medicine, American Medical Association, National Institutes of Health, World Health Organization, and American Public Health Association have all recommended that therapeutic uses of cannabinoids warrant further basic pharmacological and experimental investigation and clinical research into their effectiveness. They agree that more research is needed on the

basic neuropharmacology of tetrahydrocannabinol (THC) and other cannabinoids and related methods of administration so that better therapeutic agents can be found. A 2003 Institute of Medicine report recommended that clinical trials of cannabinoid drugs for symptom management should be conducted with the goal of developing rapid-onset, reliable, and safe delivery systems.

The active ingredient in marijuana is currently available by prescription in pill form throughout the country, under the brand name Marinol. Users of medical marijuana cite a preference for smoking the drug by asserting that taking the drug as a pill does not alleviate their symptoms or that they cannot control the dosage adequately using pills. Other forms of the drug that are in development or available in other countries, including a patch and an oral spray, may address some of the complaints about the limits of the pill.

While the benefits of medical marijuana are unclear, the potential negative health effects of smoking marijuana are serious. Smoking marijuana damages the lungs. Marijuana smoke contains cancer-causing chemicals and it deposits four times as much tar in lungs as cigarettes. Unlike any other drug approved for medical use, dosage with smoked marijuana cannot be known precisely because drug levels vary from plant to plant.

A bill in the state legislature, S.2774 / A.7347, would legalize the possession, manufacture, use, delivery, transfer, transport or administration of marijuana by a certified patient or designated caregiver for a certified medical use. Because the benefits of marijuana are not clear, and because there are known risks to smoking marijuana, the Department does not support this legislation.

Thank you again for the opportunity to testify. I would be glad to take your questions.

Marijuana Policy Project
236 Massachusetts Ave. NE, Suite 400
Washington, DC 20002
p: (202) 462-5747 • f: (202) 232-0442
info@mpp.org • www.mpp.org

"We change laws."

November 18, 2011

Dear Chairman Koppell and members of the Mental Health, Mental Retardation, Alcoholism, Drug Abuse and Disability Services Committee:

Thank you for taking up this important issue and for the Council's compassion when it stood up for medical marijuana patients in 2006 by passing a similar resolution.[1] The state Assembly heeded your call and voted in favor of medical marijuana legislation in 2007 and 2008.[2] Unfortunately, the Senate has not yet acted and has actually never even held a floor vote on this popular and science-based bill. I encourage you to again speak for the seriously ill of New York by passing Resolution No. 0094-A and calling on the legislature to vote their conscience.

29% of Americans live in medical marijuana states, including residents in neighboring Vermont and New Jersey. Canada, Israel, the Netherlands, and Germany all protect medical marijuana patients, as do 16 U.S. states and the District of Columbia.

Meanwhile, thousands of patients in New York state are living in fear that they will be arrested for using a natural medicine that in 1988 was called, "one of the safest therapeutically active substances known to man" by then-DEA Administrative Law Judge Francis Young. Some patients, like the late Barbara Jackson of the Bronx, have endured the indignity of arrest and hours spent in jail for possessing a relatively safe and effective medicine.[3]

Because medical marijuana is illegal in our state, patients have no choice but to obtain it from the criminal market or risk a felony conviction by growing it for themselves.

A. 7347 and S. 2774 would change this, by protecting patients and providing a well-regulated, safe means of accessing their medicine. A patient would only qualify if his or her physician recommends medical marijuana and certifies that the patient has a life-threatening or severe, debilitating medical condition. Patients would send in their doctors' certification to the state health department and would get a state-issued ID card. Patients, or their caregivers, would be able to get their medicine

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[1] Res. 71-A was approved on June 28, 2004 in a voice vote with four councilmembers voting against it.

[2] The Assembly voted 89-52 in favor of A. 4867B, sponsored by Assembly Health Chair Richard Gottfried (D-Manhattan), on June 18, 2008. The Assembly also approved A. 4867A on June 13, 2007.

[3] Coleman, Christina, "Weed it & weep! Granny's busted," *New York Daily News*, April 30, 2007.

from highly regulated, registered organizations or pharmacies that are licensed by the state to distribute marijuana.

Regulated access is working in other states, such as New Mexico, Colorado, and Maine. While medical marijuana is not yet legal under federal law, under the Obama administration, federal enforcement has not focused on state-licensed providers that are complying with regulations. In addition, for more than a decade during more hostile presidential administrations, brave and pioneering providers in other states have successfully operated dispensaries to provide patients with safe access to their medicine.

New York patients have waited for relief for far too long. I am personally astonished that New Jersey moved to protect their sick and dying residents before we did in New York State. We can fix that. Please stand with our state's medical community and 71% of voters by approving Resolution No. 0094-A, and let Albany know that we are tired of waiting.[4] Thank you.

[4] "New York State Voters High On Medical Marijuana, Quinnipiac University Poll Finds; Freeze State Workers' Pay, Voters Say 3-1," Quinnipiac University, February 4, 2010. The following organizations have publicly expressed support for allowing medical marijuana for people with serious medical conditions: the Pharmacists Society of the State of New York, the New York State Nurses Association, Medical Society of the State of New York, and the Hospice and Palliative Care Association of New York State.

New York State
NURSES
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PUBLIC FORUM ON MEDICAL USE OF MARIJUANA

OFFICIAL TESTIMONY

Good afternoon. My name is Ellen Brickman and I am Director of Statewide Peer Assistance for Nurses (SPAN) at the New York State Nurses Association. The Nurses Association is the oldest and largest professional organization and union for registered nurses in New York State. It represents the interests of more than 270,000 registered nurses and serves as the collective bargaining agent for more than 37,000 RNs at 150 healthcare facilities. We appreciate the opportunity to testify in support of this resolution.

The benefits of medical use of marijuana: to manage pain, nausea, migraines, wasting syndrome associated with AIDS and cancer, muscle spasticity associated with multiple sclerosis, and seizures associated with epilepsy, have been supported by clinical research. Despite the passage of New York State public health law, Article 33-A Controlled Substances Therapeutic Research Act in 1980, patients still face barriers accessing this medication. The act requires that patients be approved by a review board, resembling a clinical trial program, lengthening the time between requesting the use of a medication with proven results, and effective treatment. Thirty-one years later, prescribers and their patients still don't have access to a drug that is effective in symptomatic relief.

The safety of medical use of marijuana has been firmly demonstrated. Between 1840 and 1900, European and American medical journals published more than one hundred articles on the therapeutic use of the drug known then as Cannabis Indica, and now simply as cannabis.[1] The safety of the drug has been established by numerous studies and reports, including the LaGuardia Report of 1944, The Schafer Commission Report of 1972, a 1997 study conducted by the British House of Lords, the Institutes of Medicine report of 1999, research sponsored by Health Canada and numerous studies conducted in the Netherlands, where cannabis is currently available from pharmacies by prescription.[2]

[1] http://www.safeaccessnow.org/article.php?id=4558#comparison
[2] http://www.safeaccessnow.org/article.php?id=4558#comparison

11 Cornell Road, Latham, New York 12110-1499 ■ Phone: 518-782-9400 ■ E-mail: info@nysna.org ■ www.nysna.org
120 Wall Street, 23rd Floor, New York, NY 10005 ■ 212-785-0157

A 2010 review of research literature in Germany reports that since 2005 there have been 37 controlled studies assessing the safety and efficacy of marijuana and its naturally occurring compounds, in a total of 2,563 subjects. **By contrast, most FDA-approved drugs go through far fewer trials involving far fewer subjects.**[3] Cannabinoids have a remarkable safety record and significantly, the consumption of marijuana – regardless of quantity or potency -- cannot induce a fatal overdose.[4]

Registered nurses have a responsibility to promote health, prevent illness and alleviate suffering. The palliation of symptoms is an ethical imperative for healthcare providers in caring for patients with advanced disease. Each individual experiences disease, illness and side effects uniquely . Prescribers should have all drugs that demonstrate potential clinically effective results, available for their use, particularly when conventional therapies have proven ineffective.

In conclusion, the New York State Nurses Association supports the Council of the City of New York's proposed resolution to call upon the New York State Legislature to join the sixteen other states that allow medical use of marijuana, and to pass legislation that would legalize access to this important and effective treatment option.

Thank you for your time and consideration.

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[3] http://norml.org/component/zoo/category/recent-research-on-medical-marijuana
[4] http://norml.org/component/zoo/category/recent-research-on-medical-marijuana

RICHARD N. GOTTFRIED
75TH ASSEMBLY DISTRICT

CHAIR
COMMITTEE ON HEALTH

NEW YORK STATE ASSEMBLY

822 LEGISLATIVE OFFICE BUILDING, ALBANY, NY 12248
TEL: 518-455-4941 FAX: 518-455-5939

250 BROADWAY, RM. 2232, NEW YORK, NY 10007
TEL: 212-312-1492 FAX: 212-312-1494

E-MAIL: GOTTFRR@ASSEMBLY.STATE.NY.US

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Medical Marijuana

Testimony by Assembly Health Committee Chair Richard N. Gottfried
New York City Council Hearing
Friday, November 18, 2011

My name is Richard N. Gottfried. I chair the Health Committee in the New York State Assembly and I am the author and introducer of the New York medical marijuana bill, A. 7347. I urge the City Council to pass resolution 0094-2010 supporting the bill.

Thousands of New Yorkers who suffer from serious debilitating and life-threatening conditions would benefit from the medical use of marijuana under a physician's care. It would reduce their pain and other symptoms, enable them to tolerate their medication, and extend their lives.

Medical marijuana legislation is supported by a broad array of health and other organizations, including:

- Medical Society of the State of New York
- New York State Nurses Association
- Hospice and Palliative Care Association of New York State
- Pharmacists Society of the State of New York
- Statewide Senior Action Council
- Gay Men's Health Crisis
- New York AIDS Coalition
- New York State AIDS Institute Advisory Council
- Oncology Nursing Association (New York State chapter)
- Association of the Bar of the City of New York
- American Academy of HIV Medicine
- AFSCME District Council 37
- Housing Works

Nationally, legalizing the medical use of marijuana is supported by the American Public Health Association, the American Bar Association, and the Lymphoma Foundation of America, among others. The medical use of marijuana is recognized by the American Medical Association and the Institute of Medicine of the National Academy of Science.

Under appropriate professional care like other drugs, marijuana has important therapeutic use for many seriously ill patients. In their amicus brief to the U.S. Supreme Court in 2004, the Lymphoma Foundation of America, the HIV Medicine Association, and

the American Medical Students Association said: "For certain persons, the medical use of marijuana can literally mean the difference between life and death."

The Federal Food and Drug Administration and Drug Enforcement Agency have approved the medical use of THC, the active ingredient in marijuana, in synthetic pill form, since 1986. However, many patients and their doctors find that consuming marijuana naturally makes the dosage easier to limit and control, and that the efficacy of THC is enhanced and symptoms are easier to manage. Patients complain that the harder-to-limit dosage in pill form interferes with the patient's ability to work and live a more normal life. The choice ought to be made by the patient and physician. It should not be a law enforcement issue.

The New York medical marijuana bill has more restrictive controls than any medical marijuana law in the country, with the possible exception of New Jersey. It is more restrictive than the New York laws regulating highly dangerous drugs like morphine, oxycontin, or Valium.

The bill would set up a strict and narrow medical marijuana system. The bill allows a practitioner (who is licensed to prescribe controlled substances) to certify that a patient has a serious condition (under statutory criteria) that can and should be treated with the medical use of marijuana. A certified patient or designated caregiver who is registered with the Health Department can possess a limited amount of marijuana for the patient's medical use.

The Department of Health would license and regulate "registered organizations" to dispense medical marijuana for certified patients. Registered organizations can be: pharmacies, licensed hospitals or clinics, the state or a county health department, or not-for-profit corporations developed for this specific purpose (only if DOH finds other entities are not available in an area). DOH would also license and regulate producers.

The bill would also tax the gross receipts of registered organizations.

The notion that anyone would use the medical marijuana system to obtain marijuana for recreation use is absurd. A person would need a doctor willing to risk his or her license to certify that the person has a statutorily-defined serious condition treatable with marijuana, file his or her name and address with the state, and get the drug from a state-licensed dispenser with more state paperwork. Doing all that to get marijuana for recreational use would be a misdemeanor – tougher than the current penalty for possessing a small amount, which is like a littering ticket.

Some say that more research should be done. There is no argument against doing more research; we do research even on well-established drugs and procedures. However, since marijuana is a natural and unpatentable product, no drug company is going to spend the millions of dollars needed for clinical trials. The thousands of people whose suffering could be eased and lives prolonged by medical marijuana should not be forced to wait for research that no one has offered to fund.

The fact that smoking is not good for you is no argument against this legislation. Virtually every drug can have harmful side effects. And we are talking about relieving the suffering of people with severe, debilitating and life-threatening conditions, using marijuana under medical oversight.

Dr. Robert M. Glickman, when he was the dean of the NYU School of Medicine wrote in support of the legislation:

> "We agree that marijuana is one of the safest therapeutically active substances known and it has a wide variety of therapeutic applications for a number of medical conditions and diseases such as AIDS/HIV, glaucoma, cancer, multiple sclerosis, and epilepsy. The availability of medical marijuana will prove to be an effective pain management technique for a number of NYU's patients."

This is sensible, strict and humane legislation. The fact that this is not the law in New York is political correctness run amok, at the expense of the suffering of thousands of our fellow New Yorkers.

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Nicholas A. Pace, MD, FASAM
Clinical Associate Professor of Medicine
New York University School of Medicine

GENERAL MOTORS BUILDING
767 5TH AVENUE, 3RDFLOOR
NEW YORK, NY 10153
212-418-6450

November 16th, 2011

Dear Joint Committee Members and Subcommittee Members of the N.Y City Council,

As a physician addiction specialist and former Chairman of the NY Governor's Advisory Committee on Alcoholism and Substance, I have studied the effects of the drug marijuana for three decades and directed four international conferences on marijuana at New York University Medical Center.
Please be aware that the knowledgeable Academic Medical Community and the Addiction Treatment Community including: The AMA, American Cancer Society, National Cancer Institute, American Glaucoma Society, American Academy Of Ophthalmology, American Society of Addiction Medicine, and the New York Society of Addiction medicine, The National Council on Alcoholism and Drug Dependency, and the Alcoholism Council of New York, and The Drugs Free Schools Coalition are firmly against Medical Marijuana Laws .

The academic medical community recognizes and agrees with the Institute of Medicine that Marijuana (Cannabis) is not a harmless herb but a powerful drug "with questionable medical value that has a variety of serious side effects, and that with protracted use can lead to physiological dependence, addiction and damage to vital organ systems including the lungs, brain and reproductive system. (ref. 2)

The Medical Profession;
I. Agrees that all cannabis-based products should be subjected to the same rigorous scrutiny of the FDA regulatory process that any other medications are before being medically approved for use. In this way, patients can be protected & assured of receiving a standardized pure drug, with listed medical indications, directions & warnings about of side effects. Therefore, they oppose a law allowing the use of crude unregulated plant material containing marijuana (Cannabis) that has questionable medical value, is not FDA approved, has variable potency, is often contaminated with pathogens, pesticides, bacteria, and has severe adverse side effects including addiction. (ref. 2)

II. Rejects smoking as a safe delivery system, recognizing the public health harm of tobacco smoking; and urges people not to smoke tobacco or marijuana. Marijuana smoke is four times more toxic to the lungs than tobacco smoke because it has a larger number of carcinogens and impurities (421); it has a higher burn temperature than cigarette smoke, is inhaled more deeply, and held in the lungs longer than tobacco. (Ref 2

III. Recognizes recent studies that confirm that heavy marijuana smoking causes impairment of the Brain (MRI's show damage to the memory and emotional centers of the brain (ref 3.), Neurological/psychiatric, Pulmonary, Cardiovascular, & Reproductive Systems (abnormal sperm* Testicular Cancer.) (ref.3) Marijuana's questionable pain relief has the effectiveness of less than aspirin (ref 2) or codeine cough medicine, and is associated with significant undesirable side effects including the increased pain that comes with tolerance and drug withdrawal (ref.2)

IV. Recognizes that there is no Compassionate Medical Need for a New Medical Marijuana law, because a pure oral form (Marinol) is legally available and can be prescribed for the nausea of chemotherapy. The standardized oral form (Marinol) has a 4 hour tissue level, making it less toxic and less prone to abuse than the more irritating variable dosage smoked form with only one hour tissue levels. Most oncologists do not use Marinol because it inhibits the immune system, it does not work well and there are 30 other anti nausea drugs that work better (ref.2)

V. Recognizes that Marijuana is counter indicated in HIV/AIDS patients. Marijuana directly impairs or suppresses the immune system. Abnormal immune function leaves the patient unable to fight the infection or cancer. A recent Harvard study shows that marijuana use enhances the virus that causes Kaposi's sarcoma a serious life threatening cancer in HIV infected patients (ref. Science 8/2/07).

VI. Recognizes a great rise in teen marijuana use in states where medical marijuana laws have been adopted. In the last 8 years there has been a 492% increase in teen hospital admissions for marijuana abuse or dependence and a 136% increase in teenager's use of the emergency department for marijuana abuse compared with a 54% decline for all other substances of abuse from 1995 to 2002. (ref.4)In these states young people have the false impression that marijuana is a harmless drug that can be safely used casually for recreation.

It is obvious what is happening in those states where legislators naively believed the wealthy pro-marijuana lobbyists that medical marijuana was needed to help seriously ill, elderly people for pain relief and passed a smoking medical marijuana law. California records show elderly sick people only accounted for 2.05% of those who obtained a physician's recommendation for its use. The rest of the users were between ages of 17 and 40 and were using it for a multitude of alleged ailments with no medical supervision.

In states that have legalized medical marijuana; crime rates have gone up along with an increase in teem marijuana use. Studies suggest that when perceived risk goes down, use goes up. In addition a whole new expensive bureaucracy had to be set up, in attempt to regulate medical marijuana providers, physicians, patients, and dispensaries. In Denver Colorado there are now 809 Marijuana dispensaries outnumbering Star Bucks coffee shops. (ref.4) As a result of the amendments made to the medical marijuana bill Colorado is experiencing an increase in medical marijuana users in 2008 there were 8,957 users, by June 2010 there were 99,559 users, which indicates 2% of the entire population is using marijuana. Of additional concern in Colorado is a corresponding spike in suicide; in 2009 there were 940 suicides, nearly twice the national average.

A famous California Physician colleague of mine was asked what he thinks of marijuana as medicine" He said *"Marijuana is the most problematic drug we are dealing with today. The manifestations of the addiction are profound; the withdrawal is protracted and given the cultural reinforcement for its use, difficult to motivate an addictive patient to be involved in an ongoing connection to recovery. Every patient I admit presently has a Marijuana Prescription, nearly without exception. No one ever asked the patients at these "clinics "if they have or have had a history of addiction and as far as I can tell they never see a doctor. Clearly they do not have ANY contact with a professional with any mental health training. What I hate is bad medicine and this is the use of our profession to promote a political agenda. I hate bad medicine and this is egregious medicine. It's' worse here in California than you might imagine. And it varies district to district. It is particularly ridiculous out here in the San Gabriel Valley region of Los Angeles."*

A well known New York oncologist recently stated to me that he is acutely aware of the desperation that some patients feel, both in the treatment of their disease and symptom management. "As medical professionals we have to make decisions for our patients based on objective evidence. The case for medical marijuana lacks any compelling scientific evidence supporting benefit for cancer patients. In fact, there is more evidence supporting the harm of inhaling noxious smoke. Why should this substance be held to a different standard than others? Why should it not undergo randomized controlled studies to support its medical benefit before it can be used. He need to be objective and not emotional, otherwise, we risk harming out patients.

Sincerely,
Nicholas Pace MD FASAM
Diplomat of the American Board of Addiction Medicine
Clinical Associate Professor of Medicine
New York University Langone Medical Center.
Former Vice Chairmen American Council of Drug Education,
Co Author of "Teens under the Influence" (Random house 2003)
General Motors Bld. 3 rd Floor
767 5th Ave. New York City, N.Y.
Phone 212 418 6118
Fax 212 418 6115

Supporting References:

1).Partial list of medical organizations opposed to the New York Medical Marijuana Laws: The American Medical Association, the National Cancer Institute, the American Cancer Society, the National Multiple Sclerosis Society, the American Academy of Ophthalmology, the American Glaucoma Society, the National Eye Institute, the American Society of Addiction Medicine, the National Council on Alcoholism and Drug Dependency and NCADD NY Affiliates, the New York Society of Addiction, the Alcoholism Council of New York, and the Drug Free Schools Coalition.

2).Attached: The Medical Use of Marijuana and THC in Perspective. N. Pace Chapter 69, Marijuana & Medicine Humana Press. Molecular Basis of Therapeutic THC, N. Pace, American Society Addiction Medicine

3.) Attached a list of Abstracts of Recent scientific studies of heavy smoking marijuana patient's

a)Pulmonary impairment of large airway function with obstruction Aldington S, et al Thorax. 2007 Dec; 62(12):1058-63

b) Regional brain damage in both the hippocampus (memory& emotion) amygdala (fear & aggression) Lubman D, Arch Gen Psychiatry. 2008 Jun; 65(6):694-701.

c) Neuro-psych disorders, transient psychotic disorders, hallucinations and paranoid delusions or sustained psychotic symptoms McGuire P, Arch GenPsychiatry.2009/4; 442-51.

d)High incidence Aggressive fast-growing testicular cancer in young men as adolescents using at least once a week.2/9/09 Journal "Cancer" Hutchinson Cancer Center Se, WA.

e) Multiple Sclerosis patients had worsening of their MS symptoms increased cognitive defects & mood disorders. (Ghaffar & Feinstein, Neurology2008Jul15:164-9.

4.).Statistics from The National Center on Addiction and Substance Abuse at Columbia University (CASA) 6/18/09

69 The Medical Use of Marihuana and THC in Perspective

Nicholas Pace, Henry Clay Frick, Kenneth Sutin, William Manger, George Hyman, and Gabriel Nahas

Abstract

The curative properties attributed to marihuana for several thousand years have proved to be disappointing. The ancient oriental claims of marihuana as a pain soother and for the relief of muscle spasms, convulsions, rheumatism, epilepsy and migraine headaches were introduced into western medicine during the 19th century. The reason for the lack of success with marihuana remedies at that time was the same as the present observations encountered with THC and all of its novel applications: the variability and inconsistency of its effects associated with unwanted psychological and cardiovascular effects. The discovery of THC, the active ingredient of marihuana gave a new impetus for an intensive search for its potential therapeutic applications. THC and its psychoactive derivatives were proposed as analgesic, antidepressant, hypnotic tranquilizer, as a treatment for withdrawal symptoms, glaucoma, spasticity, nausea, vomiting, and to enhance the appetite. Marihuana smoke, in spite of its toxicity to the lung and immune system, was even advocated by some as a medically acceptable vehicle for THC. For many of these therapeutic applications, molecular pharmacologists have been able to tailor specific molecules targeted to receptor sites which control acute and inflammatory pain, nausea, vomiting, and glaucoma. These fundamental studies in molecular pharmacology have also provided for an explanation of the therapeutic inadequacy of THC. This cannabinoid deregulates the physiological signaling role of a receptor protein to which it binds and of the membrane bilipid layer which it permeates. This deregulation of membrane signaling will result in discordant and partial therapeutic effects coupled with unwanted side effects.

From: *Marihuana and Medicine*
Edited by: G. G. Nahas et al.

HISTORY

The Chinese were the first to describe the medicinal properties of oral preparations of *Cannabis* in the *Pen-ts'ao Ching* 2,000 years ago, and they were the first to discard its use a few centuries later because the substance made one see "devils." Opium with other herbal remedies and acupuncture were preferred instead.

In India and Middle Eastern countries the medicinal properties of oral preparations of *Cannabis* were still widely used in the 19th century. At that time *Cannabis* was introduced to Western medicine by William O'Shaughnessy (1842) for use as an all-purpose medication. *Cannabis indica* (from India) became a wonder drug used to treat a wide variety of ailments ranging form menstrual cramps and convulsions to inflamed tonsils and migraine headaches. It was also used to increase uterine contractions and reduce childbirth pains. Even with the low dosage (1 to 6 grains, or 65 to 400 mg, administered by mouth) this medication alleviated many aches and pains without producing any of the signs of hashish intoxication described by Moreau in 1845 *(1)*.

However, many physicians were discouraged from using the drug because of the extreme variability of potency of different lots of *Cannabis* extracts and the difficulty of obtaining reproducible effects. With the advent of more specific and effective medications like aspirin, barbiturates, and anesthetic agents, hemp preparations rapidly fell into disuse and by 1932 were dropped form the British Pharmacopoeia.

Toward the end of the 19th century the burgeoning pharmaceutical industry attempted to develop more dependable and purified compounds from *Cannabis*, but without success. Oral preparations of cannabis were used with decreasing frequency in the first part of the 20th century, and they were eliminated from the United States Pharmacopoeia in 1942. In 1960, the World Health Organization Committee on Drug dependence advised the U.N. Commission on Narcotics that cannabis preparations are practically obsolete and there is no justification for their medical use. The recommendation led the United Nations Single Convention (in 1961) held in New York to classify the flowering tops of marijuana among the drugs with high abuse potential. These drugs are to be excluded by law from commerce and medical use.

MARIHUANA SMOKING AND THC

Marihuana as medicine regained popularity in the wake of widespread recreational smoking of marihuana smoking in the United States during the second part of the 20th century. To the old claims *(2,3)*, new applications were found for the old drug in the treatment of glaucoma, and of nausea and vomiting induced by cancer chemotherapy. Concurrently, the active ingredient of marihuana, THC delta 9-tetrahydrocannabinol, was isolated.

In addition to the cannabinoids, chemicals specific to the cannabis plant, the smoke of the crude marihuana drug contains 421 different chemicals, some toxic (carbon monoxide, acetaldehyde, phenol, creosol, naphthalene) and also twice as many carcinogens as a tobacco cigarette of the same weight. The inhalation of marihuana preparations carries an additional hazard: they may be contaminated with salmonella *(5)*, or with a fungus, *Aspergillus fumigatus*, which may cause severe pulmonary disease *(6)*. For therapeutic purposes, it is important to distinguish between the use of the crude marihuana smoke and its pharmacologically pure active compound THC: the potential therapeutic applications attributed to marihuana smoke have been traced to the effect of its main psychoactive ingredient, THC, which is available as an oral preparation.

1. INTRODUCTION

It is now possible to relate the therapeutic properties of marihuana preparations to their THC content THC, because of its oily nature cannot be given parenterally in man; its pharmacokinetics and the time course of its effects when administered orally are different from those of the inhaled form. Plasma THC concentration following oral administration reaches a more sustained steady-state level, twice as long as after smoking *(7)*. The overall pharmacological and psychoactive effects of the inhaled and oral forms of THC are similar, as well as the prolonged tissue retention of the drug which has a half-life of five to eight days.

Tolerance to the effects of marihuana and THC develops rapidly, and withdrawal symptoms similar to those of other sedative-hypnotic agents are present following abstinence after chronic use. Chronic treatment of animals with CBD or with THC have resulted in alteration of spermatogenesis *(8)*. Similar observations have been reported in humans after heavy marihuana smoking (oligospermia and abnormal forms of sperm) *(9)*.

Oral THC (dronabinol) is an approved medication in the United States as a 2.5–10 mg capsule in sesame oil for oral administration. Anecdotal accounts *(10)* have claimed that marihuana smoking is more effective than oral THC.

2. THERAPEUTIC APPLICATIONS OF CANNABINOIDS

The numerous pharmacological effects produced by THC led many investigators to seek some therapeutic application for this drug and other cannabinoids as well. Extensive research programs sponsored by the pharmaceutical industry (Abbott, Squibb, Lilly, and Pfizer) and by Federal agencies were initiated to establish the efficacy of THC and of its derivatives, of their mode of action, and of their main therapeutic indications. Several related synthetic molecules were designed and tested experimentally and clinically.

Among these derivatives, nabilone, a THC-like cannabinoid developed by Lilly laboratory, was approved for medical use in 1982 *(11)*. This drug has been used in the treatment of the nausea and vomiting associated with cancer chemotherapy, in doses of 1–2 mg/day, and in the treatment of muscle spasticity.

Another THC-like synthetic derivative, levonantradol *(12)*, was developed by Pfizer laboratory. It is a very potent substance with antalgic and antiemetic activity in the milligram dose *(13,14)*. Its marked side effects prompted the interruption of its clinical trials in 1982.

The potential therapeutic applications of THC and related cannabinoids were reported in eleven symposia and monographs published in the 1970s and 1980s *(15–25)*. As a result, several hundred reports were assembled in 1500 pages of text authored by organic, analytical, and pharmaceutical chemists; experimental and clinical pharmacologists, and physicians who had specialized in the chemistry, pharmacology, and therapeutic applications of the cannabinoids. The present review is an attempt to summarize, the main findings of this data reported by scientists from the United States, United Kingdom, Sweden, France, and Israel.

3. ANALGESIC EFFECT

The analgesic action of THC reported in the experimental animal *(26)* is equivocal in clinical trials. A double-blind study by Milstein et al. *(27)* observed a significant increase in pain tolerance among marihuana smokers. Noyes et al. *(28)* reported an analgesic effect of orally administered THC in cancer patients. These effects were associated with mental clouding and other psychoactive reactions. Hill et al. *(29)* failed to detect the analgesic activity after a

dose of 12 mg THC given to 26 normal volunteers subjected to electrical stimulation of the fingers. Regelson et al. *(30)* also failed to observe analgesic effects of THC in cancer patients.

As pointed out by Clark *(31)*, the difficulty with classic threshold studies of experimental pain is that the pain threshold is influenced by both expectation and analgesia. The double-blind control is not sufficient since the psychoactive effects of marihuana may allow subjects to peak through the double-blind and distinguish between placebo and drug condition on the basis of subjective effects such as euphoria and clouding of consciousness.

Clark et al. confirmed the hyperalgesic effect of marihuana smoking reported previously by Hill et al. He recorded the effect of thermal pain in 16 heavy marihuana smokers studied in a controlled environment, evaluating the data by using a sensory decision analysis that differentiates between sensory input and subject perception. He concluded marihuana smoking has hyperalgesic activity and enhances the perception of pain (lower threshold) and increases pain-report criterion. These results are consistent with reports of heightened sensitivity or "sharpening" of perceptions produced by smoking marihuana.

4. NEUROLOGICAL DISORDERS

Consroe and Sandyk *(25)* have reviewed the potential therapeutic role of the cannabinoids (THC, its synthetic derivatives, CBD) in epilepsy, dystonia, movement disorders (Huntington's chorea, Tourette's syndrome, Parkinsonism, tardive dyskinesia), spasticity, migraine, and neuropathic pain.

They conclude that all of the clinical trials performed to treat these conditions with THC, its synthetic derivatives, or with CBD were inconclusive. They state "the realization of the potential benefits of cannabinoids in neurological disorders will depend upon a new breakthrough in research such as identification of an endogenous ligand, identification of subtypes of cannabinoid receptors, and of their selective antagonists—and agonist."

5. ANTIDEPRESSANT EFFECT

Moreau *(1)* was the first to assume that the "feeling of gaiety and joy" produced by *Cannabis* intoxication would be valuable to treat "the fixed ideas of the depressives." He treated several such cases of deep depression with increasing dosages of hashish, but with little effect. One hundred years later, a similar lack of effectiveness of *Cannabis* derivatives on the depressive state was observed. Whereas Regelson et al. *(30)* reported a significant reduction in self-related depressive symptoms in cancer patients treated with THC, Kotin et al. *(32)*, in a carefully controlled trial with four bipolar and four unipolar depressed patients, found no antidepressant activity. This latter study was confirmed by Ablon and Goodwin *(33)* who reported that THC was not effective in a group of depressed patients treated with 5–40 mg for one week, and caused dysphoria in subjects with unipolar depression.

6. ANXIOLYTIC AND SEDATIVE EFFECTS AND TREATMENT OF ALCOHOL AND OPIATE WITHDRAWAL

In normal subjects, Pillard et al. *(34)* did not find any effect of *Cannabis* (10 mg THC) on experimentally induced anxiety. Nabilone, a synthetic potent cannabinoid with THC-like activity *(35)*, was found to be less effective than diazepam in reducing induced anxiety in normal volunteers. *(36)* Furthermore, an unwanted side-effect of marihuana is to induce acute anxiety and panic attacks.

The alterations of THC on sleep EEG and its rebound effect *(37)*, its side effects before sleep induction, and its residual effects after awakening have contraindicated its clinical use as a sedative hypnotic.

It was suggested that *Cannabis* derivatives (pyrahexyl) and THC might be useful in treatment of withdrawal symptoms from alcohol. *(38,39)* A systematic evaluation failed to find *Cannabis* useful in treating this condition *(40)*. Epidemiological surveys report that the use of *Cannabis* and alcohol are combined and are frequently the gateway drugs to the usage of opiates and cocaine.

Early experimental reports suggested that *Cannabis* might be useful in alleviating the symptoms of opiate withdrawal *(41,42)*. These observations were not clinically documented.

In conclusion, THC has little therapeutic potential in treating common psychiatric disorders such as anxiety, depression, or insomnia. Currently, agents used in therapeutics are more effective, specific, and possess fewer unwanted side effects.

7. ANTIASTHMATIC EFFECT

The acute bronchodilator action of inhaled or oral *Cannabis* was observed in normal and asthmatic subjects *(43)*. However, Tashkin et al. *(44)* reported that chronic smoking of marihuana was associated with increased airway resistance and symptoms of irritation and inflammation of large bronchi. Such observations led other investigators to test oral THC. Abboud and Sander *(45)*, using a double-blind randomized crossover design, compared the bronchodilating effects of placebo and oral THC in normal subjects and asthmatic patients. They concluded that oral administration of THC would have doubtful therapeutic value in treating asthma because its bronchodilating action was mild, unpredictable, and associated with significant disturbing central nervous system effects.

8. ANTIEMETIC EFFECT

Several controlled studies have reported that THC in 15–20 mg oral dose exerts an antiemetic effect in cancer patients undergoing chemotherapy *(45,46)*. Some clinical trials have indicated that THC is more effective than prochlorperazine, the most commonly used antiemetic in the United States *(47–50)*, whereas others reported less effectiveness and more side effects *(51)*. However, THC is not as effective as metoclopramide against emesis produced by cisplatin therapy. Gralla et al. *(52)* and Carey et al. *(53)* made a critical review of 19 studies performed on 951 cancer patients between 1975 and 1982 to assess the antiemetic properties of THC, as compared to that of other medications, during chemotherapy. The authors concluded that the different studies showed "considerable inconsistencies," THC being claimed equal, superior, or inferior to other medications, and they recommended additional controlled trials. Subsequent studies indicated that a 5-HT_3 receptor antagonist (ondansetron) that is administered intravenously is the most effective antiemetic for cancer chemotherapy *(54)*. It is effective for high-dose cisplatin therapy with a global satisfaction of nausea and vomiting control of 85%. Another serotonin-receptor antagonist, granisetron (1 mg intravenously), results in a 93% complete control of nausea after cisplatin therapy.

In 1987 an oral preparation of THC, dronabinol (marinol) was declassified from schedule I to schedule II and made available to relieve the vomiting of cancer chemotherapy and as an appetite stimulant. After its commercial release, the Food and Drug Administration (FDA) formulated the following guidelines *(55)*.

Marinol is not indicated as first-line treatment for nausea and vomiting associated with cancer chemotherapy. (It is only indicated) in patients who have failed to respond adequately to conventional antiemetic treatments. Because of the limitations of its indication, comparisons of Marinol to conventional antiemetics are inappropriate. Marinol is not a therapeutic alternative to Compazine (prochlorperazine) or other conventional antiemetic treatments (metoclopramide, ondansetron).... Patients using Marinol should

actions of THC with some of the other many medications taken by these patients should also be considered.

10. GLAUCOMA

A chance observation by Hepler *(67)* on subjects smoking marihuana (0.9–1.5% THC) showed a lowering of intraocular pressure. Subsequent studies *(68)* indicated that the smoking of *Cannabis* 1–2% THC decreased the intraocular pressure by 30%, and that this effect lasted four to five hour, and a ceiling effect was observed after two cigarettes (30 mg THC). There was no tolerance development to the lowering of intraocular pressure among marihuana smokers studied in a controlled environment during a period of 94 days. However, Dawson et al. *(69)* and Flom et al. *(70)* observed reduced intraocular pressure in smokers with little experience of use, but little or no change in subjects with extensive history of use. Dawson et al. compared 10 nonsmokers of marihuana with 10 matched subjects who had smoked marihuana for an average of 10 years or more. The smokers presented a *higher* intraocular pressure than the control group, along with a greater incidence of abnormalities of the anterior chamber of the eye.

The lowering of intraocular pressure by *Cannabis* smoking was attributed to THC or its 11-hydroxymethyl metabolite, which when infused intravenously to volunteers reduced ocular tension *(71)*. Nonpsychoactive cannabinoids have little effect. Smoking *Cannabis* (20–30 mg THC) reduced ocular tension *and* blood pressure in marihuana-naive, heterogeneous glaucoma subjects, and in subjects with open-angle glaucoma *(72,73)*. The reduction in blood pressure that reached basal levels, lasted four to five hours or longer. Associated hypotension may be severe; 6 of the 32 subjects experienced syncopal episodes. The systemic hypotensive effect is greatest in glaucoma subjects who are hypertensive. Oral administration of THC capsules significantly reduced ocular tension in healthy marihuana-naive volunteers only when administered in doses greater than 20 mg *(74)*. Marked side-effects were observed, including acute panic reactions, tachycardia, palpitations, depersonalization, and paranoia. These reactions were more common in subjects who were naive to marihuana.

In a randomized, double-blind study using 10 marihuana-naive nonsmokers with glaucoma, 5 and 10 mg THC administered per dose was not more effective than placebo in lowering intraocular pressure, although systematic hypotension was a problem.

Most antiglaucoma agents are administered topically and are effective by this route. This is not the case of THC *(75)*. Topical THC in light mineral oil vehicle (0.05–0.1%) when administered to six subjects with open-angle glaucoma was not more effective than placebo.

In summary, smoking THC containing *Cannabis* lowers intraocular pressure in glaucoma patients, producing unwanted psychoactive and cardiovascular side-effects, especially hypotension in older patients. The drug is ineffective when topically applied. Its oral administration is only effective in dosage associated with significant side-effects. There are many other effective preparations containing pilocarpine and beta-blockers that are available to treat glaucoma and have less systemic side-effects.

11. INTERACTIONS OF *CANNABIS* WITH SEDATIVES, OPIATES, AND HYPNOTICS

Dalton et al. *(76)* administered secobarbital, 150 mg/70 kg orally, to young males 50 minutes before a marihuana cigarette (THC, 25 µg/kg). The magnitude of the depressant effect of the drug combination on measures of standing steadiness and psychomotor and

could not be considered perfectly representative of oncologists at large. Among respondents, 44% acknowledged having used marihuana for at least one patient and 40% of the respondents had the "feeling" that marihuana smoking was more effective than oral THC.

In another survey *(84)*, oncologists were asked to state their drug of choice against emesis. Marihuana or THC was rated sixth and this survey was made before the availability of ondansetron, the current drug of choice, which would have displaced THC to the seventh rank. The cannabinoid antiemetic property, whatever the vehicle for THC might be, oral or inhaled, is only partially effective in cancer chemotherapy and it is ineffective in cisplatin therapy.

The pharmacokinetics of oral versus smoked THC in humans indicate that plasma levels of THC reach a more sustained level following oral administration *(7)*. Since a saturation of receptors in the chemoreceptor trigger zone (CTZ) of nausea and vomiting is the goal of the antiemetic medication, a more prolonged plasma and tissue concentration (four hours) following marinol should be more appropriate than the rapid short concentration peak (one hour) of smoked THC. It is unlikely that "smoking marihuana produces a rapid increase in the blood level of THC and is thus more likely to be therapeutic." On the basis of pharmacokinetics, the opposite should be true.

Additional studies to compare the respective efficacy of smoked marihuana versus THC delivered orally or in suppositories have been suggested. Such a comparison would have to take in account multiple confounding variables. The following factors would have to be controlled:

- Standardized marihuana cigarettes of known THC content sterilized in order to eliminate contaminants should be made available to all investigators. Several concentrations should be available in order to assess dose-response relationships.
- Measurements of the cannabinoids in body fluids, which present wide individual variations related to pharmacogenetics and method of inhalation (naive patients will have to be taught how to inhale marihuana smoke). Associated medications constitute another variable.
- The differences in pharmacological response related to previous exposure to the drug, (whether the subject is naive or tolerant to marihuana smoke).
- Objective measurements of drug response are only quantifiable in the case of vomiting (amount frequency and duration of episodes) or of glaucoma. For other conditions markers are missing or blurred.
- Independent evaluation of subjective responses would require groups treated with placebo in double-blind studies.

Methodological difficulties and statistical uncertainties would hamper an objective evaluation of such studies. How does one, for instance, perform a double double-blind study on the same subject between a placebo cigarette and a marihuana cigarette and one between a placebo pill and a marinol pill? How does one perform a crossover study from marihuana smoking to marinol ingestion? How does a physician evaluate the relief and well being reported by subjects after marihuana smoking against the toxic effects on lung and aveolar macrophage, which cannot be felt by the subject? Should a physician conform to the law?

13. CONCLUSION

The curative properties attributed to *Cannabis* oral preparations during the 19th century proved to be disappointing. Despite initial claims for its effectiveness as an analgesic, or for the treatment of tetanus, epilepsy, rheumatism, and many other ailments, *Cannabis* did not establish itself as a dependable remedy, unlike other dependence-producing drugs like opium or cocaine or over-the-counter drugs like aspirin.

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Nicholas A. Pace, MD, FASAM
Clinical Associate Professor of Medicine
New York University School of Medicine

GENERAL MOTORS BUILDING
767 5TH AVENUE, 3RD FLOOR
NEW YORK, NY 10153
212-418-6450

The Medical Consequences of Marijuana Use 10/19/11

Nicholas Pace,MD,FASAM,ABAM,

Abstract

A review of the recent medical literature regarding medical complications occurring in heavy marijuana smoking patients show the following:

- Regional Brain damage with reduced brain volume in both the hippocampus(mediates memory & emotion) and the amygdala (mediates fear and aggression)
- Neuropsychiatric disorders with transient signs of psychotic disorders hallucinations and paranoid delusions or more sustained psychotic symptoms as seen in schizophrenia.
- Implicated in the etiology of many major long- term psychiatric conditions including depression, anxiety, psychosis, bipolar disorder, a- motivational syndrome & a significant association with suicidal ideation .
- Pulmonary Impairment of large airway function with pulmonary obstruction and hyperinflation and linked with respiratory conditions such as reduced lung density, lung cysts, chronic bronchitis
- Testicular Cancer in young men who began using marijuana as adolescents once a week & is linked to cancers in eight sites, including children after in uterus exposure
- Multiple Sclerosis patients had worsening of their MS symptoms with increased cognitive defects and mood disorders.
- Marijuana has an adverse effect on both male and female reproductive organs including none ovulatory cycles, abnormal sperm, and aggressive testicular cancers in adolescents.
- A dose dependent link with elevated rates of myocardial infarction, arrhythmia & strokes

A REVIEW OF SOME RECENT SCIENTIFIC STUDIES IN HEAVY MARIJUANA SMOKING PATIENTS

Prior to passing new smoking medical marijuana laws ,Legislators should be made aware of what some of the recent scientific studies show regarding what some of medical complications occurring in heavy marijuana smoking patients. Prolonged heavy smoking of marijuana can not only cause pulmonary impairment of large airway function with obstruction but also cause regional brain damage in both the hippocampus (mediating memory and emotion) and the amygdala (mediating fear and aggression),Neuophyychiatric disorders with either transient signs of psychotic disorders with hallucinations and paranoid delusions or more sustained psychotic symptoms. There is a high incidence of an aggressive fast-growing testicular cancer in young men who as adolescents began using at least once a week. Multiple Sclerosis patients had worsening of their MS symptoms with increased cognitive defects and mood disorders.

- Regional Brain damage with reduced brain volume in both the hippocampus (mediating memory and emotion) and the amygdala (mediating fear and aggression). Lubman DArch Gen Psychiatry. 2008 Jun; 65(6):694-701
- Neuropsychiatric disorders are more likely to exhibit transient signs of psychotic disorders with hallucinations and paranoid delusions, and may also suffer more sustained psychotic symptoms. Mcguire p Arch Gen Psychiatry. 2009 Apr; 442-51.
- Pulmonary Impairment of large airway function with obstruction and hyperinflation. Aldington S, et al Thorax. 2007 Dec; 62(12):1058-63
- Testicular Cancer Can Increased risk of developing an aggressive, fast-growing testicular cancer in young men who began using marijuana as adolescents at least once a week ((2/9/09 journal "Cancer" Hutchinson Cancer Research center Seattle WA)
- Multiple Sclerosis patients had worsening of their MS symptoms with increased cognitive defects and mood disorders, (ghaffar & Feinstein Neurology.2008Jul.15:164-9.
- There was **175% jump in marijuana's potency** (3.2 to 8.8%) and a **492% increase** in the proportion of **teen treatment admissions** with a medical diagnosis of marijuana abuse or dependence compared with a 54 % decline for all other substances of abuse from 1995 to 2002; (CASA 6/18/08)
- There was a **136% increase in the proportion of emergency department findings of marijuana as a major substance of abuse among teens** with a more than five time increase in such findings for all other substances of abuse.(CASA 6/18/09)

ABSTRACTS ATTACHED

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#22 Select 1 document(s) 1
#21 Search (#19) AND (#20) 4
#19 PubMed for Journals Archives of General Psychiatry (Select 744) 7714

1: Arch Gen Psychiatry. 2008 Jun;65(6):694-701.

Regional brain abnormalities associated with long-term heavy cannabis use.

YÃ¼cel M, Solowij N, Respondek C, Whittle S, Fornito A, Pantelis C, Lubman DI.

MAPS, ORYGEN Research Centre, 35 Poplar Rd, Melbourne, Victoria, Australia. murat@unimelb.edu.au

CONTEXT: Cannabis is the most widely used illicit drug in the developed world. Despite this, there is a paucity of research examining its long-term effect on the human brain. OBJECTIVE: To determine whether long-term heavy cannabis use is associated with gross anatomical abnormalities in 2 cannabinoid receptor-rich regions of the brain, the hippocampus and the amygdala. DESIGN: Cross-sectional design using high-resolution (3-T) structural magnetic resonance imaging. SETTING: Participants were recruited from the general community and underwent imaging at a hospital research facility. PARTICIPANTS: Fifteen carefully selected long-term (>10 years) and heavy (>5 joints daily) cannabis-using men (mean age, 39.8 years; mean duration of regular use, 19.7 years) with no history of polydrug abuse or neurologic/mental disorder and 16 matched nonusing control subjects (mean age, 36.4 years). MAIN OUTCOME MEASURES: Volumetric measures of the hippocampus and the amygdala combined with measures of cannabis use. Subthreshold psychotic symptoms and verbal learning ability were also measured. RESULTS: Cannabis users had bilaterally reduced hippocampal and amygdala volumes (P = .001), with a relatively (and significantly [P = .02]) greater magnitude of reduction in the former (12.0% vs 7.1%). Left hemisphere hippocampal volume was inversely associated with cumulative exposure to cannabis during the previous 10 years (P = .01) and subthreshold positive psychotic symptoms (P < .001). Positive symptom scores were also associated with cumulative exposure to cannabis (P = .048). Although cannabis users performed significantly worse than controls on verbal learning (P < .001), this did not correlate with regional brain volumes in either group. CONCLUSIONS: These results provide new evidence of exposure-related structural abnormalities in the hippocampus and amygdala in long-term heavy cannabis users and corroborate similar findings in the animal literature. These findings indicate that heavy daily cannabis use across protracted periods exerts harmful effects on brain tissue and mental health.

Publication Types:
Research Support, Non-U.S. Gov't

PMID: 18519827 [PubMed - indexed for MEDLINE]

London SE5 8AF, UK. m.broome@iop.kcl.ac.uk

It has become increasingly clear that the simple neurodevelopmental model fails to explain many aspects of schizophrenia including the timing of the onset, and the nature of the abnormal perceptions. Furthermore, we do not know why some members of the general population have anomalous experiences but remain well, while others enter the prodrome of psychosis, and a minority progress to frank schizophrenia. We suggest that genes or developmental damage result in individuals vulnerable to dopamine deregulation. In contemporary society, this is often compounded by abuse of drugs such as amphetamines and cannabis, which then propel the individual into a state of dopamine-induced misinterpretation of the environment. Certain types of social adversity such as migration and social isolation, as well as affective change can also contribute to this. Thereafter, biased cognitive appraisal processes result in delusional interpretation of the abnormal perceptual experiences. Thus, a plausible model of the onset of psychosis needs to draw not only on neuroscience, but also on the insights of social psychiatry and cognitive psychology.

Publication Types:
Review

PMID: 16198238 [PubMed - indexed for MEDLINE]

4: Rev Bras Psiquiatr. 2005 Mar;27(1):3-4. Epub 2005 Apr 18.

Comment on:
Rev Bras Psiquiatr. 2005 Mar;27(1):70-8.

Effect of cannabis use in human brain activity.

MartÃ-n-Santos R, Atakan Z, McGuire P.

Publication Types:
Comment
Editorial

PMID: 15867974 [PubMed - indexed for MEDLINE]

5: Schizophr Res. 1995 May;15(3):277-81.

Morbid risk of schizophrenia for relatives of patients with cannabis-associated psychosis.

McGuire PK, Jones P, Harvey I, Williams M, McGuffin P, Murray RM.

Department of Psychological Medicine, Institute of Psychiatry, De Crespigny Park, London, UK.

Twenty-three patients admitted with acute psychosis who were cannabis positive on urinary screening were each matched, with respect to sex, with two psychotic controls who screened negatively for all substances. The lifetime morbid risk of psychiatric disorder was estimated among the first degree relatives of cases and controls, using RDC-FH criteria to define diagnoses, and Weinberg's shorter method of age correction. The cases had a significantly greater familial morbid risk of schizophrenia (7.1%) than the controls (0.7%), while the risks of other

psychoses, and of non-psychotic conditions were similar. The same pattern of familial risk was evident when the analysis was restricted to patients with DSM-III schizophrenia. The data suggest that the development or recurrence of acute psychosis in the context of cannabis use may be associated with a genetic predisposition to schizophrenia.

PMID: 7632625 [PubMed - indexed for MEDLINE]

6: Schizophr Res. 1994 Sep;13(2):161-7.

Cannabis and acute psychosis.

McGuire PK, Jones P, Harvey I, Bebbington P, Toone B, Lewis S, Murray RM.

Department of Psychological Medicine and Genetics, Institute of Psychiatry and King's College Hospital, London, UK.

The Present State Examination was used to assess the psychopathology of 23 psychotic patients who were cannabis positive on urinary screening, and 46 matched drug-free controls. Cases and controls were indistinguishable in terms of psychopathology, DSMIII diagnoses, onset of recent illness, the proportion of first admissions, ethnicity, and socio-economic class, differing only in their histories of substance use. These data suggest that psychosis which develops or recurs in the context of cannabis use does not have a characteristic psychopathology or mode of onset, and is not restricted to a particular ethnic or socio-demographic group. There is thus little evidence to support the validity of 'cannabis psychosis' as a diagnostic entity.

PMID: 7986773 [PubMed - indexed for MEDLINE]

7: Br J Psychiatry. 1993 Nov;163:698.

Comment on:
Br J Psychiatry. 1993 Aug;163:141-9.

Psychiatric symptoms in cannabis users.

McGuire P, Jones P, Murray R.

Publication Types:
Comment
Letter

PMID: 8298853 [PubMed - indexed for MEDLINE]

2: Arch Gen Psychiatry. 2009 Jan;66(1):95-105.

Distinct effects of {delta}9-tetrahydrocannabinol and cannabidiol on neural activation during emotional processing.

Fusar-Poli P, Crippa JA, Bhattacharyya S, Borgwardt SJ, Allen P, Martin-Santos R, Seal M, Surguladze SA, O'Carrol C, Atakan Z, Zuardi AW, McGuire PK.

Neuroimaging Section, Division of Psychological Medicine, PO67, Institute of Psychiatry, London SE58AF, England. p.fusar@libero.it

CONTEXT: Cannabis use can both increase and reduce anxiety in humans. The neurophysiological substrates of these effects are unknown. OBJECTIVE: To investigate the effects of 2 main psychoactive constituents of Cannabis sativa (Delta9-tetrahydrocannabinol [Delta9-THC] and cannabidiol [CBD]) on regional brain function during emotional processing. DESIGN: Subjects were studied on 3 separate occasions using an event-related functional magnetic resonance imaging paradigm while viewing faces that implicitly elicited different levels of anxiety. Each scanning session was preceded by the ingestion of either 10 mg of Delta9-THC, 600 mg of CBD, or a placebo in a double-blind, randomized, placebo-controlled design. PARTICIPANTS: Fifteen healthy, English-native, right-handed men who had used cannabis 15 times or less in their life. MAIN OUTCOME MEASURES: Regional brain activation (blood oxygenation level-dependent response), electrodermal activity (skin conductance response [SCR]), and objective and subjective ratings of anxiety. RESULTS: Delta9-Tetrahydrocannabinol increased anxiety, as well as levels of intoxication, sedation, and psychotic symptoms, whereas there was a trend for a reduction in anxiety following administration of CBD. The number of SCR fluctuations during the processing of intensely fearful faces increased following administration of Delta9-THC but decreased following administration of CBD. Cannabidiol attenuated the blood oxygenation level-dependent signal in the amygdala and the anterior and posterior cingulate cortex while subjects were processing intensely fearful faces, and its suppression of the amygdalar and anterior cingulate responses was correlated with the concurrent reduction in SCR fluctuations. Delta9-Tetrahydrocannabinol mainly modulated activation in frontal and parietal areas. CONCLUSIONS: Delta9-Tetrahydrocannabinol and CBD had clearly distinct effects on the neural, electrodermal, and symptomatic response to fearful faces. The effects of CBD on activation in limbic and paralimbic regions may contribute to its ability to reduce autonomic arousal and subjective anxiety, whereas the anxiogenic effects of Delta9-THC may be related to effects in other brain regions.

Publication Types:
Randomized Controlled Trial
Research Support, Non-U.S. Gov't

PMID: 19124693 [PubMed - indexed for MEDLINE]

3: Schizophr Res. 2005 Nov 1;79(1):23-34.

What causes the onset of psychosis?

Broome MR, Woolley JB, Tabraham P, Johns LC, Bramon E, Murray GK, Pariante C, McGuire PK, Murray RM.

Division of Psychological Medicine, Institute of Psychiatry, De Crespigny Park,

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mcguire p[au] AND marijuana 7

1: Arch Gen Psychiatry. 2009 Apr;66(4):442-51.

Modulation of mediotemporal and ventrostriatal function in humans by Delta9-tetrahydrocannabinol: a neural basis for the effects of Cannabis sativa on learning and psychosis.

Bhattacharyya S, Fusar-Poli P, Borgwardt S, Martin-Santos R, Nosarti C, O'Carroll C, Allen P, Seal ML, Fletcher PC, Crippa JA, Giampietro V, Mechelli A, Atakan Z, McGuire P.

Section of Neuroimaging, Division of Psychological Medicine and Psychiatry, Institute of Psychiatry, King's College London, Box P067, De Crespigny Park, London SE5 8AF, England. s.bhattacharyya@iop.kcl.ac.uk

CONTEXT: Cannabis sativa use can impair verbal learning, provoke acute psychosis, and increase the risk of schizophrenia. It is unclear where C. sativa acts in the human brain to modulate verbal learning and to induce psychotic symptoms. OBJECTIVES: To investigate the effects of 2 main psychoactive constituents of C. sativa, Delta9-tetrahydrocannabinol (Delta9-THC) and cannabidiol, on regional brain function during verbal paired associate learning. DESIGN: Subjects were studied on 3 separate occasions using a block design functional magnetic resonance imaging paradigm while performing a verbal paired associate learning task. Each imaging session was preceded by the ingestion of Delta9-THC (10 mg), cannabidiol (600 mg), or placebo in a double-blind, randomized, placebo-controlled, repeated-measures, within-subject design. SETTING: University research center. PARTICIPANTS: Fifteen healthy, native English-speaking, right-handed men of white race/ethnicity who had used C. sativa 15 times or less and had minimal exposure to other illicit drugs in their lifetime. MAIN OUTCOME MEASURES: Regional brain activation (blood oxygen level-dependent response), performance in a verbal learning task, and objective and subjective ratings of psychotic symptoms, anxiety, intoxication, and sedation. RESULTS: Delta9-Tetrahydrocannabinol increased psychotic symptoms and levels of anxiety, intoxication, and sedation, whereas no significant effect was noted on these parameters following administration of cannabidiol. Performance in the verbal learning task was not significantly modulated by either drug. Administration of Delta9-THC augmented activation in the parahippocampal gyrus during blocks 2 and 3 such that the normal linear decrement in activation across repeated encoding blocks was no longer evident. Delta9-Tetrahydrocannabinol also attenuated the normal time-dependent change in ventrostriatal activation during retrieval of word pairs, which was directly correlated with concurrently induced psychotic symptoms. In contrast, administration of cannabidiol had no such effect. CONCLUSION: The modulation of mediotemporal and ventrostriatal function by Delta9-THC may underlie the effects of C. sativa on verbal learning and psychotic symptoms, respectively.

Publication Types:
Comparative Study
Randomized Controlled Trial
Research Support, Non-U.S. Gov't

PMID: 19349314 [PubMed - indexed for MEDLINE]

#13 Select 1 document(s) 1
#12 Search (#9) AND (#11) 34
#9 PubMed for Journals Thorax (Select 7730) 10402
#11 Search beasley r[au] 404

1: Thorax. 2007 Dec;62(12):1058-63. Epub 2007 Jul 31.

Erratum in:
Thorax. 2008 Apr;63(4):385.

Comment in:
Thorax. 2007 Dec;62(12):1036-7.

Effects of cannabis on pulmonary structure, function and symptoms.

Aldington S, Williams M, Nowitz M, Weatherall M, Pritchard A, McNaughton A, Robinson G, Beasley R.

Medical Research Institute of New Zealand, P O Box 10055, Wellington 6143, New Zealand.

BACKGROUND: Cannabis is the most widely used illegal drug worldwide. Long-term use of cannabis is known to cause chronic bronchitis and airflow obstruction, but the prevalence of macroscopic emphysema, the dose-response relationship and the dose equivalence of cannabis with tobacco has not been determined. METHODS: A convenience sample of adults from the Greater Wellington region was recruited into four smoking groups: cannabis only, tobacco only, combined cannabis and tobacco and non-smokers of either substance. Their respiratory status was assessed using high-resolution CT (HRCT) scanning, pulmonary function tests and a respiratory and smoking questionnaire. Associations between respiratory status and cannabis use were examined by analysis of covariance and logistic regression. RESULTS: 339 subjects were recruited into the four groups. A dose-response relationship was found between cannabis smoking and reduced forced expiratory volume in 1 s to forced vital capacity ratio and specific airways conductance, and increased total lung capacity. For measures of airflow obstruction, one cannabis joint had a similar effect to 2.5-5 tobacco cigarettes. Cannabis smoking was associated with decreased lung density on HRCT scans. Macroscopic emphysema was detected in 1/75 (1.3%), 15/92 (16.3%), 17/91 (18.9%) and 0/81 subjects in the cannabis only, combined cannabis and tobacco, tobacco alone and non-smoking groups, respectively. CONCLUSIONS: Smoking cannabis was associated with a dose-related impairment of large airways function resulting in airflow obstruction and hyperinflation. In contrast, cannabis smoking was seldom associated with macroscopic emphysema. The 1:2.5-5 dose equivalence between cannabis joints and tobacco cigarettes for adverse effects on lung function is of major public health significance.

Publication Types:
Research Support, Non-U.S. Gov't

PMID: 17666437 [PubMed - indexed for MEDLINE]

1: Cancer. 2009 Mar 15;115(6):1215-23.

Association of marijuana use and the incidence of testicular germ cell tumors.

Daling JR, Doody DR, Sun X, Trabert BL, Weiss NS, Chen C, Biggs ML, Starr JR, Dey
SK, Schwartz SM.

Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, Washington 98109, USA. jdaling@fhcrc.org

BACKGROUND: The incidence of testicular germ cell tumors (TGCTs) has been increasing the past 4 to 6 decades; however, exposures that account for this rise
have not been identified. Marijuana use also grew during the same period, and it
has been established that chronic marijuana use produces adverse effects on the
human endocrine and reproductive systems. In this study, the authors tested the
hypothesis that marijuana use is a risk factor for TGCT. METHODS: A
population-based, case-control study of 369 men ages 18 to 44 years who were diagnosed with TGCT from January 1999 through January 2006 was conducted in King,
Pierce and Snohomish Counties in Washington State. The responses of these men to
questions on their lifetime marijuana use were compared with the responses of 979
age-matched controls who resided in the same 3 counties during the case diagnosis
period. RESULTS: Men with a TGCT were more likely to be current marijuana smokers
at the reference date compared with controls (odds ratio [OR], 1.7; 95% confidence interval [95% CI], 1.1-2.5). In analyses according to histologic type,
most of the association between current marijuana use and TGCT was observed in men who had nonseminomas/mixed histology tumors (current use: OR, 2.3; 95% CI, 1.3-4.0). Age at first use among current users (age<18 years [OR, 2.8] vs age>or=18 years [OR, 1.3]) and frequency of use (daily or weekly [OR, 3.0] vs less than once per week [OR, 1.8]) appeared to modify the risk. CONCLUSIONS: An
association was observed between marijuana use and the occurrence of nonseminoma
TGCTs. Additional studies of TGCTs will be needed to test this hypothesis, including molecular analyses of cannabinoid receptors and endocannabinoid signaling, which may provide clues regarding the biologic mechanisms of TGCTs.

Publication Types:
    Research Support, N.I.H., Extramural
    Research Support, Non-U.S. Gov't

PMID: 19204904 [PubMed - indexed for MEDLIN

#6 Search (#4) AND (#5) 12:13:10 2
#4 PubMed for Journals (Select 6069) 27761
#5 Search ghaffar[au] AND feinstein[au] 6

1: Neurology. 2008 Jul 15;71(3):164-9. Epub 2008 Feb 13.

Comment in:
Neurology. 2008 Jul 15;71(3):160-1. Neurology. 2009 Jan 6;72(1):100-1; author reply 101.

Multiple sclerosis and cannabis: a cognitive and psychiatric study.

Ghaffar O, Feinstein A.

Department of Psychiatry, Sunnybrook Health Sciences Centre, FG08-2075 Bayview Avenue, Toronto, ON, Canada.

BACKGROUND: A significant minority of patients with multiple sclerosis (MS) use cannabis, yet no study has examined the possible effects on mentation. Here, we report the emotional and cognitive correlates of street cannabis use in patients with MS. METHODS: A sample of 140 consecutive patients with MS were interviewed with the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) Axis I disorders (SCID-IV) from which details of cannabis use were recorded. Cognition was assessed using the Neuropsychological Battery for MS supplemented with the Symbol Digit Modalities Test (SDMT), an index of information processing speed, working memory, and sustained attention. RESULTS: Ten subjects (7.7%) were defined as current cannabis users based on use within the last month. Compared to non-cannabis users (n = 130), they were younger ($p = 0.001$). Each of the 10 current cannabis users was matched on demographic and disease variables to four subjects with MS who did not use cannabis (total control sample n = 40). Group comparisons revealed that the proportion of patients meeting DSM-IV criteria for a psychiatric diagnosis was higher in cannabis users ($p = 0.04$). In addition, on the SDMT, cannabis users had a slower mean performance time ($p = 0.006$) and a different pattern of response compared to matched controls (group x time interaction; $p = 0.001$). CONCLUSIONS: Inhaled cannabis is associated with impaired mentation in patients with multiple sclerosis, particularly with respect to cognition. Future studies are required to clarify the direction of this relationship.

PMID: 18272863 [PubMed - indexed for MEDLINE]

Related Links

Cognitive functioning and depression in patients with chronic fatigue syndrome and multiple sclerosis. [Arch Neurol. 1994] PMID:8018045

[Validation of the Short Cognitive Battery (B2C). Value in screening for Alzheimer's disease and depressive disorders in psychiatric practice] [Encephale. 2003] PMID:12876552

[Interest of a new instrument to assess cognition in schizophrenia: The Brief Assessment of Cognition in Schizophrenia (BACS)] [Encephale. 2008] PMID:19081451

Repeated assessment of neuropsychological deficits in multiple sclerosis using the Symbol Digit Modalities Test and the MS Neuropsychological Screening Questionnaire. [Mult Scler. 2008] PMID:18573822

[Effect of comorbid substance use on neuropsychological performance in subjects with psychotic or mood disorders] [Encephale. 2002] PMID:11972143

From the University of Colorado Health Sciences Center

Medical Marijuana Use and Suicide Attempt in a Patient With Major Depressive Disorder

Abraham Nussbaum, M.D.

Christian Thurstone, M.D.

Ingrid Binswanger, M.D., M.P.H.

Case Presentation

"Ms. H," a 29-year-old woman, presented to the emergency department with epigastric distress 2 hours after intentionally ingesting ethylene glycol in an admitted suicide attempt. After being stabilized, she was admitted to the inpatient psychiatric service.

Ms. H reported 3 weeks of depressed mood, anhedonia, decreased appetite with subjective weight loss of 7 lb, insomnia, decreased energy, and thoughts of suicide. She denied manic and psychotic symptoms. She denied any family history of suicide but reported that her mother had experienced episodes of depression. On the night before her presentation, she reported drinking eight beers, ingesting the various pills in her cousin's medicine cabinet, and falling asleep with the hope of death. When she awoke the next morning, she returned to her apartment, smoked marijuana, and attempted suicide with ethylene glycol.

She denied ever using cocaine, hallucinogens, heroin, or methamphetamine. Her urine drug screen on admission was positive for amphetamines; she attributed this to the medications in her cousin's medicine cabinet. She reported three to four binge drinking episodes annually but denied symptoms of alcohol abuse or dependence.

Ms. H denied episodes of depression before her first use of marijuana at age 18. By age 23, she was smoking two to three joints daily. She made her first suicide attempt at age 23 by acetaminophen overdose; she was admitted to a community hospital, where she was diagnosed with major depressive disorder, but she never received treatment after discharge. Ms. H said that marijuana relaxed her and made her "less worried" but interfered with her work as a massage therapist. Ms. H discontinued weekday use at age 24 but continued to smoke marijuana on weekends until early 2010, when she obtained her medical marijuana license. She reported that from February 2010 until her suicide attempts 7 months later, she smoked at least a joint of marijuana daily, and she doubled her use in the month preceding her suicide attempt.

Ms. H acknowledged the temporal association between her suicide attempts and episodes of increased marijuana use, but she was precontemplative about abstinence. She was referred to an outpatient substance abuse program, but declined to attend, saying, "Marijuana is prescribed by a doctor, so I don't think it's a problem." She was discharged to her father's home with a prescription for 20 mg/day of citalopram and an appointment with a primary care provider.

Diagnosis

Ms. H drank to excess during the evening before ingesting ethylene glycol. However, she did not experience alcohol withdrawal and denied legal or interpersonal problems related to alcohol. While she was advised to address her binge drinking, there was no evidence that alcohol directly caused her depression.

Ms. H acknowledged that her primary substance use was with marijuana, first for a decade as a recreational drug and then for the 7 months preceding her suicide attempts as a registered medical marijuana user. She acknowledged that it now took escalating amounts of marijuana for her to feel relief, that she often used more than she intended to, and that marijuana use interfered with her occupational and social life. Her self-admitted periods of heaviest marijuana use were temporally associated with depressive episodes and suicide attempts, and she identified an additional episode of depression while smoking marijuana only on weekends.

While the possibility that she was experiencing a substance-induced mood disorder with depressive features could not be definitively excluded, Ms. H was diagnosed with major depressive disorder, recurrent, severe without psychotic features, and cannabis dependence.

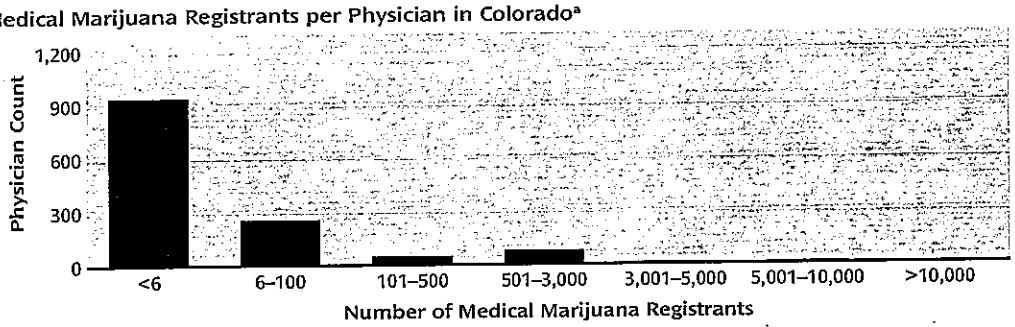
Marijuana and Mental Illness

The associations between marijuana use and mental illness are numerous. In the United States, marijuana is the most frequently abused illicit substance, with over 16.7 million Americans reporting past-month use (1), and it is identified as the primary substance of abuse in 17.1% of substance treatment admissions (2). A growing body of evidence associates marijuana use with an earlier onset and more adverse course of psychotic disorders (3).

What is less well known is that longitudinal studies associate marijuana use with depression. While infrequent marijuana use does not appear to be associated with depressive disorders (4), the medicalization of marijuana encourages regular use, and regular use has a modest but

This article is featured in this month's AJP Audio

FIGURE 1. Medical Marijuana Registrants per Physician in Colorado[a]



[a] Data from the Colorado Department of Public Health and the Environment, provided to the authors in December 2010. The Ns for the seven categories in the bar graph are, from left to right, 911, 242, 39, 49, 2, 2, and 1.

significant association with depression that endures even after controlling for possible confounders. A recent prospective cohort study of 7,735 adults with no history of anxiety or mood disorders (5) found that adults who used marijuana at the beginning of the 3-year study period were at an increased risk of having a first depressive episode (odds ratio=1.62, 95% CI=1.06–2.48) in comparison to nonusers, and this association was stronger with more frequent use. Animal models have found that both activation and blockade of the endocannabinoid system can lead to depression (6).

Ms. H says she smoked marijuana before ingesting ethylene glycol in part to "steady" herself for her suicide attempt. This statement is intriguing, because while acute intoxication can induce euphoria, several studies have found a robust association between frequent marijuana use and suicidality, often in the absence of depression (7–9). A longitudinal study (10) that followed a cohort of 2,033 Norwegians over 13 years from late adolescence into their late twenties found a significant association between using marijuana one to 10 times by age 21 and suicidal ideation by age 27 (odds ratio=2.4, 95% CI=1.3–4.3) after controlling for confounding factors such as conduct disorder, parental divorce and unemployment, school performance, and alcohol and nicotine use. Among those who had used marijuana 11 or more times by age 21, the researchers identified a significant association between both suicidal ideation (odds ratio=2.7, 95% CI=2.8–6.4) and suicide attempt (odds ratio=2.9, 95% CI=1.3–6.1) by age 27. Growing evidence associates hyperactivity of the endocannabinoid system with impulsivity and suicidality; for example, postmortem studies have found up-regulated cannabinoid receptors in the prefrontal cortex of individuals who died by suicide (6). For someone like Ms. H, using marijuana may both relieve acute distress and increase the long-term risk of suicide and depression through chronic activation of the endocannabinoid system.

Medical Marijuana in Colorado

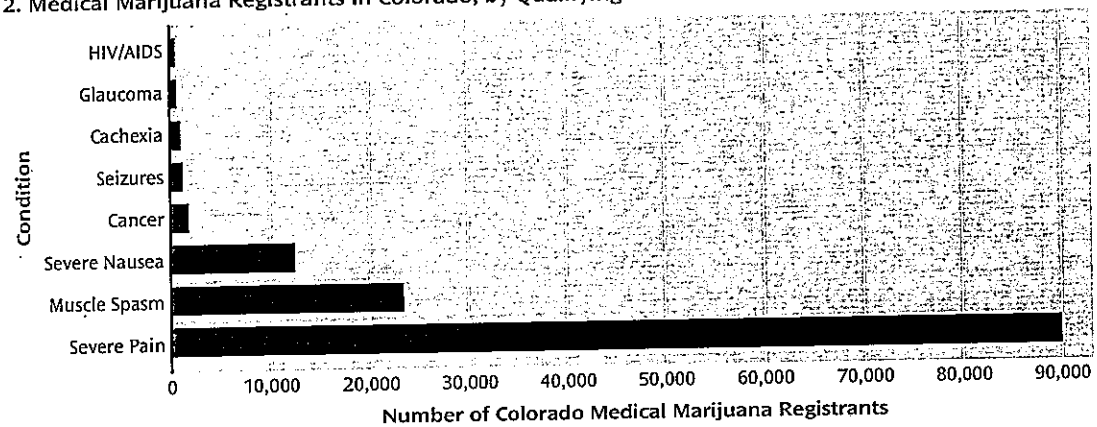
While medical marijuana has been legal in California since 1996, its widespread use began in March 2009, when the federal government announced that it would not prosecute medical marijuana users and distributors in states where the medical use of marijuana is legal (11). At the time of this writing, the District of Columbia and 14 states, including Colorado, have legalized medical marijuana (12).

In November 2000, the Colorado electorate passed Amendment 20 with 54% of the vote (12). Amendment 20 legalized the possession of marijuana by a person diagnosed with a "serious or chronic illness" whose doctor will attest that he or she "might benefit from medical use of marijuana" (www.cdphe.state.co.us/hs/medicalmarijuana/amendment.html). The qualifying conditions are cancer, cachexia, HIV/AIDS, glaucoma, epilepsy, muscle spasms, severe nausea, and severe pain. As of September 2010, the state had 809 dispensaries—licensed stores that sell marijuana to registered users—which constituted more than a third of the nation's 2,192 dispensaries (12).

The Colorado Department of Public Health and the Environment (CDPHE) compiles data on the age, gender, and qualifying condition of individuals registered for medical marijuana use; the number of physicians recommending marijuana; and the conditions for which physicians recommend marijuana. In the applications processed by the CDPHE, the average age of registrants is 40 years, and 71% of registrants are male. From 2000 through 2008, 8,957 people in Colorado registered to use medical marijuana. By June 2010, this figure had increased to an estimated 99,559 (Colorado Department of Public Health and Environment, private communication, December 2010). Approximately 2% of the state's population is now registered to use medical marijuana, and on a per capita basis, Colorado has twice as many medical marijuana users as California (12). Medical marijuana registration is highest in Colorado's ski counties, where median income and education levels are highest (13).

CDPHE data indicate that as of December 2010, 1,246 doctors have signed the medical marijuana registry forms the department has processed, which is approximately 9% of Colorado's licensed physicians. However, the practice has largely been limited to a small coterie of physicians, as illustrated in Figure 1.

FIGURE 2. Medical Marijuana Registrants in Colorado, by Qualifying Condition[a]



[a] Data from the Colorado Department of Public Health and the Environment, provided to the authors in December 2010.

In the applications processed by the CDPHE, 94% of Colorado medical marijuana registrants are qualified for severe pain. Figure 2 enumerates the medical conditions for which users are qualified to take medical marijuana; note that users can be qualified for more than one condition.

Like the majority of medical marijuana users in Colorado, Ms. H was licensed to use marijuana for severe pain. In fact, studies of cannabinoid-mediated analgesia suggest benefit for neuropathic pain in multiple sclerosis. Investigators are interested in designing peripheral cannabinoid agonists to treat pain syndromes, but the available literature is limited by small sample sizes, heterogeneous populations, subjective outcome measures, difficulty maintaining the study blind, and variable concentrations of cannabinoids in smoked marijuana (14). Ms. H identified her own pain as daily headaches that developed after her husband struck her in the head during a domestic dispute that occurred 6 months before she registered to use medical marijuana. She was not asked about the cause of her headaches when she registered.

Treatment of Cannabis Dependence

The treatment of cannabis dependence and withdrawal remains nonspecific. When withdrawing from marijuana, users can experience a variety of symptoms, including anger, anorexia, craving, dysphoric mood, insomnia, irritability, and restlessness. Symptoms begin within a day of discontinuing marijuana, peak approximately 5 days after discontinuation, and extend for 1 to 3 weeks (15). While many psychotropic agents have been studied for the treatment of cannabis dependence, greater efficacy has been demonstrated with behavioral psychotherapies, especially motivational interviewing, cognitive-behavioral therapy, and contingency management. Marijuana-specific manuals exist for these interventions. The best practice remains behavioral psychotherapy alongside treatment of co-occurring mental health and substance use conditions (16).

Ms. H received citalopram to target depressive symptoms and as-needed doses of hydroxyzine and trazodone to ameliorate insomnia, irritability, and restlessness. The treating psychiatrist employed motivational interviewing techniques with Ms. H, expressed empathy for her many psychosocial stresses, and attempted to develop a discrepancy between her desire to continue using cannabis and its association with her two suicide attempts.

Discussion

As Ms. H's case illustrates, the rapid expansion of medical marijuana use raises concerns about the psychiatric complications of marijuana use, the relationship between patients and physicians, and the need for additional services and research.

The use of medical marijuana in the context of mental illness or substance abuse can be dangerous. While we cannot directly attribute Ms. H's two suicide attempts to marijuana use, the association between her increased use of marijuana and her suicide attempts is concerning, especially given the growing concern that frequent marijuana use is associated with suicide. This is especially concerning in Colorado, where the CDPHE recorded 940 suicides in 2009, a suicide rate of 18.4 deaths per 100,000 residents, the highest rate in Colorado since 1988 and nearly twice the national average (17). Medical marijuana systems should attempt to identify not only the people who might benefit from medical marijuana but also those who might suffer from its use.

Amendment 20 does not require a laboratory, mental, physical, or other examination, only a physician's signature indicating that the user has a debilitating medical condition that "may be alleviated by the medical use of marijuana." Ms. H saw the referring doctor only a single time and reports that she did not receive a physical examination. Until recently, physicians recommending marijuana were not required to seek or review the person's medi-

cal, substance use, or psychiatric records; to be available if complications arose; or to coordinate care with other physicians treating the patient. Permission to possess and use marijuana is excluded from the state's Prescription Drug Monitoring Program, which reports all other prescriptions for controlled substances.

Finally, Ms. H's case shows our need for rigorous investigations into the effects of marijuana on medical and psychiatric conditions, especially its association with impulsivity and suicidality. The medical marijuana industry, a system that encourages chronic and frequent use of marijuana, has expanded dramatically, and the ways in which this development will alter patterns of marijuana use and abuse remain unclear.

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REVIEW

Chronic toxicology of cannabis

ALBERT STUART REECE

Medical School, University of Queensland, Highgate Hill, Brisbane, QLD, Australia

Introduction. Cannabis is the most widely used illicit drug worldwide. As societies reconsider the legal status of cannabis, policy makers and clinicians require sound knowledge of the acute and chronic effects of cannabis. This review focuses on the latter. *Methods.* A systematic review of Medline, PubMed, PsychInfo, and Google Scholar using the search terms "cannabis," "marijuana," "marihuana," "toxicity," "complications," and "mechanisms" identified 5,198 papers. This list was screened by hand, and papers describing mechanisms and those published in more recent years were chosen preferentially for inclusion in this review. *Findings.* There is evidence of psychiatric, respiratory, cardiovascular, and bone toxicity associated with chronic cannabis use. Cannabis has now been implicated in the etiology of many major long-term psychiatric conditions including depression, anxiety, psychosis, bipolar disorder, and an amotivational state. Respiratory conditions linked with cannabis include reduced lung density, lung cysts, and chronic bronchitis. Cannabis has been linked in a dose-dependent manner with elevated rates of myocardial infarction and cardiac arrythmias. It is known to affect bone metabolism and also has teratogenic effects on the developing brain following perinatal exposure. Cannabis has been linked to cancers at eight sites, including children after *in utero* maternal exposure, and multiple molecular pathways to oncogenesis exist. *Conclusion.* Chronic cannabis use is associated with psychiatric, respiratory, cardiovascular, and bone effects. It also has oncogenic, teratogenic, and mutagenic effects all of which depend upon dose and duration of use.

Keywords Cannabis; Psychopathology; Respiratory pathology; Psychosis; Depression; Chronic bronchitis; Chronic asthma; Genotoxicity; Oncogenesis; Toxicity; Toxicology

Introduction

According to the United Nations Office of Drugs and Crime, there are some 165 million users of cannabis worldwide, making it the most widely used illicit drug.[1] This review examines the psychiatric, respiratory, cardiovascular, and bone effects associated with chronic cannabis use and the neurodevelopmental, genotoxic, mutagenic, and oncogenic effects of cannabis.

Methodology

A systematic review of Medline, PubMed, PsychInfo, Google Scholar, Scopus, Proquest, Web of Knowledge, and Ebsco-Host using the search terms "cannabis," "marijuana," or "marihuana" identified 14,065 papers, excluding duplicates. When the search terms "toxicity," "complications," and "mechanisms" were added, the list narrowed to 5,198 papers. This list was screened by hand, and original papers describing mechanisms and those published in more recent years were chosen preferentially. Review papers are cited where appropriate to introduce a large or detailed field for the interested reader. Few case reports are included and they are specifically flagged where they occur; those that are cited have been included largely because they suggest important pathophysiological mechanisms.

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Address correspondence to Albert Stuart Reece, Medical School, University of Queensland, 39 Gladstone Road, Highgate Hill, Brisbane, QLD 4101, Australia. E-mail: sreece@bigpond.net.au; asreece@bigpond.net.au.

Psychiatric and social disorders

An authoritative meta-analysis of cannabis-related psychopathology has been published,[2] with an accompanying editorial.[3] Another review found an elevated risk of psychosis in many studies, with an odds ratio (OR) of about 2.3.[4] A similar meta-analysis from the Netherlands found a pooled OR for psychosis of 2.1.[5] Several studies from diverse cultures have confirmed the elevated risk of psychosis and schizophreniform spectrum disorders[5–17] following high levels of cannabis use, particularly when cannabis consumption has commenced at a young age.[14,18] Cannabis use has been found to exacerbate pre-existing psychotic disorders.[5,15]

There is a similar and increasing literature around both bipolar disorder[19–21] and depression.[22–25] Although the psychoneurological effects of cannabis are usually stereotypically characterized as a depressant, both its use and the

withdrawal state are accompanied frequently by psychomotor agitation, which has been implicated causally with interpersonal violence.[26] Interestingly, in a series of forensic examinations of suicide, cannabis use was associated with the most violent means of death, particularly severe motor vehicle accidents.[27]

In 1972 Nahas[28] drew attention to the devastating effects of cannabis in Egypt as quantified by carefully prepared and formally psychologically documented surveys from that country. Higher levels of anxiety, impaired memory, poor concentration, impaired learning ability, and psychomotor impairment including reduced quality and quantity of work were seen in these users. In addition, a common dependency syndrome was observed, which made exit from the dependent state both difficult and rare.[28] Geographical microclustering of cannabis use has been demonstrated, which has the effect of establishing local socially normative use patterns.[29] Both in northern Africa and in New Zealand communities exist where cannabis use is common, and intellectual impairment, psychomotor slowing, poor work capacity, and severe social deprivation are entrenched.[30–32]

Lee and colleagues[33,34] have published several descriptions of heavy, problematic, and refractory cannabis use in remote indigenous communities of the Northern Territory and across northern Australia more generally. A substantial proportion (31–62%) of users' median weekly income and up to 10% of the total community income were spent on cannabis. Ninety percent smoked cannabis heavily (more than six cones daily) and were not able to cease use. Severe mental illness was commonplace, as were depression, suicidal ideation, auditory hallucinations, and imprisonment. There was less participation in employment, education, or training. Community violence escalated when cannabis supplies from distant centers were interrupted. Most users had not "matured out" of dependent cannabis use even 5 years later. It is particularly noteworthy that these same communities had largely successfully defeated alcohol abuse, primarily by tight restrictive policies aimed at severely curtailing alcohol supply. The authors concluded that cannabis was both an important cause and a consequence of ongoing severe social disadvantage and deprivation.

Respiratory effects

Both the Thoracic Society of Australia and New Zealand[35] and the British Lung Foundation[4] have issued major statements in recent years acknowledging the known deleterious effects of cannabis on the lungs. Cannabis is smoked differently from tobacco. Users commonly inhale deeply to a maximal breath and then retain the smoke in the lungs, which generates higher pressures during breath holding and on expiration.[35–37]

Cannabis smoke stimulates inflammation in the airways so that its long-term use is associated with the development of chronic bronchitis. A New Zealand study[38] demonstrated large airway inflammation and obstruction and hyperinflation but was seldom associated with macroscopic emphysema, with a dose equivalence of one cannabis joint to 2.5–5 cigarettes. These findings were supported by an accompanying editorial[39] and press release.[40] Decreased lung density has also been noted with increased lung volumes, signs of destruction of lung tissue, cyst formation, and emphysematous change with secondary pneumothorax because of bullous rupture.[41–43]

Cannabis smoke is known to contain several potent carcinogens including anthrocyclines, nitrosamines, polycyclic aromatic hydrocarbons, terpenes, and vinyl chloride.[4,35,44–47] As a consequence, cannabis use is associated with cancer of the lung.[30–32]

Cardiovascular effects

Cannabis exposure is known to cause phasic systemic vasodilation, mild hypertension, and tachycardia often associated with postural hypotension, and a reduced duration and increased heart rate response to exercise.[48–51] Some but not all these effects are mediated by the autonomic nervous system. Tolerance to many of these acute effects with time appears. In most young healthy patients such changes are clearly generally well tolerated,[48,50] but this is not universally true and several exceptions cited below are of considerable pathophysiological interest. Such generic reassurances cannot be provided to patients with pre-existing coronary or atherosclerotic disease.[50,52]

Several case reports associate cannabis use with infarctions of kidney,[53] brain,[54–60] heart[61–65], and digits,[66,67] and of priapism in humans with sickle cell disease.[68] An association between cannabis use and pedal gangrene has also been described in a 27-year old.[67] Some 50 cases of cannabis arteritis have been reported in the literature.[67] Cannabis use can acutely trigger myocardial infarction,[69] which has also been documented in a 25-year-old man with no other cardiac risk factors and normal coronary arteries at angiography.[62] Coronary no-flow phenomenon has been observed after acute cannabis use.[57] Cardiomyopathy has also been reported in a young man.[70] One large study of 1,913 adults conducted in the United States found both a significant association between myocardial infarction and cannabis use, and a dose–response effect, with adjusted hazard ratios of 2.5 and 4.2 for less than weekly and weekly use, respectively.[52]

Reversible cerebral vasospasm[71] as well as slowing and flow reversal in the middle cerebral artery[72] has also been documented and attributed to cannabis use. On the contrary, the same authors also reported an increase of blood flow in the cerebral frontal lobes.[73] Several case reports have described a cannabis-associated inflammatory angiitis,[61,74,75] which can be so severe as to mimic Buerger's disease (thromboangiitis obliterans or "disappearing artery syndrome").

In a study in 19 patients, alterations of the cardiac pressure cycle were found with a highly significant prolongation of

both electromechanical systole (by 17 ms) and left ventricular ejection time, in the context of a reduced pre-ejection period (systolic pressure upstroke), a tachycardia of 132 bpm, and unchanged brachial systemic pressures.[76] These more abrupt cardiac pressure changes imply increased cardiac work in the context of a prolonged QTc interval and reduced opportunity for myocardial perfusion (the "Buckberg index"), which is limited to the diastolic phase of the cardiac cycle.[77,78] Hence, this scenario combines both an adverse mechanical and electrical profile in the context of reduced coronary perfusion and an altered endothelial, coagulation, angiogenic,[79] and inflammatory milieu.

Cannabis has also been linked with elevated rates of cardiac arrhythmias in several case reports.[80] Generally, these are supraventricular and trivial,[81–83] but well-documented cases of lethal ventricular arrythmias do exist[57] and one such was recently reported from a man who survived and whose episode was recorded on his implantable defibrillator.[84]

Elevated plasma concentrations of the endocannabinoid 2-arachidonylglycerol status have been associated in an Italian study of 62 patients with an exacerbation of the cardiovascular risk profile with worse concentrations of total cholesterol, high-density lipoprotein cholesterol, body mass index, intra-abdominal obesity, and adiponectin.[85]

Bones

Cannabinoid receptors are present on bones. Physiological studies have shown that cannabinoids have an important role in the regulation of bone density[86]; blockade or modulation of CB1 cannabinoid activity protects from bone loss.[87] Heavy cannabis use in humans is associated with substantial bone loss.[54] Interestingly, CB2 stimulation appears to be causally associated with stimulation of both endosteal and periosteal bone growth by mechanisms involving inhibition of osteoclastogenesis, osteoblast stimulation, and favorable modulation of the RANKL (receptor activated NF-kB ligand) – osteoprotegerin system, matrix metalloproteinase inhibition, inhibition of adrenergic sympathetic signaling to bone, and inhibition of bone marrow monocyte-directed hemopoiesis[88–99] (the bone marrow-derived monocyte is believed to be the immediate precursor of the multinucleate osteoclast). Cannabis use is also known to be associated with profound loss of alveolar bone from the jaws,[100–103] often in the context of severe erosive periodontitis.[104,105]

Maternal cannabis use and fetal development

Not all the studies in this field have returned results confirming a link between maternal cannabis use and later deleterious changes in the offspring.[106] However, maternal cannabis use has been shown to reduce body weight at birth.[107] Many birth abnormalities were identified in a large Hawaiian sample over 6 years. Of 54 birth defects studies, 39% were noted in cannabis-exposed babies.[108] Many of these defects were major and involved the brain (encephalocoele, hydrocephaly, microcephaly, anophthalmia/microphthalmia), cardiovasculature (tetralogy of Fallot, ventricular septal defect, atrial septal defect, and right and left heart atretic syndromes), gastrointestinal system (pyloric stenosis, intestinal atresias and stenoses, and gastroschisis), and limbs (polydatyly, syndactyly, and reduction deformities of the upper and lower limbs); oro-facial clefts were also reported. One large American study found a somewhat elevated risk of anencephaly (OR = 1.7, CI = 0.9–3.4).[109] The association with gastroschisis has been confirmed by other investigators.[110]

The dominant theme to emerge from studies of perinatal exposure is that of impaired executive cortical functioning reflected in reduced attention and analytical behavior and visuospatial analysis and hypothesis testing;[111] parent-rated behavioral problems, language comprehension, and distractibility[112]; and inattention, hyperactivity, impulsivity, and substance use disorders.[113] Indeed, close agreement between human and animal studies of perinatal exposure has been shown.[113] Such changes emerge from as early as the first weeks of life and persist in children in longitudinal studies into the school ages. Importantly, cannabis seemed to potentiate other causes of disadvantage such as smoking, low protein nutrition, and early age of first maternal pregnancy, and child sexual abuse implying that cannabis use by disadvantaged groups compounds other functional deficits.[112,114] Lower school age child IQ was also noted in another large longitudinal follow-up study.[115] It is important to note, however, that such reductions in intellectual performance, executive function, memory, sustained attention, and verbal ability are also seen in samples of low-risk upper middle class children of school age.[116] Equally, it is important to note that careful studies controlling for such pertinent confounding psychosocial variables find strong persistent effects of cannabis exposure.[117]

Maternal prenatal cannabis use has been found to predict later cannabis use during adolescence both as age of onset and frequency of use, a relationship that persisted after adjustment for many other risk factors.[118]

Genotoxicity, mutagenicity, and oncogenesis

Cannabis use is associated with cancer of the lung[30–32] (OR = 2.3, 4.1, and 5.7), head and neck[44,119] (OR = 4.1, 2.6, and 3.1), larynx (OR = 1.7 and 2.3), prostate (OR = 3.1)[120], cervix (OR = 1.4),[120] testes (OR = 1.7),[121] and brain (OR = 2.8).[122] Cannabis has also been linked with tumors of the urothelial tracts.[123–125] Several authors have also found evidence of a dose–response relationship, either with dose, duration, or the combined lifetime total duration of cannabis consumption.[31,32,44,121] A report from Tunisia showed an eightfold rise in lung cancer risk, but initially did not demonstrate a dose–response relationship; tobacco is frequently mixed with cannabis in that country.[30] A later expanded revision of these

data from the same area in northern Africa was able to demonstrate a relationship with the total dose duration of cannabis exposure.[121]

Of great concern is the evidence of inheritable tumors such as childhood neuroblastoma (OR = 1.8, 4.7),[126] rhabdomyosarcoma,[45] and leukemia (OR = 11), particularly non-lymphoblastic leukemia,[127] in cannabis-exposed pregnant mothers.

It should be noted that not all epidemiological studies have been positive,[128] with some studies failing to demonstrate such a link, possibly because cannabis exposure in the study population was limited.[45] For example, a study conducted in Los Angeles did not observe an association with lung cancer, which the authors attributed to the relatively few cases exposed to significant amounts of cannabis.[129] Similarly, a New Zealand study of head and neck cancer was recently found to be negative, a finding attributed by the authors to uncontrolled confounding and inadequate sampling of the New Zealand population.[128]

Cannabinoids liberate radical species both by receptor binding (nitrogen-centered species[130–132]) and by uncoupling mitochondrial oxidative phosphorylation via stimulation of the matrix protein uncoupling protein 2.[133,134] Nitric oxide generation at the cell membrane occurs via both CB1[130] and non-CB1/2 receptor-mediated[131] mechanisms. Indeed, it has been shown that oxidation[135] of the DNA base guanosine to oxo-guanosine is a *normal* part of endocannabinoid signaling. This potentially very serious and inherently mutagenic defect is overcome during normal signaling by activation of the base excision DNA repair pathway within cells. The capacity of such DNA repair pathways is well known to be limited, so the possibility exists that with pathological overstimulation, as might occur during substantial cannabis use, the resulting major genetic defects would become fixed and eventually translated into altered mRNAs, micro-RNAs, genetic expression, and protein sequences.

Cannabis is known to stimulate the oncogenic MAP kinase pathway,[136] which is potently oncogenic, and to be involved particularly in the genesis of non-lymphocytic leukemias.[137] A strongly positive association between cannabis consumption and this tumor has been found.[127] Cannabinoids block topoisomerase II, an enzyme that untwists and makes accessible the dominant coding DNA strand and plays a vital role in DNA repair, meiotic chromosomal replication, mRNA transcription, and DNA hypermutation in prelymphocytes.[138,139] Cannabinoids also impair RAD-51, another enzyme involved in the accurate repair of DNA breaks. Mice chromosomal studies imply that cannabinoids also interfere with the normal maintenance of the ends of chromosomes.[140]

Chromosomal ends or telomeres are made up of many copies of a 6-nt repeat structure (T–T–A–G–G–G) and are protected by a complex of proteins collectively called "shelterin."[141,142] Telomeres are maintained by an enzyme called telomerase, which is absent from most cells but is present in stem cells, gonads (testes and ovaries), and cancers.[143,144] The length of the telomeres has been shown recently to be proportional to the age, the health, and the reproductive fitness of stem cells in a variety of *in vivo* tissue niches.[145] It is of concern that the chromosomal damage was shown in mice not only for tetrahydrocannabinol but also for cannabidiol (and cannabinol),[140] a non-psychoactive cannabinoid that has been added to commercial cannabis sprays supposedly to confer safety![146]

The involvement of cannabinoids with at least three enzymes involved in DNA repair raises questions about their potential genetic toxicity, a subject that remains largely uninvestigated. Gonadal stem cell and genetic toxicity have implications for cell growth inhibition, fetal malformations, and inheritable defects including cancers. Indeed, evidence of cannabis-induced altered DNA expression,[147] a higher incidence of 21 birth defects,[107] and an 11-fold rise in inherited leukemias in the offspring of cannabis users[127] have been documented. Other studies have produced similar findings,[148] including tissues of the germ line.[149] The presence of such major chromosomal abnormalities in sperm cells but not in circulating white blood cells[149] is consistent with the inhibition by cannabinoids of telomerase, which is well known to be present in stem cells, germ cells, and cancer cells but not in the nuclei of normal tissue.[150–152]

Conclusions

In summary, now there is evidence for the implication of cannabis in various psychiatric, respiratory, cardiovascular, and bone pathologies.[153,154] The reports of social disruption, disorganization, and deprivation consequent on widespread heavy cannabis use from a number of communities around the world are of substantial concern. The features associated with chronic cannabis use imply that a clear public health cautionary message is warranted along the lines employed for other environmental intoxicants such as tobacco, which should be targeted strategically to young and otherwise vulnerable populations.

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COLUMBIA UNIVERSITY
College of Physicians and Surgeons

Herbert D. Kleber, MD
Professor of Psychiatry
Department of Psychiatry
Division on Substance Abuse

1051 Riverside Drive, #66
New York, NY 10032
Telephone: (212) 543-5570
Fax: (212) 543-6018
Email: hdk3@columbia.edu
www.columbia.edu

November 16, 2011

To: Committee on Mental Health, Mental Retardation, Alcoholism, Drug Abuse and Disability Services

Regarding: Proposed Res. No. 94-A- Resolution calling upon the N.Y. State Legislature to pass A. 7347/S.2774, legislation that would legalize the medicinal use of marijuana

This letter is in opposition to the proposed legislation that would legalize the medicinal use of marijuana. I have been in the field of substance abuse treatment, research, prevention and policy for over 4 decades as spelled out in my enclosed biosketch. My reasons for opposing the legislation are as follows:

1) Much of the "evidence" for the medical effectiveness of marijuana is anecdotal. Controlled studies are few and indicate effectiveness primarily for the nausea/vomiting of cancer chemotherapy, AIDS wasting, and neuropathic pain. Most of the reasons people give for wanting to use it do not involve the above and are readily treated by existing FDA approved medications.
2) The marijuana available in the dispensaries is usually of unknown potency, purity, and composition. There are over 60 cannabinoids in the cannabis plant and any given batch may contain unknown percentages of each.
3) The U.S. has one of the safest systems in the world, via the FDA, to provide patients with medications of known purity and composition that have been shown by controlled trials to be effective. The FDA has not approved any medication by the smoked route nor any that have not met rigorous standards.. The last time the country tried to circumvent the FDA was in the 1980's with an agent called Laetrile that got on the market via state referenda. It turned out to be toxic and potentially lethal. Why would New York want to circumvent the FDA? I encourage the development of potential medications from the cannabis plant and such research is ongoing.
4) The potency of marijuana today is sharply different from the 1970's and 80's when it was 2-3% THC. Now the average M.J. seized by the DEA is 7-10% THC and dispensaries have signs indicating potencies of 15-20%. We are seeing a rise in marijuana dependence, withdrawal and toxicity due to this.
5) In contrast to claims of marijuana's safety because, unlike narcotics, there are not overdose deaths, m.j. does have potential serious and even lethal side effects. The latter would include automobile accidents associated with "driving while drugged." The former would include earlier onset of schizophrenia, a 2-fold increase in risk of psychotic disorders, short term memory impairment and cognitive impairment, among others.
6) New York should learn from the examples of California and Colorado where after initial enthusiasm, communities are trying to close dispensaries and then find themselves in expensive lawsuits by the very profitable dispensary operators.

7) Adolescent M.J. use has been rising. Such use is related to perceived risk and perceived social disapproval. Passage of this referenda increases both.
8) In these difficult economic times, the allure of taxes from M.J. sales is tempting. The example of alcohol should be kept in mind here. For every $1 – from taxes on alcohol, over $8 - $10 is spent coping with the health, legal and driving consequences related to alcohol.

Thank you for your attention to the above. I apologize for not being able to attend the hearing and present the points in person.

Yours Sincerely,

HDKleber, M.D.

Herbert D. Kleber, MD
Professor of Psychiatry
Director, Division on Substance Abuse
Columbia University/ New York State Psychiatric Institute

Herbert D. Kleber, M.D.

Biographical Sketch

Dr. Herbert Kleber is Professor of Psychiatry at the Columbia University College of Physicians and Surgeons and the New York State Psychiatric Institute, and Director of the Division on Substance Abuse there, a Division he founded in 1992. The Division has consistently been considered as one of the top ones in the country as ranked by U.S. News and World Reports. Also in 1992, he co-founded CASA with Joe Califano and served as its Executive Vice-President until 2001. He has been a pioneer in the treatment and research of substance abuse for over 40 years.

Prior to coming to New York, he served for 2 ½ years as the 1st Deputy Director for Demand Reduction at the Office of National Drug Control Policy in the White House under President George H.W. Bush and Director William Bennett. Before that, Dr. Kleber was Professor of Psychiatry at Yale University School of Medicine (1966-89) where he founded and directed the Substance Abuse Treatment Unit. Currently he oversees research on new medications to treat cocaine, heroin, prescription opioids, or marijuana problems.

Dr. Kleber is the author or co-author of more than 275 papers, chapters, and books dealing with all aspects of substance abuse, and the co-Editor of the American Psychiatric Press Textbook of Substance Abuse Treatment, now in its 4th edition. He has received numerous awards from scientific societies and medical schools, is listed as one of the "Best Doctors in America," and was elected in 1996 to be a member of The Institute of Medicine of the National Academy of Science. He serves on a number of national boards in the areas of treatment, prevention, research, and policy. These include the Betty Ford Institute, Partnership for a Drug-Free America, D.A.R.E., APA Council on Addiction, and the Monitoring the Future Project at the University of Michigan. At the New York State level he is on the Medical Advisory Board for the Office of Alcohol and Substance Abuse Services (OASAS).

164 West 74th Street
New York, NY 10023

T 646 505 2100
F 212 787 5295
www.phoenixhouse.org

Phoenix House

OFFICE OF THE FOUNDER

November 18, 2011

Committee on Mental Health, Mental Retardation
Alcoholism, Drug Abuse and Disability Service

Subcommittee on Drug Abuse

Dear Committee Members,

I am so sorry I am not able to be there personally. I was looking forward to seeing you, and I wanted very much to let you know how deeply concerned I am about legislation that might authorize the lawful distribution of "medical marijuana."

You've got some of the nation's leading experts in your office, and they can tell you what bad medicine and health practice this would be. From my perspective at Phoenix, it would be a disaster. At our adolescent residential programs in New York and nationally, marijuana is the primary drug of abuse for the overwhelming majority of admissions.

The social and family dysfunction, educational toll, and health consequences that relate directly to marijuana use are already staggering.

The political forces pushing this legislation wish to legalize marijuana (and, eventually, other drugs) and are using "compassion" as a protective shield.

With personal best wishes,

MSRosenthal MD

Mitchell S. Rosenthal, M.D.

SHEILA B. BLUME M.D.

284 Greene Avenue

Sayville, New York, 11782

(631) 589-7853

sheila_blume@post.harvard.edu

November 17, 2011

New York City Council Subcommittee on Drug Abuse

Considering Res. No. 94-A

Re: "medical" marijuana

Dear Members of the committee:

I am a retired psychiatrist specializing in addictions. I served as director of the NYS Division of Alcoholism and Alcohol Abuse in the cabinet of Governor Hugh Carey, from 1979—1983.

I am active in many medical organizations including the New York State and Suffolk County Medical Societies, the American Society of Addiction Medicine (of which I have been president) and the American Psychiatric Association, in which I have held several positions. I am writing today to ask you to resist to supporting the adoption of any bill permitting "medical" marijuana in New York.

As a physician, when I prescribe a medication, I do so with the assurance that it has been approved by the FDA, and therefore that its efficacy has been demonstrated in a sufficient number of controlled studies, and that its purity and side effects are known to me. I specify the dose of the medicine and how many doses are to be dispensed. When the patient may need more of the medicine, he or she makes a medical visit at which we discuss the efficacy of the medication in this particular situation and the patient's reactions, so that I may decide on whether to prescribe more of the same, discontinue, or change the medication. None of these basic ingredients of medical practice would be present in the proposed "medical" marijuana legislation.

The FDA has not approved marijuana in its smoked form, although its most important active ingredient, THC, is available in pill form for prescription to those patients who may receive relief from it. Smoked marijuana is not approved because it is a highly addictive drug whose efficacy has not been scientifically established, and whose dosage cannot be easily controlled. You may also note that all of the thousands of medicines approved by the FDA are approved for oral or

injected use, or via an inhaler, but none are approved to be taken as part of a cigarette. This is true because smoking exposes the patient to a large number of cancer-causing substances along with the desired medication. There is at least one study that shows that marijuana cigarettes are more carcinogenic than tobacco cigarettes. While it is true that other addictive drugs, such as opiate analgesics, are approved by the FDA, these medicines must be specially prescribed under a significant number of legal restrictions. I am sure you are aware that even with these restrictions, prescription opiates are currently creating a significant societal problem because of abuse and addiction.

Because it is clear that smoked marijuana will not be approved by the FDA, there are New Yorkers who would like to make it available for "medical" usage, outside of the federal laws set up to protect the public health, as it has been in several other states. This legislation would enable a physician to "prescribe" (or more realistically approve) the use of marijuana for any adult patient. There is no uniformity of THC content, so the dose is not controlled. There is virtually no requirement for legitimate medical care or follow-up, and the range of diagnoses for which marijuana may be approved is so wide that almost anyone can qualify. Furthermore, there are no diagnostic tests that would tell the doctor whether or not the patient is truly suffering from such conditions as as chronic pain or frequent headaches.

The experience of other states should tell us that marijuana becomes widely available in such states, and its use goes far beyond the range of people with severe illness. Certain practitioners specialize in giving out marijuana permissions with few of any questions asked, and with no legitimate medical workup and no follow-up.

I have treated many marijuana addicts during my career in medicine, most of them young people, and I can tell you that increasing the availability of this drug and branding it as a medicine will not benefit our youth. I would just ask you to consider this question very carefully and recommend against allowing an increase in the availability of this dangerous drug.

Please feel free to contact me for any other assistance I might give.

Yours sincerely,

Sheila B. Blume, M.D.

(sent as an Email attachment to Nicholas Pace MD)

Don Abrahms paper
Madras, Bertha Kalifon

to:
Pace, Nicholas
11/17/2011 02:09 PM
Show Details

BK Madras Comment on:

Cannabis in painful HIV-associated sensory neuropathy:
A randomized placebo-controlled trial
Abrams et al., Neurology 68: 515-521, 2007

First draft 2/13/07
Edited slightly 2/23/07

The FDA, the federal agency responsible for reviewing the safety and efficacy of drugs, does not support the use of smoked marijuana for medical purposes. A recent article in the journal Neurology fuels the medical marijuana debate, but adds nothing substantive. What is the public to think? Although marijuana has been proposed as a medication for several disorders, marijuana is not superior to pure prescription drug and has serious detrimental effects.

The article concluded that smoked cannabis effectively relieved chronic neuropathic pain from HIV-associated neuropathy, *with findings comparable to oral drugs used for chronic pain.* This pivotal sentence is instructive. Weigh the two options: if a marijuana cigarette is comparable to a safe and effective oral pain-killer with a low propensity to intoxicate, should physicians prescribe an impure, intoxicating smoked leaf instead of a pure drug? Would they be willing to introduce cigarette smoke into a patient's system? All study patients were required to have prior experience smoking marijuana, because they needed to know how to inhale deeply. If broadly approved, would this require training drug-naïve patients on how to smoke cigarettes and inhale deeply? How can an impure cigarette be supported by healthcare professionals, in the midst of a 40-year anti-smoking campaign that is achieving significant public health gains?

The marijuana smoking patients reported increased anxiety, sedation, disorientation, paranoia, confusion and dizziness, albeit in low numbers. In fact, the placebo group showed a larger reduction in depression/dejection. Should an intoxicating cigarette, that impairs thinking, concentration and perception, be introduced to patients at risk for AIDS-induced dementia? Should marijuana be used, even if it produces tolerance that compels the smoker to compensate by smoking more often, or seeking higher potency intoxicants? Research has demonstrated that cannabis can compromise brain, heart, lung, function and possibly immune system response. Shouldn't this information inform the debate?

The study design had several concerns.

Length of study: A five-day study of a cigarette delivery system, to be smoked indefinitely for neuropathic pain is inadequate to yield data on long term consequences, [to be verified: particularly as HIV patients who use reportedly have a higher death rate compared with non-users.]

Effectiveness of smoked marijuana: In the study, 7 more people who smoked marijuana-laced cigarettes (25 subjects) than placebo cigarettes (25 subjects) reported a reduction in neuropathic pain. ***But smoked marijuana was no more effective than smoked placebo in reducing pain, if pain was induced in the***

forearm of subjects.

Drug abstinence: A study of this nature requires a detailed history of drug use and current drug use and inclusion, exclusion criteria need to be carefully justified. The report states that patients were in stable health without current substance abuse. A few lines later the authors state that "Current users were asked to discontinue any cannabis use". In addition to this inconsistency, it is not clear how long after users abstained that the study was initiated. This is a concern because of the long half-life of marijuana in the body. Did the study begin only after all traces of the drug were gone from users? There was no mention of biological testing to confirm self-reports of drug use – an essential procedure for this type of study.

Random controlled study? How "blind" and random was the study, when the majority of patients were marijuana smokers who are able to distinguish smoked placebo from smoked marijuana?

Differences between the marijuana group and placebo group could skew the data. Only 7 more marijuana smokers responded with significant reductions in pain than the placebo smokers. But 78% of the marijuana cigarette group and 68% percent of the placebo cigarette group were current users. The actual difference is small, 2 people, but add to this difference the fact that 6 more patients in the placebo group than in the marijuana group were administered HAART. HAART is an AIDS cocktail that can induce neuropathic pain, raising the possibility that the placebo group was at higher risk for neuropathic pain, which could affect placebo response. Also, 3 more people in the placebo group were current users of opioid pain-killers than the marijuana group, again potentially affecting the placebo data. About half of the patients were on pain medications during the study, but we do not know whether the placebo control and drug groups were taking the same doses. When the difference between marijuana smoking responders and placebo smoking non-responders is only seven people, small population differences in the two groups may significantly skew the data. There is a way to address these weaknesses in matched controls: a cross-over repeat study in which the placebo group becomes the drug group and vice versa. This was not done.

No drugs in leaf form are being approved as prescription pharmaceuticals, because plants such as marijuana contain a complex mixture of compounds of uncertain concentrations, the majority of which have unknown pharmacological effects, metabolism, metabolites, side-effect profiles, toxicology and drug interactions. In growing marijuana plants, you cannot with certainty regulate the relative concentrations of the hundreds of compounds produced by the plant. These factors were the critical incentive for medicinal chemists and pharmacologists to isolate active ingredients in plants, study them alone and produce a pure product with a much higher certainty of its effects. A good analogy is the medicinal history of coca leaves. They produce cocaine, which is not only a stimulant and an intoxicant, but a good local anesthetic. Building on the core cocaine structure, researchers designed local anesthetics with low psychoactive and addictive properties, but high local anesthetic properties – for example novocaine. Current cannabinoid research shares this goal of developing alternative, pure medications, by isolating and changing active ingredients, to avoid the adverse consequences of smoked marijuana. A smokable plant is not modern medicine. It harkens a return to pre-scientific pharmacology.

Bertha K Madras, PhD
Professor of Psychobiology
Department of Psychiatry
Harvard Medical School
1 Pine Hill Drive
Southborough, MA 01772
(508) 624-8073
bertha_madras@hms.harvard.edu

HARVARD MEDICAL SCHOOL
NEW ENGLAND PRIMATE RESEARCH CENTER

BERTHA K. MADRAS, PhD
Professor of Psychobiology
Department of Psychiatry

Address: HMS-NEPRC
One Pine Hill Drive,
Southborough, Massachusetts 01772-9102
Tel: 508-624-8073 or 508-624-8100
E-mail: bertha_madras@hms.harvard.edu

November 17, 2011

To: The Committee on Mental Health, Mental Retardation, Alcoholism, Drug Abuse and Disability Services, jointly with the Subcommittee on Drug Abuse hearing: November 18, 2011, 10:00 a.m, 16th Floor Committee Room, 250 Broadway, New York, NY.
Re: Proposed Res. No. 94-A: Resolution calling upon the New York State Legislature to pass A.7347/S.2774, legislation that would legalize the medicinal use of marijuana.

I strongly oppose any legislation that would legalize the use of marijuana as medicine. My reasons are outlined below. Additional information can be obtained by contacting me.

SMOKING AN IMPURE PRODUCT AND DELIVERY OF *ANY MEDICINE* BY SMOKE IS NOT MODERN MEDICINE.
IT RUNS COUNTER TO A *50 YEAR PUBLIC HEALTH CAMPAIGN TO END SMOKING*

- **New York bans smoking in restaurants, bars, public places, 1,700 parks, on the city's 14 miles of public beaches, in pedestrian plazas (Times Square), to prevent harm associated with second hand smoke.**
- **Approval of marijuana smoking is a complete contradiction of this sound public health policy and a reversal in efforts to reduce smoking and second hand smoke.**

IT IS POOR PUBLIC POLICY AND MEDICAL PRACTICE TO PERMIT MARIJUANA TO BE USED AS A SMOKED OR ANY OTHER FORM, FOR MEDICAL PURPOSES IF IT IS:

- **Not FDA-approved**
- **Ingested by smoking of hundreds of chemicals – some hazardous**
- **Not subject to product liability regulations**
- **Exempt from quality control standards**
- **Not governed by dose, frequency of dosing, longitudinal effects**
- **Provided at unknown strengths of THC**
- **Self-prescribed and self-administered by the patient**
- **Marinol is approved**
- **The scientific evidence does not achieve FDA standards for safety, efficacy**
- **The intoxicating effects of marijuana on cognition are unacceptable**
- **Long term psychological, physiological effects in sick populations unknown**
- **Clinical trials require subjects to be experienced marijuana users**
- **Majority of trials do not provide side effect profile e.g. cognition**

FDA IS THE *SOLE* FEDERAL AGENCY THAT APPROVES DRUGS AS SAFE AND EFFECTIVE FOR INTENDED INDICATIONS. FDA REQUIRES THAT SCHEDULED DRUGS FOR APPROVAL:

- **Are pure compound(s)**
- **Are produced with controlled chemistry, manufacturing, composition of matter; known shelf life**
- **Have reproducible and validated production methods**
- **Have distribution by a regulated chain of custody**
- **Have documented pharmacology and toxicology in animals at various doses**
- **Have documented human pharmacokinetics, bioavailability for a wide range of doses**
- **Have documented clinical microbiology**
- **Have proven dose response effects, efficacy, safety for all medical indications**
- **Have documented side effect profile**
- **Have in place post-approval processes to report adverse events, safety updates**

DOES MARIJUANA FULFILL FDA CRITERIA FOR DOSE REQUIREMENTS?

- **Production is not standardized**
- **There is no quality control; (bacteria, chemical , cleanliness, are not regulated)**
- **Dose is not regulated; doses can range from 2-20%**
- **Dosage forms unregulated: marijuana can be smoked, vaporized, baked products, teas.**
- **Marijuana is impure: it contains ~ 80 cannabinoids; (a) ammonia in marijuana smoke up to 20-times greater than in tobacco smoke; (b) hydrogen cyanide is 3–5 times higher than in tobacco smoke; (c) marijuana cigarette smoke contains known carcinogens and other chemicals implicated in respiratory diseases[1].**

DOES MARIJUANA FULFILL FDA REQUIREMENTS FOR DRUG APPROVAL? 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 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; it has no currently accepted medical use in treatment in the United States**
- **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**

FDA STATEMENT ON BALLOT INITIATIVESM LEGISLATIVE ACTIONS FOR 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.

MARIJUANA AS "MEDICINE" IN THE PRACTICE OF MEDICINE IS MEDICAL FICTION

- Composition of matter: completely unregulated for purity, potency, quality,
- Medical indications; for each of the medical conditions listed in ballot initiatives or legislative actions, the evidence is absent or inadequate
- Medical education: Medical education focuses on evidence-based diagnosis and treatment, but marijuana has no scholarly presence in medical training
- Medical practice is compromised because there are no: requirements to extract medical history or give a detailed medical exam, discuss long term treatment, effects or follow-up, provide informed consent, consult with other physicians, keep proper records that support recommending marijuana instead of safe approved alternatives, have an "in good faith" relationship with patient rather than a "pill mill", be able to identify substance abusers, addicted.
- Marijuana Production: Dispensaries had no product liability, no product regulation , no chain of custody, no accountability to physicians or their patients.

MARIJUANA BIOLOGY
CANNABINOID SYSTEM IN THE BRAIN AND BODY AFFECTS:

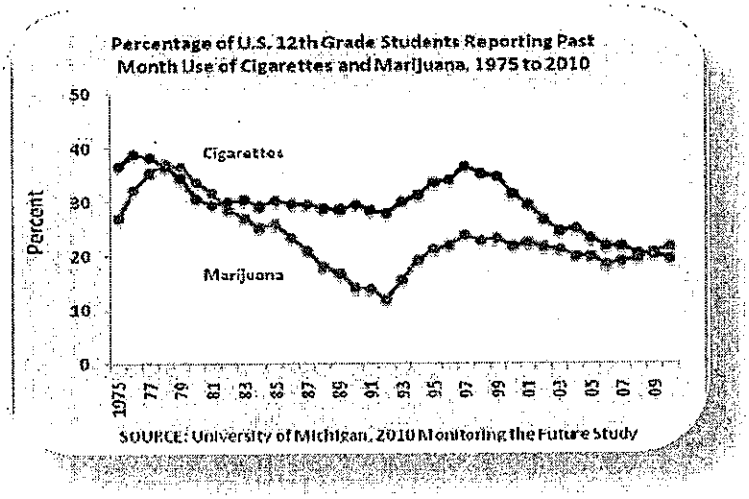
- Brain cell function
- Production of new brain cells
- Appetite, pain
- Learning, memory
- Early pregnancy, fertility, implantation sucking, maintenance of pregnancy
- Skeletal nerve terminals
- Immune system function
- Inflammatory response
- Gastrointestinal tract
- Liver function
- Cardiovascular system
- Lung airways

MARIJUANA, ACUTELY, HAS ADVERSE EFFECTS ON BRAIN FUNCTION

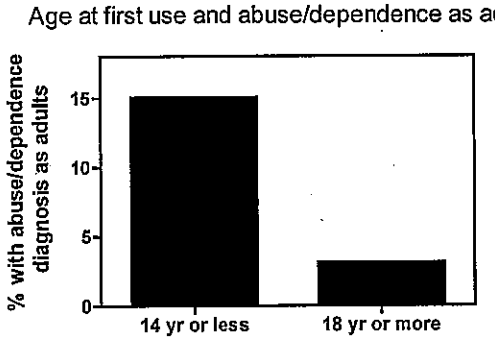
Impairs memory
Impairs attention
Impairs judgment
Impairs motor coordination
Impairs cognition
Impairs attention
Impairs time sense
Impairs self-perception
Impairs complex tasks
Impairs sleep
Impairs balance
Disjointed thoughts
Causes dizziness

MARIJUANA AND ADOLESCENTS

MARIJUANA USE (PAST 30 DAYS) IS HIGHER THAN CIGARETTE SMOKING (12TH GRADERS)[2]



IF MARIJUANA IS INITIATED AT AGE 14 OR YOUNGER, PREVALENCE OF ABUSE/ADDICTION IS 5-6 TIMES HIGHER IN THE ADULT[3]



ADOLESCENTS IN TREATMENT WHO OBTAIN MARIJUANA DIVERTED FROM A "MEDICAL" USER HAVE INCREASED CONSEQUENCES

MEASURE	SOURCE DIVERTED	SOURCE NOT DIVERTED	CONCLUSION
	48.8%	16.6%	
Use more than 20 times/month	83.8%	56.1%**	Much higher use rates if marijuana obtained from diverted source.
Perceived risk of using	15.4%	14.6%	No differences
Friends don't disapprove regular use	79.5%	56.1%*	More associates approve of use by user with diverted source of marijuana.
Substance use problems, score	46.5	37.6**	More substance use problems if marijuana obtained from diverted source.
Other problems, score	46.3	37.6*	More problems if marijuana obtained from diverted sources.
Very easy access to marijuana	84.6%	43.9%***	More reported access if marijuana obtained from diverted source.

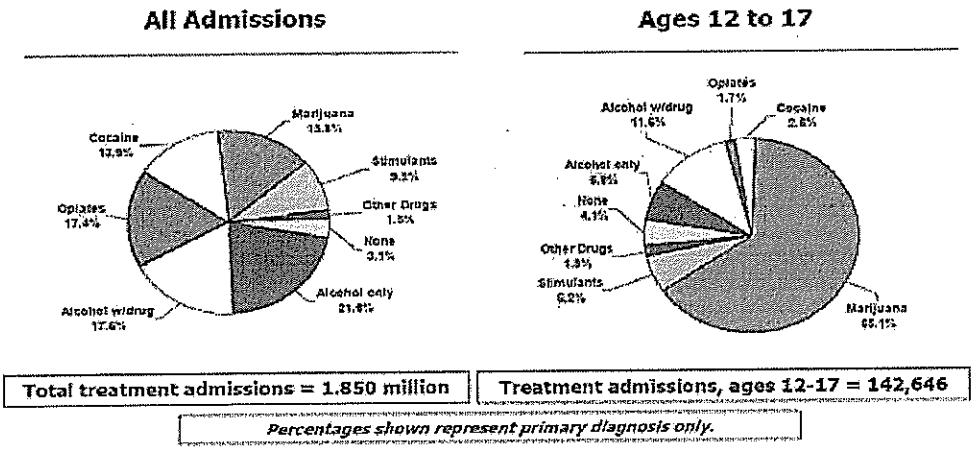
MENTAL HEALTH PROBLEMS IN MARIJUANA-USING COLLEGE STUDENTS

Percent endorsement of marijuana-related problems.

	Any marijuana use (n=487)	Infrequent marijuana use (n=323)	Frequent marijuana use (n=164)
Problems with partner	15.4	15.1	16.1
Problems with family	12.3	8.8	19.1[b]
Neglect family	10.2	6.3	17.9[b]
Problems with friends	10.9	9.8	13.0
Miss days of work/class	20.2	13.8	32.7[b]
Lose a job	2.9	2.2	4.3
Lower productivity	30.4	21.1	48.8[b]
Medical problems	3.3	2.2	5.6
Withdrawal symptoms	4.0	1.9	8.0[b]
Blackouts or flashbacks	4.9	4.1	6.8
Memory loss	24.2	15.4	41.4[b]
Difficulty sleeping	11.5	9.1	16.0[b]
Financial difficulties	12.9	6.0	26.5[b]
Legal problems	7.5	4.4	13.6[b]
Lower energy	31.2	23.9	45.7[b]
Feel bad about use	17.2	16.0	21.6
Lowered self-esteem	10.2	7.9	14.8[b]
Procrastinate	41.7	28.6	67.3[b]
Lack self-confidence	11.9	8.8	17.9[b]

Buckner JD, Ecker AH, Cohen AS. Mental health problems and interest in marijuana treatment among marijuana-using college students. Addict Behav. 2010 Sep;35(9):826-33. Epub 2010 May 18.

A HIGH PROPORTION OF YOUTH ARE IN TREATMENT PRIMARILY FOR MARIJUANA, NOT ALCOHOL



Source: SAMHSA, *2005 Treatment Episode Data Set.*

- ~23,770 treatment admissions were adolescents 12-14 years[4]
- 63% were for marijuana; 20.8% for alcohol
- 45.5% reported multiple drug use
- 24.7% had a psychiatric disorder
- 17.3% had a prior admission

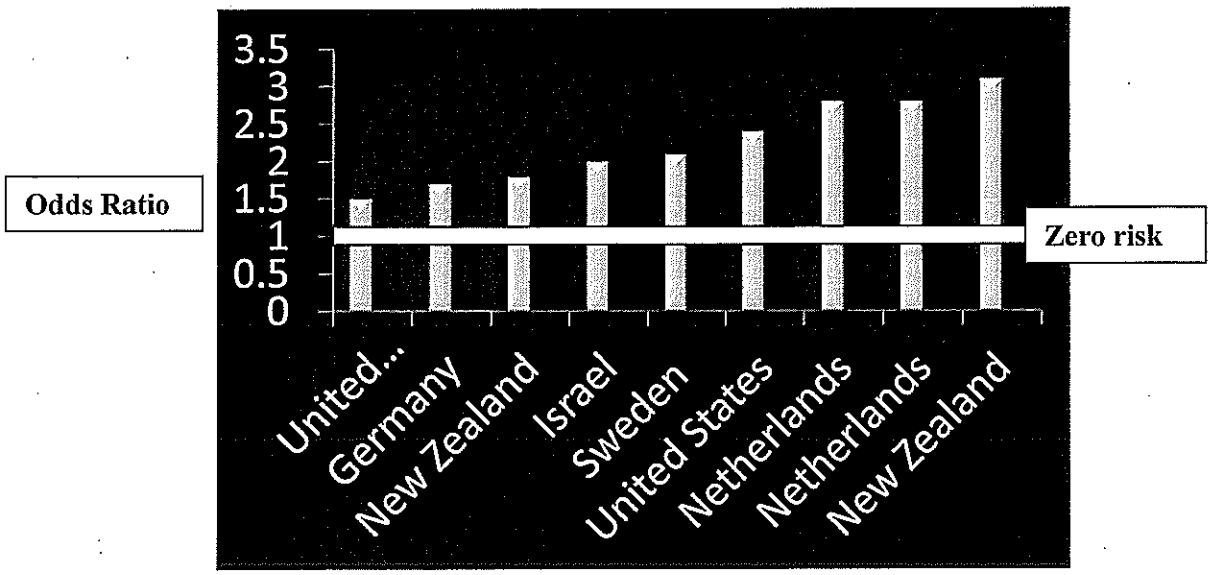
MARIJUANA IS ADDICTIVE AND CAN RESULT IN WITHDRAWAL SYMPTOMS

- Progression to chronic use can be as rapid as nicotine, more rapid than alcohol
- Tolerance and withdrawal may reflect more severe addiction
- Progression to addiction *more rapid in youth*
- Cognitive-behavioral treatment reduces marijuana use, but only 15% remain abstinent 6-12 months after treatment
- <u>Withdrawal from marijuana can result in:</u>
- Irritability, Anxiety, Nervousness, Restlessness, sleep disturbances
- Aggression, Sadness, Boredom, Anger
- Weight gain, headaches, GI problems discomfort, craving, appetite change,
- <u>Improved memory (after 12 days for 1 year)</u>

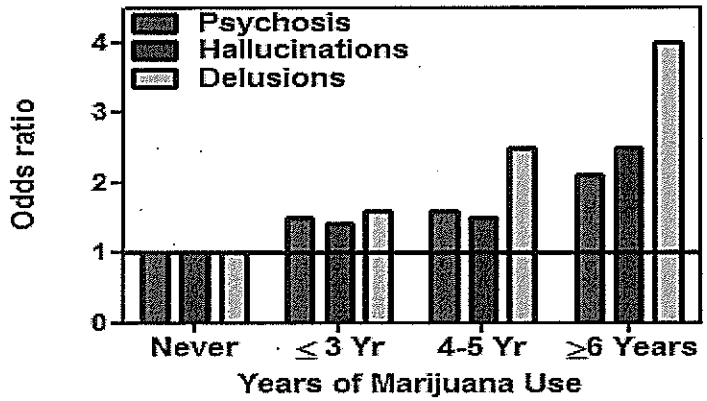
MARIJUANA USE IS ASSOCIATED WITH BRAIN CHANGES[5]

- Marijuana users had bilaterally reduced volumes of hippocampus and amygdala.
- Reduced volume in brain region critical for learning and memory depended on how long the person smoked marijuana during previous 10 years.
- Positive psychotic symptoms were associated with cumulative exposure to marijuana.
- Marijuana users performed significantly worse than controls on verbal learning.
- Study suggests that heavy daily marijuana use – [such as for "medical indications] for prolonged periods can exert harmful effects on brain tissue and mental health.

MARIJUANA USE IS ASSOCIATED WITH INCREASED RISK FOR PSYCHOSIS[6]



LENGTH OF MARIJUANA USE IS ASSOCIATED WITH INCREASED RISK FOR PSYCHOSIS, HALLUCINATIONS, DELUSIONS[7]



MARIJUANA USE IS ASSOCIATED WITH INCREASED HEALTH RISKS

- Bronchitis, compromised pulmonary function
- Strokes
- Heart attack (4.8 times higher in susceptible) and angina
- Adverse effects on pregnancy and developing fetus
- Hormonal effects
- Higher rates of hospitalizations, car accidents

References. Others available upon request

1. Moir et al, A Comparison of Mainstream and Sidestream Marijuana and Tobacco Cigarette Smoke Produced under Two Machine Smoking Conditions. *Chem. Res. Toxicol.*, 2008, *21* (2), pp 494–502
2. University of Michigan, 2010, Monitoring the Future
3. National Survey on drug use and health, 2010, NSDUH, Sept 2011
4. The TEDS Report, SAMHSA, May 3, 2011
5. Yucel et al, Regional brain abnormalities associated with long-term heavy cannabis use. Arch Gen Psychiatry. 2008 Jun;65(6):694-701.
6. Adapted from Murray RM, Morrison PD, Henquet C, Di Forti MCannabis, the mind and society: the hash realities. Nat Rev Neurosci. 2007 Nov;8(11):885-95.
7. McGrath et al, Association Between Cannabis use and Psychosis-related outcomes using sibling pair analysis in a cohort of young adults. Arch Gen Psychiatry 2010: 67: 440-447

LONG TERM USE OF MARIJUANA CAN ADVERSELY AFFECT THE MENTAL HEALTH AND HALTH OF PEOPLE WHO USE IT DAILY FOR MEDICAL CONDITIONS.
USE OF MARIJUANA FOR MEDICAL PURPOSES IS UNSAFE,
POOR PUBLIC HEALTH, POOR PUBLIC POLICY AND POOR MEDICINE

Sincerely,

Bertha K. Madras, PhD
Professor of Psychobiology, Department of Psychiatry, Harvard Medical School/NEPRC

North Shore LIJ Center for Advanced Medicine

North Shore-Long Island Jewish Health System

450 Lakeville Road
Lake Success, New York 11042
Tel (516) 734-8900

Monter Cancer Center

Department of Medicine
North Shore University Hospital

Don Monti Division of
Medical Oncology
Division of Hematology

Harry Raftopoulos, M.D.
Associate Attending Physician

October 3, 2011

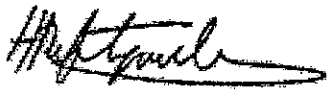
Nicholas A. Pace, MD, FASAM
Clinical Associate Professor of Medicine
New York University School of Medicine

Dear Dr Pace:

I am writing to strongly endorse your efforts to prevent medical marijuana becoming available in New York State. As a medical oncologist who focuses exclusively on the treatment of lung cancer, I am acutely aware of the desperation that some patients feel both in the treatment of their disease and symptom management. However, as professionals, we have to make decisions for our patients based on objective evidence. The case for medical marijuana lacks ANY compelling, scientific evidence supporting benefit for cancer patients. In fact there is more evidence supporting the harm of inhaling noxious smoke. Why should this substance be held to a different standard than others? Why should it not have to undergo randomized, controlled studies to support benefit BEFORE it can be used? We need to be objective and not emotional, otherwise we risk harming our patients.

I urge you to do your utmost to prevent legislators from embarking on this distraction which can only impede legitimate products with far better promise of helping patients from moving forward.

Sincerely,



Institute For Behavior and Health
Creating Tomorrow's Drug Policy

September 29, 2011

Governor Andrew Cuomo
Office of the Governor
The State of New York
Albany, New York

Dear Governor Cuomo:

By way of introduction, I was the first Director of the National Institute on Drug Abuse (NIDA), the nation's principal agency devoted to scientific research on drugs of abuse, including marijuana. I am currently the President of the Institute for Behavior and Health, Inc., a non-profit organization devoted to reducing illegal drug use, and Clinical Professor of Psychiatry at Georgetown Medical School. I also served as co-chair of the American Society of Addiction Medicine (ASAM) Task Force that reviewed the issue of marijuana as a medicine and produced the recently released White Paper on marijuana as medicine.

The conclusions of the ASAM Task Force support those of the Institute of Medicine (IOM) Report issued in 1999. There is no future in smoked marijuana as medicine. "Medical marijuana" in is neither good public health policy nor compassionate healthcare for the sick. Marijuana is a Schedule I drug of abuse. Sixty one percent of Americans suffering from a substance use disorder other than alcohol are suffering from marijuana dependence or marijuana abuse. Marijuana is not *medicine*.

New York must not circumvent the important role of the Food and Drug Administration (FDA) to study and approve medicines as safe for use. It is unwise for medicines to be approved by ballot initiative or legislative action. Abused drugs must be provided to appropriate patients by physicians' prescriptions and distributed in the closed system of professional pharmacies that reduce abuse and misuse. State legislators and New York residents have been mislead by unfounded claims of marijuana's health benefits. The truth is crude marijuana should not be used for any medical purpose. Some of the chemicals in marijuana may one day be approved for the treatment of specific disorders at specific doses within the well-established system of drug approval. They could then be dispensed by physicians' prescriptions in the controlled system that has served this country well for a century. Undermining that system is bad public policy, bad medicine and bad politics.

6191 Executive Boulevard, Rockville, Maryland 20852
Ph: 301.231.9010 Fax: 301.770.6876 www.ibhinc.org

For decades the debate over "medical marijuana" focused on research and claims. Today the landscape of this debate is defined by the actual practice of "medical marijuana" as can be plainly seen in the states which have legalized this hoax. The reality is that "medical marijuana" is available in these states for virtually anyone who wants to use it for virtually any reason in any dose they chose and they are free to give it away or sell it to anyone they choose to pass it on to. New York needs to learn from these experiences and put this issue back on track for a careful scientific review by the FDA and any product approved by the FDA must be distributed under physicians' prescriptions through registered pharmacies.

Many proponents of "medical marijuana" are using these state-based initiatives to promote marijuana legalization. It is vital that New York not follow down the same path, opening a door to new marijuana legalization initiatives.

A well-known drug legalization initiative is that of the self-appointed Global Commission on Drug Policy which published a report in June 2011 proposing eleven recommendations to achieve its goal of "reducing the harm caused by drugs to people and societies". Some the recommendations are appealing in that they advocate improving treatment, increasing youth drug use prevention, and using evidence-based practices. However, the foundation on which the Global Commission's proposals rest is both subtle and ominous: the Commission does not seek to reduce the use of illegal drugs, but instead proposes strategies to normalize and to reduce the "harms" resulting from illegal drug use, largely through legalization and decriminalization of illegal drugs, including marijuana. These recommendations are a threat to public health and to public safety. The unarticulated consequence of the Global Commission's recommendations is that illegal drugs would become more widely and cheaply available, inevitably leading to increased drug-caused harm. This consequence is not simply conjecture, but is based on the recent experience with the rapid rise in death rates due to the non-medical use of prescription opioids drugs that parallels their increased availability.

The Obama Administration's White House Office of National Drug Control Policy (ONDCP) does not support the Global Commission's report. An ONDCP spokesman has stated, "Drug addiction is a disease that can be successfully prevented and treated. Making drugs more available – as this report suggests – will make it harder to keep our communities healthy and safe."

The Institute for Behavior and Health, Inc. (IBH) concurs with the ONDCP position and support building upon and improving the current United States drug policy which seeks to reduce illegal drug use. Surrendering to the modern drug epidemic is not consistent with the IBH mission. IBH identifies and promotes new, effective strategies to reduce the demand for illegal drugs and to improve drug policy.

I urge you to support programs and policies that seek to reduce drug use and improve public health. "Medical marijuana" and marijuana legalization initiatives are not in the interest of public health or the practice of medicine.

Sincerely,

Robert L. DuPont, M.D.
President

RLD:cs
Enclosure

6191 Executive Boulevard, Rockville, Maryland 20852
Ph: 301.231.9010 Fax: 301.770.6876 www.ibhinc.org

The Institute on Global Drug Policy

October 2, 2011

Dear Governor Cuomo:
I ask that you oppose medical excuse marijuana legislation, and further ask that you endorse the recommendations of the American Society of Addiction Medicine.

It is most important to understand that legislative actions giving access to marijuana seriously jeopardize consumer protection. Our processes for bringing medicine to the public have been established so that science, not emotion, prevails. Medicine needs come through the FDA to assure safety and efficacy. The FDA opposes medical excuse marijuana and such legislative actions. More importantly, the recent legislative initiatives create medicine by popular vote. Marijuana is not a safe drug, and is far from clearly effective. The active ingredients of marijuana are already available to the public by medical prescription. There is no advantage, and indeed there is a disadvantage, to smoking marijuana over available medications.

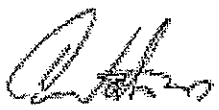
Marijuana advocates allege benefits of marijuana use with little or no clear scientific basis. Neither Marijuana nor pure THC has ever been compared to effective new anti-nausea medications. Cannabis can actually enhance pain because of a very narrow therapeutic window. The progression of glaucoma is not slowed, and ophthalmologists do not consider it a reasonable treatment. Cannabinoids may reduce muscle spasm, but they damage gait and mental status in Multiple Sclerosis patients. While cannabinoids stimulate appetite, it appears to increase body fat rather than lean body mass. There exists no credible evident that marijuana is beneficial for depression, drug abuse, headaches, or menstrual cramps.

Allowing such legislation to become law is riding a wave of emotion and mob psychology that has been carefully crafted, financed, and driven by the marijuana lobby. The advocates' strategy remains the same; play to emotion, overstate the benefits of marijuana, use the medical excuse to get the camel's nose under the tent and then push for more legal access to pot.

Some of the most consistently identified problems with marijuana are the effect on memory, concentration, and coordination. The effects on driving skills and coordination are extremely serious, and marijuana is regularly implicated in trauma. Since marijuana dispensaries became legal in California, marijuana-related fatal trauma has doubled. Marijuana also has effects on the lungs, and has been found to damage lung immunity and function. Marijuana has serious effects on the fetus that have been documented not only at birth, but have also been seen in the children who used during pregnancy.

Medicine and policy makers must stop this circus of medicine by popular vote which is dangerous and which plays in to the pot legalization lobby.

For a detailed scientific discussion of the medical excuse issue see www.globaldrugpolicy.org
Sincerely,



Eric A. Voth, M.D., FACP
Chairman, The Institute on Global Drug Policy
5999 Central Ave
St. Petersburg, FL 33710

Office of the
Special Narcotics Prosecutor
for the City of New York
Bridget G. Brennan, Special Narcotics Prosecutor

80 CENTRE STREET, SIXTH FLOOR
NEW YORK, NY 10013
212-815-0413, OFFICE
212- 815-0144, FAX

November 18, 2011

Re: New York City Council Resolution No. 94-A
Resolution calling upon the New York State Legislature to pass A.7374/S.2774

Dear Council Members:

I am sorry that a prior commitment prevents me from attending today's hearing. Please accept this letter, and its attachments in lieu of my testimony.

I am writing to express concern for the public health and safety of all New Yorkers, if A.7374/S.2774 , the "medical marijuana bill" should pass. I have deep compassion for those afflicted with life threatening diseases or debilitating physical pain. I strongly believe that marijuana should be rigorously researched for therapeutic components which could be distilled and hygienically delivered to patients. I advocate removing all obstacles to the scientific study of the remedial potential of marijuana, and I urge the New York State Legislature to do the same.

However, smokable marijuana is not a proven medicine. In fact, marijuana is the most commonly reported drug of addiction in our Alternative to Incarceration programs. In New York City, defendants who sell cocaine and heroin, and are sent to rehabilitation programs, report an addiction to marijuana more frequently than to any other drug. Overwhelming, the cost of treatment in lieu of incarceration for narcotic sales is born by publicly funded insurance programs. It makes little sense to recognize marijuana as addictive enough to motivate criminal behavior, and at the same time advocate that it be considered a therapeutic herb. We are currently experiencing an epidemic of prescription drug abuse in our city, and designating as a medicine yet another drug which we know to be highly addictive will only contribute to our problems.

The "medical marijuana bill", in its present form, is far too loosely drawn, and offers no safeguards to protect the health of those who use it, and the safety of the communities where marijuana dispensaries would be located. For example, it:

- Allows an unlimited number of unregulated marijuana dispensaries to proliferate anywhere, including next to schools, public parks, and other highly inappropriate locations. Dispensaries have proven to be public nuisances and magnets for crime in states where they have been permitted.
- Does not require a physician in good standing to meet with a patient before providing a "certification" for marijuana, and allows nurse practitioners to provide a certification;
- Has a broad, loose definition of conditions for which marijuana can be certified.

Nationwide, the FDA oversees approval and monitors quality and effectiveness for legal prescription drugs. Since marijuana is illegal under federal law and can not be distributed in licensed pharmacies, the oversight of distribution, as well as monitoring and testing of marijuana would fall to the New York State Department of Health. The Department is designated under the bill as the only agency responsible for administering the program. To responsibly implement this bill, the Department of Health must develop protocols to approve marijuana for distribution, test THC levels, monitor quality and oversee dispensaries. No protocols currently exist, so the cost in training, equipment, and personnel will be enormous.

I have consulted with Los Angeles City Attorney Carmen Trutanich, whose office has struggled to oversee an explosion of medical marijuana dispensaries. He has compared smoking marijuana purchased in Los Angeles dispensaries to spraying ***Raid*** ant killer on your salad and eating it. To monitor marijuana quality, Trutanich sent undercover officers to purchase three marijuana samples in local dispensaries. Two of the samples came back with extraordinarily high levels of the insecticide Bifenthrin. One sample was found to have 1600 times the legal digestible limit of Bifenthrin, the other just over 85 times. These kinds of ingredients pose a real health and safety risk to those patients taking the medical marijuana.

In New York City, we seize illegal marijuana laced with cocaine, PCP (angel dust), and many other illegal substances. We have never tested for pesticides. Since there is no way to determine what marijuana contains by looking at it, the Heath Department would have to rigorously oversee dispensaries and test all marijuana before distribution.

New York City will have to absorb millions of dollars in law enforcement costs and civil litigation. There is simply no way, upon visual inspection, to differentiate marijuana raised by authorized growers from marijuana grown in Mexico. Any governmental attempt to control the supply of marijuana to dispensaries would be challenged by international drug traffickers. The bill sets no limits on the number of dispensaries, and is bound to lead to an explosion similar to what occurred in Los Angeles. There are no protections for our schools, parks and children in the current New York State proposal. In addition, the marijuana industry is well funded and litigious. If the New York City attempts to limit dispensaries, it will undoubtedly face costly litigation. The neighborhoods which are the most likely sites for the dispensaries are impoverished areas where rents are low.

I have attached a resolution passed by the Baptist Ministers' Conference of Greater New York and Vicinity stating their strong opposition to the medical marijuana proposal. I urge you to solicit opinions from those in the communities most likely to be affected by the proliferation of dispensaries which would result from the passage of this bill.

In conclusion, the current legislation sets up the same flawed distribution structure that has led to escalating crime and health problems in other states. We must learn from that experience and, at the very least, incorporate the protections they have belatedly adopted. It is not too late for New York State. Please do not urge passage of medical marijuana legislation unless you can be sure that it protects the health and safety of all New Yorkers.

Sincerely,

Bridget G. Brennan

Bridget G. Brennan
Special Narcotics Prosecutor
for the City of New York

The Baptist Ministers' Conference
of
Greater New York & Vicinity.

Headquarters-Convent Avenue Baptist Church
420 W. 145th Street, New York City 10031

Whereas,
We, the official staff and members of The Baptist Ministers' Conference of Greater New York & Vicinity are NOT in support of passing this to become legal.

Whereas,
The affects that the Medical Marijuana would bring to our people is Not what we as Christians practice as Godly and Morally correct behavior.

Whereas,
The impact and exposure that this would bring into our various communities would pose great danger and threats to all concerned. Potential robberies of both vendors, and recipients. Gang territorial drug wars and eventually mass imprisonment and even murders.

Whereas,
Our Youth will be vastly affected, as today peer pressure causes many to experiment and consume un-prescribed medications left unsecured.

Therefore Be It Resolved,
That we embrace the confidence of the Medical Professionals, to find alternative methods of which to cure and treat the conditions at hand, WITHOUT the use of Marijuana.

Be It Further Resolved,
That each of the Clergy will set apart quality time in each of the individual churches to inform our congregants of the traumatic affects that this will cause to our people and our communities. We will take whatever steps necessary as a unit of Christian believers to STOP Medical Marijuana from becoming legal.

And So on this 16th day of July, 2010. It Is Written!

President, Rev. Dr. Calvin E. Owens, Sr.
1st Vice, Rev. Dr. Shellie Sampson, Jr.
2nd Vice, Rev. James D. Morrison
Political Activist, Rev. Dr. John Scott

NADCP
National Association of Drug Court Professionals

need to Know

The Facts On Marijuana

*By **Douglas B. Marlowe**, J.D., Ph.D.*
Chief of Science, Law & Policy
December 2010

Several jurisdictions in the U.S. have taken steps toward decriminalizing marijuana possession for personal use or when recommended by a physician for medicinal purposes. Other jurisdictions have pending ballot initiatives or legislative bills proposing such changes in the law.

The Board of Directors of the National Association of Drug Court Professionals (NADCP) has determined that it is essential for Drug Court practitioners to be fully and objectively informed about the effects of marijuana on their participants and the public at-large. This document briefly reviews the scientific evidence concerning the effects of marijuana.

Incarceration for Marijuana Possession

It is exceedingly rare to be incarcerated in the U.S. for the use or possession of marijuana. According to the National Center on Addiction & Substance Abuse at Columbia University (CASA, 2010), less than 1 percent (0.9%) of jail and prison inmates in the U.S. were incarcerated for marijuana possession as their sole offense.

It is exceedingly rare to be incarcerated in the U.S. for the use or possession of marijuana.

Excluding jail detainees who may be held pending booking or release on bond, the rates are even lower. Prison inmates sentenced for marijuana possession account for 0.7 percent of state prisoners and 0.8 percent of federal prisoners (see Table). And, considering that many of those prisoners pled down from more serious charges, the true incarceration rate for marijuana possession can only be described as negligible.

Prison inmates sentenced for marijuana possession account for 0.7 percent of state prisoners and 0.8 percent of federal prisoners.

	State Prisoners	Federal Prisoners
Marijuana offence only	1.6%	N.R.
Marijuana possession only	0.7%	0.8%
First-time marijuana possession	0.3%	N.R.

Source: Office of National Drug Control Policy, Who's Really in Prison for Marijuana? [NCJ #204299] (citing BJS, 1999, Substance abuse and treatment, state and federal prisoners, 1997 [NCJ #172871]; U.S. Sentencing Commission, 2001 Sourcebook of Federal Sentencing Statistics). N.R. = not reported.

LAW ENFORCEMENT AGAINST PROHIBITION

121 Mystic Avenue, Medford, Massachusetts 02155 - Tele: 781.393.6985 Fax: 781.393.2964 info@leap.cc www.leap.cc

Statement in Support of Proposed Res. No. 94-A
Resolution calling upon the New York State Legislature to pass A.7347/S.2774, legislation that would legalize the medicinal use of marijuana

To:
Ruben Wills, Chairperson
New York City Council Subcommittee on Drug Abuse
And the Committee on Mental Health, Mental Retardation, Alcoholism, Drug Abuse and Disability Services

Submitted By: Lieutenant Joanne Naughton (Ret.), on behalf of
LAW ENFORCEMENT AGAINST PROHIBITON (LEAP)

Friday, November 18, 2011 at 10:00 a.m.
16th Floor Committee Room, 250 Broadway, New York, NY

Thank you for the opportunity to present the views of Law Enforcement Against Prohibition (LEAP) in favor of Proposed Res. No. 94-A. I was a member of the New York Police Department for over 20 years, starting as a police officer and retiring a lieutenant in 1987. I worked in the narcotics bureau making undercover street-level buys for three years. I am a speaker for LEAP, an organization of current and former criminal justice professionals and civilian supporters. We are cops, sheriffs, prosecutors, judges, prison guards and others from nearly every level of law enforcement. Like other law enforcement organizations, LEAP does not endorse or condone the use of marijuana or any other drug.

As a former officer, I know that the voice of police is crucial in the dialogue about our current drug policy, which is wasteful and ineffective. But in the case of medical marijuana, the patient, physician, and caregivers are the ones who should be making decisions about medical care. It is inappropriate for the police to substitute our judgment for that of physicians and those in need of medical care.

One area where law enforcement is qualified to speak regarding medical marijuana is in the area of public safety. Current drug policy prevents police from solving significant crimes because their time is squandered chasing marijuana law violators. This is an especially absurd waste of time when the so-called violators are medical marijuana patients simply trying to obtain the medication recommended by their doctors. This bill and the regulated system established by the New York State Department of Health under this bill will give clear direction to law enforcement on all types of procedural matters surrounding medical marijuana patients

We urge all of you to ratify this legislation, taking into consideration the opinions of doctors, caregivers, patients, and the multiple public health and advocacy organizations that support this legislation. Thank you for your time.

11/13/2011

To Chair G. Oliver Koppel and members of the Committee on Mental Health, Mental Retardation, Alcoholism, Drug Abuse and Disability Services and Chair Ruben Wills and members of the Subcommittee on Drug Abuse,

My name is Sunil Kumar Aggarwal, MD, PhD, and I am a registered voter residing at 564 First Ave, Apt#13H in the Manhattan district of Councilmember Daniel R. Garodnick. Please accept this statement as part of the record for the hearing of 11/18/2011 10:00 AM regarding reaffirming support for Proposed Res. No. 94-A calling upon the New York State Legislature to pass A.7347/S.2774, legislation that would legalize the medicinal use of marijuana. I would ideally like to present this testimony in person, but hospital work duties prevent this.

I am presently a resident physician in the Department of Rehabilitation Medicine at New York University Medical Center. My research activities in medicine and science have led to peer-reviewed publications on cannabinoid medical science, dosing, and health and human rights published in journals of Pain medicine, Hospice and Palliative Medicine, General Medicine, and Law, in addition to a book chapter for the general public. My papers have been cited by State Boards of Pharmacy and have been cited in introductory level college psychology textbooks. For my doctoral dissertation research in medical geography, I studied 176 subjects recruited both from sites of both cannabis delivery and medical consultation. Three years ago, as a medical student delegate, I was the lead author on resolution that called on American Medical Association to urge federal regulatory authorities to review their scheduled drug classification of the botanical marijuana /cannabis based on accumulated evidence from basic science and clinical trials which demonstrate its unambiguous medical utility for a host of difficult-to-treat maladies. Despite this resolution's passage and an ensuing letter from the AMA to federal drug regulatory authorities, and despite statements of support for the immediate allowance of the therapeutic use of marijuana by the Institute of Medicine and American College of Physicians, the federal agencies have maintained an increasingly unscientific and unjust classification of Schedule I for this botanical in federal law, thereby substantially restricting research, impeding the development of a pharmacy stocking system needed for inpatient and outpatient empiric treatment trials, and placing cannabinoid botanical-using patients at risk for criminal sanction.

As we are citizens of the United States of America, where the federal government has failed to follow scientific fact and instead has succumb to obstinacy and politicization, thereby sacrificing people's right to all possible treatment options, we have no choice but to turn to our state governments for help. They have it in their power the ability to choose not comply with this remarkably corrupt system that classifies a long-known commons resource therapeutic botanical as irredeemably dangerous in the highest degree, all the while allowing pharmaceutical corporations free license to bring to market extractions of the same botanical, which the federal government is doing. States are obligated to look after the health and welfare of their citizens and are tasked with the regulation of medical practice. New York City has a long tradition of challenging the irrationality of federal marijuana policy dating back to Mayor Fiorella La Guardia's valiant efforts in the 1940's to use scientific research through the NY Academy of Sciences to rebut earlier claims by the US Department of Treasury that marijuana use led to

homicidal mania, to more recent medical research at Columbia University in the 21st century that proved the appetite and weight-gain stimulating properties of cannabis used therapeutically by patients with HIV/AIDS patients in inpatient clinical trials. Our city must once again stand up for rational policy when it comes to marijuana.

Respectfully Submitted,

Sunil Kumar Aggarwal, MD, PhD

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also cited in The Medical Letter 52:1330, Jan. 25, 2010. This publication has a circulation of 450,000 in 125 countries.

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THE COUNCIL
THE CITY OF NEW YORK

Appearance Card

I intend to appear and speak on Int. No. _____ Res. No. _____

☐ in favor ☐ in opposition

Date: 9/18/11

(PLEASE PRINT)

Name: Adam Karpati

Address: Executive Deputy Commissioner, DoHMH

I represent: _____

Address: 42-09 28th St, Long Island City, NY

THE COUNCIL
THE CITY OF NEW YORK

Appearance Card

I intend to appear and speak on Int. No. _____ Res. No. 94-A

☒ in favor ☐ in opposition

Date: 11/18/11

(PLEASE PRINT)

Name: Ellen B Brickman

Address: 11 Cornell Rd Latham NY 12110

I represent: NYS Nurses Ass'n

Address: _____

THE COUNCIL
THE CITY OF NEW YORK

Appearance Card

I intend to appear and speak on Int. No. _____ Res. No. _____

☑ in favor ☐ in opposition

Date: 11/18/11

(PLEASE PRINT)

Name: Arlene Williams

Address: 301 E. 79th St #36N 10075

I represent: MPP

Address: _____

Please complete this card and return to the Sergeant-at-Arms

THE COUNCIL
THE CITY OF NEW YORK

Appearance Card

I intend to appear and speak on Int. No. _____ Res. No. 94

☑ in favor ☐ in opposition

Date: 11/18/11

(PLEASE PRINT)

Name: Senator Thomas K. Duane

Address: 322 8th Ave, #1700

I represent: _____

Address: _____

THE COUNCIL
THE CITY OF NEW YORK

Appearance Card

I intend to appear and speak on Int. No. _____ Res. No. _____

☒ in favor ☐ in opposition

Date: _____

(PLEASE PRINT)

Name: Hon Richard Gottfried

Address: 242 W 27 St.

I represent: NYS Assembly Committee on Health, Chair

Address: _____

THE COUNCIL
THE CITY OF NEW YORK

Appearance Card

I intend to appear and speak on Int. No. _____ Res. No. 0094-A

☑ in favor ☐ in opposition

Date: 11/18/11

(PLEASE PRINT)

Name: KELLEY GROSSON

Address: 375 SOUTH END AVENUE 8C NYC

I represent: MPP

Address: 236 Massachusetts Ave NE Washington DC

Please complete this card and return to the Sergeant-at-Arms

THE COUNCIL
THE CITY OF NEW YORK

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I intend to appear and speak on Int. No. _____ Res. No. _____

☐ in favor ☑ in opposition

Date: 11/18/11

(PLEASE PRINT)

Name: Greg Bunt MD

Address: 54 W 40th St, NY NY

I represent: NY Society Addiction Medicine

Address: Albany NY

THE COUNCIL
THE CITY OF NEW YORK

Appearance Card

I intend to appear and speak on Int. No. _____ Res. No. 94-A

☐ in favor ☐ in opposition

Date: 11-18-11

(PLEASE PRINT)

Name: JOANNE NAUGHTON

Address: 121 Medford Ave, Mystic, Mass

I represent: LEAP

Address: 121 Medford Ave, Mystic, Mass.

THE COUNCIL
THE CITY OF NEW YORK

Appearance Card

I intend to appear and speak on Int. No. A.7347/S.2774 Res. No. 94-A

☐ in favor ☒ in opposition

Date: 11/18/11

(PLEASE PRINT)

Name: MAX Schwartzberg

Address: 3514 Ave M Bklyn NY 11234

I represent: self

Address: _____

Please complete this card and return to the Sergeant-at-Arms

THE COUNCIL
THE CITY OF NEW YORK

Appearance Card

I intend to appear and speak on Int. No. _____ Res. No. _____

☒ in favor ☐ in opposition

Date: 11/18/11

(PLEASE PRINT)

Name: ILANA LANDECKER

Address: 32-20 33 St. 2Fl, Astoria, NY 11106

I represent: _____

Address: _____

THE COUNCIL
THE CITY OF NEW YORK

Appearance Card

I intend to appear and speak on Int. No. _____ Res. No. _____

☐ in favor ☒ in opposition

Date: 11/18/11

(PLEASE PRINT)

Name: MICHOLAS PACE

Address: 760 5th Ave NYC NY

I represent: Self - as plaintiff

Address: _____

THE COUNCIL
THE CITY OF NEW YORK

Appearance Card

I intend to appear and speak on Int. No. _____ Res. No. _____

☒ in favor ☐ in opposition

Date: 11/18/11

(PLEASE PRINT)

Name: NOAH POTTER, ESQ.

Address: 350 HEMPSTEAD AVENUE, WEST HEMPSTEAD NY 11552

I represent: SELF

Address: _____

Please complete this card and return to the Sergeant-at-Arms