MEDICAL MARIJUANA: FAQS

House Bill 291

Senate Bill 308

Why is it important to legalize marijuana for medical use?

Medical marijuana can relieve suffering and help many people cope with serious medical conditions when conventional treatments have failed.

What does the public think?

The public overwhelmingly favors regulated use of marijuana for medical purposes. An ABC News-Washington Post poll (1/18/10) showed that 81% of Americans favor medical marijuana. In Maryland, the Baltimore Sun's on-line poll had 90% and WBFF-Fox 45 TV poll had 89% in favor of making medical marijuana available to needy patients. This is reflected in the bi-partisan co-sponsorship of House Bill (HB) 291 and Senate Bill (SB) 308.

Doesn't Maryland law already permit medical marijuana?

No. Under current Maryland law, a judge may reduce the sentence of a person convicted of possession of marijuana if there is evidence of medical need. Thus, Maryland already recognizes medical use as legitimate, but the patient is forced to enter the illegal and dangerous drug market to obtain medical marijuana. Further, the person is still left with a criminal conviction and the expense and stress of going to court.

Why is this bill being introduced to the Maryland legislature?

Recently several things have changed.

1) US Attorney General Eric Holder has stated that the federal government will not prosecute in states that have responsible medical marijuana laws.

2) In a major policy shift, the American Medical Association (AMA) has asked that the Drug Enforcement Agency (DEA) consider downgrading marijuana from DEA Schedule 1 to Schedule 2. (See attachment explaining DEA drug schedules for more detail.)

3) 15 states, in addition to the District of Columbia, have medical marijuana laws, the most recent being Arizona, enacted on December 14, 2010. HB 291 seeks to avoid the mistakes of other states. It builds on the New Jersey law, the most narrowly drafted of all states, and also includes provisions and amendments to be even more specific that were added to last year's bill that passed the Maryland State Senate.

What are some examples of diseases or conditions that would benefit from medical marijuana use?

Medical marijuana has helped patients with cancer, cancer treatment and chemotherapy, severe wasting diseases, AIDS, and multiple sclerosis, to name a few. Like any other medication, medical marijuana should be used judiciously, safely, appropriately, and with a doctor's supervision (HB 291, page 6, lines 8-19). Medical marijuana ought to be considered like any other tool in the medical toolbox. As with any treatment, the doctor and patient must weigh risk and benefits, effects and side effects, and alternatives.

How does medical marijuana improve a disease process or help with symptom management, especially compared with medications currently available?

Medical marijuana stimulates specific receptors in the brain and throughout the body. This can help relieve many symptoms including intractable nausea and muscle spasms, and it can improve appetite. For example, one patient with leukemia used medical marijuana after a bone-marrow transplant. It was the only medication that relieved her symptoms of severe bone pain, nausea, and loss of appetite. She used it sparingly for a four-month period. Once her recovery began, she was able to discontinue use.

What is Marinol? Shouldn't it be used first?

Marinol is an oral form of some ingredients in marijuana. It is prescribed legally throughout the United States. Marinol should be tried before medical marijuana is recommended. However, many patients have problems with Marinol: it needs to be taken orally (not easy for patients with severe nausea from cancer chemotherapy); has delayed onset of action; and prolonged activity (up to 6-8 hours) continuing

after the patient's symptoms have eased. Interestingly, Marinol is listed by the Drug Enforcement Agency as Schedule 3, indicating that its risk-safely profile is moderate.

Where would the medical marijuana come from under this bill?

Medical marijuana would be grown in facilities jointly certified by the state Department of Health and Department of Agriculture. This would ensure that the product is pure and of consistent pharmacologic quality (HB 291, page 8, lines 14-23). The bill also requires security measures and background checks for anyone involved in the growing or dispensing of medical marijuana. This would keep the economic activity of medical marijuana within the state instead of funding illegal drug entities.

Would patients be allowed to grow their own marijuana plants?

No. This is illegal now and would continue to be.

Would patients have to see their doctor to get medical marijuana?

Yes. Under this bill, medical marijuana would only be available to a patient who received instructions as part of a bona-fide physician-patient relationship when conventional treatments have failed (HB 291, page 6, lines 4-19 and page 7, lines 17-20).

After seeing a physician, how would a patient get medical marijuana?

Medical marijuana would only be dispensed through state certified dispensaries or by pharmacies that chose to participate. The dispensaries would be licensed by the Department of Health, and demonstrate security measures including background checks on all employees (HB 291, page 10, lines 16-19). Pharmacies would participate only on a voluntary basis. Pharmacies routinely dispense medications, such as narcotics, amphetamines, sedatives, and tranquilizers, with greater risks than those posed by medical marijuana. There are already comprehensive rules and regulations to assure safety and accountability (HB 291, page 9, lines 21-32). Additionally, pharmacists are an integral part of the health care team and are experienced in counseling patients.

What if the patient is too ill to get to a dispensary or pharmacy?

The legislation allows a patient to designate a primary caregiver who can obtain the medical marijuana on the patient's behalf. Unlike other states, HB 219 allows the patient to designate only one primary care giver at a time (HB 291 page 7, lines 7-8), and a caregiver can only fulfill this role for one patient at a time.

How is medical marijuana administered?

Medical marijuana can be administered by several methods. Some patients smoke it. Others use vaporizers to inhale it as a mist. It can also be taken orally: cooked into food or taken as a liquid tincture.

Aren't there side effects and risks with medical marijuana?

Yes, as there are when any medication is taken. That's why the legislation requires that the physician and patient review these. It's important to remember that many medical marijuana users already have serious, debilitating, and sometimes terminal diseases. Medical marijuana can ease their symptoms.

Comparisons to tobacco use don't hold up. Even when inhaled, marijuana is less toxic to the lungs than tobacco, and the amounts used are significantly less.

Can marijuana impair a patient?

Yes, medical marijuana can impair a patient, and so it should be used judiciously and responsibly. All laws concerning use of legal or illegal substances while driving or operating machinery still apply in full force (HB 291, page 21, lines 16-22). Many prescribed medications (narcotics, sedatives, etc.) can impair patients. That's why use of those medications should only be done under a doctor's care and with careful instructions, as this legislation contemplates for medical marijuana.

Shouldn't there be more research on its medicinal use before legalization is considered?

Certainly more research on medical marijuana is needed, but a large body of scientific evidence and clinical experience indicates that medical marijuana has appropriate uses for conditions where conventional treatments have failed. There are over 17,000 published medical articles on marijuana. Some examples are attached.

What do doctors think?

Medical marijuana was legal until the 1940's. Up to that time, it had been used for a wide variety of ailments. After it became illegal, physicians ceased to recommend its use. Today many physicians support its use, some oppose it, and others are undecided. Nothing in the bill requires a physician to recommend medical marijuana use. As with all medications, physicians would be required to follow standards of medical practice, record keeping, and privacy.

Would there be any legal risks to doctors and pharmacists?

The legislation prevents state prosecution of health professionals solely for the reason of recommending or providing medical marijuana (HB 291, page 18, lines 7-24). All standards of care and documentation would continue in full force. As stated above, the federal government has decided not to pursue medical marijuana prosecutions in states where it is legal.

Is this a step towards legalizing marijuana?

That is not the purpose of this legislation, any more than recommending morphine for pain relief should be considered as an endorsement to legalize heroin.

How will this be paid for? Is there any cost to state agencies?

Any state agency costs will be paid by reasonable fees to be set by the agency. We do not anticipate any fiscal note from the Department of Budget and Management.

What are the costs to patients?

Currently Marylanders seeking medical marijuana have to go to the illegal market, with all the attendant risks of cash transactions with dealers and potentially adulterated product. One economic effect of this legislation would be that these funds would stay in Maryland instead of going to overseas drug lords.

While it's impossible to predict exactly what medical marijuana would cost to patients, the experience of other states suggests that it would be less than the current street price (HB 291, page 12, lines 14-16 and page 23 lines 17-19).

There are reports of problems with the medical marijuana system in California. What would prevent Maryland from having a similar situation?

There are many safeguards in this bill that would prevent California's situation from being repeated here. Among these are: state certified growers only; limiting patients to using only one dispensary (HB 291, page 20, lines 11-12); medical marijuana only available in bona-fide doctor-patient relationships; controls on the amount dispensed; only one caregiver listed per patient; and one patient per caregiver.

What is the Drug Enforcement Agency drug schedule?

This is a method of listing drugs by their potential uses and dangers. Drugs are rated from Schedule 1 (most dangerous and without medical use, e.g. heroin) to 5 (least dangerous). Only drugs on Schedules 2-5 can be prescribed to patients. See attached list of drug schedule examples. On the state level, HB 291/SB 308 would move medical marijuana from its current Schedule 1 listing to a more appropriate Schedule 2 status. Again, note that Marinol is a Schedule 3 drug.

What if the next U.S. Attorney General chooses to reverse the current stand on medical marijuana?

If this were to happen, it would impact millions of Americans struggling with serious illness. As more states find responsible ways to permit their citizens to benefit from legal medical marijuana, they are providing examples of how best to implement this policy. As this process continues, it becomes less likely that the federal government would change its current position.

List of Commonly Used Controlled Drugs

Generic Name	Brand Name/Street Name/Common Examples
Schedule 1	
3,4-methylenedioxymethamphetamine (MDMA)	Ecstasy
Alpha-methylfentanyl	China White
Bufotenin	Psychoactive Toad
Gamma-hydroxybutyric acid	GHB, Date Rape Drug, Liquid Ecstasy
Heroin	
Lysergic acid diethylamide	LSD, Acid
Marijuana	
Para-methoxyamphetamine	Dr. Death, Chicken Powder
Psilocybin	Magic Mushrooms, "Shrooms"
Tetrahydrogestrinone	THG, The Clear

Schedule 2	
Amphetamine	Adderall
Cocaine	
Fentanyl	Duragesic
Hydromorphone	Dilaudid
Meperidine	Demerol
Methadone	
Methamphetamine	Meth, Speed, Crank, Crystal Meth
Methylphenidate	Ritalin, Concerta
Morphine	
Phencyclidine	PCP, Angel Dust
Opium (raw, extracts, powder, liquid)	
Oxycodone	OxyContin, Roxicet, Percocet

Schedule 3	
Anabolic Steroids	Testosterone, Body Building Drugs
Buprenorphine	Bupe
Hydrocodone/Acetaminophen	Lortab
Dronabinol	**Marinol**
Dextropropoxyphene	Darvocet
Ketamine	K, Special K, Vitamin K
Paracetamol/Acetaminophen	Tylenol 3
Paracetamol/Hydrocodone	Vicodin

Schedule 4	
Benzodiazepine class	Xanax, Valium, Klonopin, Librium, Ativan, Versed
Phenobarbital	
Phentermine	
Zaleplon	Sonata
Zolpidem	Ambien

Schedule 5	
Codeine	Robitussin AC
Diphenoxylate	Lomotil
Pregabalin	Lyrica

LIGHT FOR ALL
THE BALTIMORE SUN

Marijuana conundrum

Our view: We don't want to emulate California's freewheeling medical cannabis program, but doctors, not judges, should decide when a drug is medically necessary

February 1, 2010

Everyone has heard the horror stories from California, which after passing a 1996 law legalizing the medical use of marijuana for patients with cancer and other serious illnesses found itself awash in pot shops and physicians who seemed all too eager to hand out cannabis prescriptions to anyone who asked, regardless of the complaint. California is belatedly moving to correct the worst abuses of that law, but the sheer number of loosely regulated pot dispensaries and pharmacies that sprang up after its passage is making reform an uphill struggle.

We certainly don't want to see California's experience replicated in Maryland, where a proposal to legalize marijuana for medical use is pending in the General Assembly this year. Opinion remains divided among the medical community over the potential therapeutic benefits and risks of medical marijuana. Yet there's enough anecdotal and other evidence suggesting it can ease the suffering of some patients diagnosed with chronic and terminal illnesses that the idea shouldn't be dismissed out of hand.

Maryland already acknowledges -- and in some ways actually encourages -- this ambivalence. The state's current law on the subject, passed six years ago, doesn't explicitly exempt the medical use of marijuana from criminal prosecution, but it does allow people accused of possessing small quantities of the drug to claim "medical necessity" as a defense. If a judge accepts their claim, they can get off with a fine not exceeding $100 -- less than some parking tickets. The problem with the current statute, of course, is that it still forces people who do have a genuine medical necessity to break the law -- and risk being slapped with a criminal record -- simply in order to get the treatment they need. And it makes judges, rather than doctors, the ultimate arbiters of what is medically necessary.

That's unacceptable, especially given last year's decision by the Justice Department to stop aggressively pursuing medical marijuana patients in the 14 states that have laws allowing the drug's use. We always thought the Bush administration's claim that medical marijuana was a mortal threat to the republic was overblown. Doctors routinely prescribe far more potent medications to patients -- including derivatives of cocaine -- and the country hasn't collapsed.

The legislation proposed by Del. Dan Morhaim, a Baltimore County Democrat, and Republican Sen. David Brinkley of Frederick would allow patients with debilitating illnesses such as seizures, severe chronic pain or severe nausea as a result of cancer treatment to register with the state and to purchase marijuana from state-licensed dispensaries and pharmacies. Mr. Morhaim, an internist and emergency medical physician, says the goal is to make medical marijuana as readily available as other medications currently in use by physicians, and with the same legal and medical safeguards.

To avoid the problems of the California law, the bill would require patients to get approval only from doctors with whom they have a long-standing relationship, and it would also prohibit them from growing marijuana on their own. As long as the controls are in place to restrict purchases to patients with valid prescriptions at authorized dispensaries and pharmacies, we see little chance of this turning into a California-style debacle or even the opening skirmish in a full-scale legalization campaign.

No one would deny a seriously ill patient the benefits of anesthesia during major surgery, or arrest him or her for taking painkillers afterward. To the extent that medical marijuana holds the potential to provide a similar therapeutic benefit, why should anyone have to risk going to jail for taking a medication that his or her doctor has decided is medically necessary?

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February 15, 2010

Delegate Dan Morhaim, MD
House of Delegates
6 Bladen Street, #362
Annapolis, Maryland 21401

Dear Delegate Morhaim:

I am happy to provide this letter of support for the legalization of marijuana for medical use (House Bills 712/713; Senate Bills 579/627). I find it intriguing that in Maryland we recognize the medical usefulness of marijuana, but it remains a federal offense for a patient to obtain marijuana. When we use any medication to treat a patient, we must carefully consider the benefits and burdens of therapy, and the use (and legalization) of marijuana is no different. I am currently employed as a Professor at the University of Maryland School of Pharmacy, and my practice is both in ambulatory care and working with hospice patients. I serve as the Chairman of the Board of the American Society of Pain Educators and I am on the Board of the Hospice and Palliative Care Network of Maryland. The views in this letter are entirely my own opinion.

At present we have two synthetic oral cannabinoids available in the US – **dronabinol** (Marinol) and **nabilone** (Cesamet); both are FDA approved for chemotherapy-induced nausea and vomiting. Dronabinol is also approved for the treatment of anorexia with weight loss in AIDS patients; this medication has been shown to be safe and it is rarely abused. Disadvantages to dronabinol include its variable absorption, slow rate of onset and a long duration of action, which makes it difficult to titrate to an effective dose. As an oral dosage form, it is frequently not well tolerated by patients with nausea and vomiting. An oromucosal cannabinoid spray has been approved for use in Canada (nabiximols; Sativex) for the management of neuropathic pain in multiple sclerosis patients, and it is currently being evaluated for intractable cancer pain in the US.

When we consider the **benefits** and **burdens** of smoked marijuana we find that there are numerous clinical trials that have more than adequately demonstrated equivalent or superior efficacy as compared to FDA-approved medications currently on the market. The therapeutic benefit of smoked marijuana as an **antiemetic** following cancer chemotherapy has been demonstrated conclusively. Some of these data show a better clinical effect with smoked marijuana than with more traditional antiemetic agents. Smoked marijuana has also been shown to have a positive effect in the management of **refractory pain** (especially neuropathic pain) and **loss of appetite**. When we consider a difficult to manage pain such as neuropathic pain, a “clinically significant” response is considered to be a 30% reduction in pain. A recent study compared smoked marijuana to placebo in HIV patients with significant neuropathic pain. Results showed

that **46% of patients achieved at least a 30% reduction in pain**.[1] This is better data than we have for many analgesics approved by the FDA, medications that enjoy wide-spread prescribing. Additional clinical trials have demonstrated the therapeutic potential of smoked marijuana in the management of multiple sclerosis, spinal cord injuries, Tourette's syndrome, epilepsy and glaucoma.

Obviously there are burdens associated with medical marijuana treatment as well. As I mentioned in the first paragraph, even though we recognize the therapeutic benefits of marijuana in Maryland, it is still illegal to buy or grow this drug. Further, there is no standardization in dosing, and certainly no quality assurance in production. I strongly support these legislative proposals that include guidelines on how and where medical marijuana would be grown and distributed. This would greatly reduce the risks associated with acquiring marijuana from presently available sources.

All medications have adverse effects and marijuana is no exception. Any psychoactive medication should be prescribed and dispensed judiciously, after thorough examination by an independent licensed practitioner. We have a huge drug abuse and diversion problem in this country; one of our best strategies is to insist on adherence to good principles of patient assessment and follow-up and the use of medical marijuana is no exception.

Delegate Morhaim, I have spent my entire career working with patients in pain, both ambulatory patients, and to a greater degree patients with advanced illness receiving hospice care. **Access to pain relief is a basic and essential human right**, endorsed by numerous groups including the International Association for Hospice and Palliative Care and the World Hospice and Palliative Care groups. You have never in your life seen a group of practitioners who are stronger patient advocates that those who care for the terminally ill. We work ceaselessly to provide care and comfort when a cure is no longer possible. Advanced cancer patients, those with end-stage HIV, and patients with other diseases suffer and endure debility, anorexia and cachexia, neuropathic and refractory pain. My resident recently conducted a survey of hospice practitioners, and over **86% of respondents agreed that marijuana has medical benefits**, and **87% of respondents felt that prescribers should be allowed to order smoked marijuana without fear of prosecution** (unpublished data). These are health care practitioners who work "in the trenches" and any tool we can add to our armamentarium to treat pain and suffering is a welcome one. I strongly support this legislation, I believe the data attesting to the therapeutic benefits of medical marijuana, and I would welcome the guidelines and restrictions for growing and distributing this important medication. No drug is the right drug for all patients; medical marijuana is no exception. Thank you for your work in this important area.

Sincerely,

Mary Lynn McPherson

Mary Lynn McPherson, Pharm.D., BCPS, CPE

1. Ellis RJ et al. Smoked medicinal cannabis for neuropathic pain in HIV: a randomized, crossover clinical trial. Neuropsychopharmacology 2009;34:672-680.

MEDCHI, THE MARYLAND STATE MEDICAL SOCIETY
HOUSE OF DELEGATES

Resolution 12-10

INTRODUCED BY: Baltimore County Medical Association

SUBJECT: Medical Marijuana

REFERRED TO: Reference Committee B

Whereas, medical marijuana can relieve suffering and help patients cope with serious medical conditions when conventional treatments have failed; and

Whereas, current evidence suggests that medical marijuana can relieve intractable nausea, muscle spasms, and improve appetite in patients with debilitating chronic illnesses including cancer, multiple sclerosis, and AIDS; and

Whereas, medical marijuana should be available for prescription to patients after careful consideration of the benefits and risks, including side effects, with their physician; and

Whereas, dronabinol, the currently available oral form of one of the ingredients of medical marijuana, needs to be taken orally, has a delayed onset of action, has a prolonged duration, and may not be as effective; and

Whereas, the safety of medical marijuana is demonstrated by the fact that there has never been a documented fatality due to overdose of dronabinol or cannabis; and

Whereas, patients are forced to enter the illegal and dangerous street drug market to obtain marijuana of uncertain quality for medical use, and can be convicted of a crime in Maryland as a result; and

Whereas, Our AMA has policy in place which supports well-controlled studies of marijuana in patients who have serious medical conditions for which current evidence suggests efficacy; therefore be it

Resolved, that MedChi, The Maryland State Medical Society, affirm and support the principles embodied in AMA Policy H-95.952, in particular the need for full objective investigation of the clinical benefits and risks of marijuana in patients who have serious medical conditions.

As amended and adopted by the House of Delegates at its meeting on September 26, 2010.

ORIGINAL ARTICLE

Medicinal use of cannabis in the United States: Historical perspectives, current trends, and future directions

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ABSTRACT

Cannabis (marijuana) has been used for medicinal purposes for millennia, said to be first noted by the Chinese in c. 2737 BCE. Medicinal cannabis arrived in the United States much later, burdened with a remarkably checkered, yet colorful, history. Despite early robust use, after the advent of opioids and aspirin, medicinal cannabis use faded. Cannabis was criminalized in the United States in 1937, against the advice of the American Medical Association submitted on record to Congress. The past few decades have seen renewed interest in medicinal cannabis, with the National Institutes of Health, the Institute of Medicine, and the American College of Physicians, all issuing statements of support for further research and development. The recently discovered endocannabinoid system has greatly increased our understanding of the actions of exogenous cannabis. Endocannabinoids appear to control pain, muscle tone, mood state, appetite, and inflammation, among other effects. Cannabis contains more than 100 different cannabinoids and has the capacity for analgesia through neuromodulation in ascending and descending pain pathways, neuroprotection, and anti-inflammatory mechanisms. This article reviews the current and emerging research on the physiological mechanisms of cannabinoids and their applications in managing chronic pain, muscle spasticity, cachexia, and other debilitating problems.

Key words: cannabinoids, cannabis, marijuana, chronic pain, opioids, opiates, botanical medicine

INTRODUCTION: AN OVERVIEW OF CANNABINOID MEDICINE IN THE UNITED STATES

Though disrupted by a post-1937 *Cannabis sativa* L. prohibition, the emerging field of cannabinoid medicine is growing in the United States (see Figure 1) as ever greater numbers of healthcare providers become educated about the physiologic importance of the endogenous cannabinoid system[1-3] and about the wide safety margins[4] and broad clinical efficacies[5-8] of cannabinoid drugs. Cannabinoid medicines are available in both purely botanical and purely chemical varieties and are useful for managing pain and other conditions in the growing chronically and critically ill patient population.[9] This article provides a current and historical perspective of the use of cannabinoid therapies in the United States.

The following is a brief overview of the various cannabinoid medicines currently utilized in the American healthcare sector. They fall into three categories: single molecule pharmaceuticals, cannabis-based liquid extracts, and phytocannabinoid-dense botanicals—the main focus of this article (Figure 2). The first category includes US Food and Drug Administration (FDA)-approved synthetic or semi-synthetic single molecule cannabinoid pharmaceuticals available by prescription. Currently, these are dronabinol, a Schedule III drug and nabilone, a Schedule II drug. Though both are also used off-label, dronabinol, a (-)*trans*-Δ9-tetrahydrocannabinol (THC) isomer found in natural cannabis, has been approved for two uses since 1985 and 1992,

department patients from the Drug Abuse Warning Network (DAWN) for the period 1994-2002 were examined in three metropolitan areas in California (Los Angeles, San Diego, San Francisco), one in Colorado (Denver), and one in Washington State (Seattle). The analysis followed an interrupted time-series design. There was no statistically significant pre-medical marijuana law versus post-medical marijuana law differences found in any of the ADAM or DAWN sites. Thus, consistent with other studies of the liberalization of cannabis laws, medical cannabis laws do not appear to increase use of the drug. The authors theorized that the use of medical cannabis by "sick" patients might "de-glamorize" its use and thereby actually discourage use among others.

The scientific process continues to evaluate the therapeutic effects of marijuana through ongoing research and assessment of available data. With regard to the medicinal use of marijuana, our legal system should take a similar approach, using amassed scientific evidence and logic as the basis of policy-making rather than political views and societal trends that are more reflective of the ongoing debate over any potential harmful effects of recreational marijuana use. At the same time, physicians and medical students should make extra efforts to fill in the gaps in their training and knowledge base by educating themselves in the art and science of cannabinoid medicine.

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Smoked Medicinal Cannabis for Neuropathic Pain in HIV: A Randomized, Crossover Clinical Trial

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Despite management with opioids and other pain modifying therapies, neuropathic pain continues to reduce the quality of life and daily functioning in HIV-infected individuals. Cannabinoid receptors in the central and peripheral nervous systems have been shown to modulate pain perception. We conducted a clinical trial to assess the impact of smoked cannabis on neuropathic pain in HIV. This was a phase II, double-blind, placebo-controlled, crossover trial of analgesia with smoked cannabis in HIV-associated distal sensory predominant polyneuropathy (DSPN). Eligible subjects had neuropathic pain refractory to at least two previous analgesic classes; they continued on their prestudy analgesic regimens throughout the trial. Regulatory considerations dictated that subjects smoke under direct observation in a hospital setting. Treatments were placebo and active cannabis ranging in potency between 1 and 8% Δ-9-tetrahydrocannabinol, four times daily for 5 consecutive days during each of 2 treatment weeks, separated by a 2-week washout. The primary outcome was change in pain intensity as measured by the Descriptor Differential Scale (DDS) from a pretreatment baseline to the end of each treatment week. Secondary measures included assessments of mood and daily functioning. Of 127 volunteers screened, 34 eligible subjects enrolled and 28 completed both cannabis and placebo treatments. Among the completers, pain relief was greater with cannabis than placebo (median difference in DDS pain intensity change, 3.3 points, effect size = 0.60; $p = 0.016$). The proportions of subjects achieving at least 30% pain relief with cannabis versus placebo were 0.46 (95%CI 0.28, 0.65) and 0.18 (0.03, 0.32). Mood and daily functioning improved to a similar extent during both treatment periods. Although most side effects were mild and self-limited, two subjects experienced treatment-limiting toxicities. Smoked cannabis was generally well tolerated and effective when added to concomitant analgesic therapy in patients with medically refractory pain due to HIV DSPN.
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Keywords: HIV; clinical; neuropathic pain; cannabis; polyneuropathy

INTRODUCTION

In 1999, a report of the United States Institute of Medicine (Watson *et al*, 2000) recommended further investigations of the possible benefits of cannabis (marijuana) as a medicinal agent for a variety of conditions, including neuropathic pain due to HIV distal sensory polyneuropathy (DSPN). The most abundant active ingredient in cannabis, tetrahydrocannabinol (THC), and its synthetic derivatives, produce effective analgesia in most animal models of pain (Mao *et al*, 2000; Martin and Lichtman, 1998). The antinociceptive effects of THC are mediated through cannabinoid receptors (CB1, CB2) in the central and peripheral nervous systems (Calignano *et al*, 1998), which in turn interact with noradrenergic and κ-opioid systems in the spinal cord to modulate the perception of painful stimuli. The endogenous ligand of CB1, anandamide, itself is an effective antinociceptive agent (Calignano *et al*, 1998). In open-label clinical trials and one recent controlled trial (Abrams *et al*, 2007), medicinal cannabis has shown preliminary efficacy in relieving neuropathic pain.

Neuropathic pain in HIV is an important and persisting clinical problem, affecting 30% or more of HIV-infected individuals. Although combination antiretroviral (ARV) therapy has improved immunity and survival in HIV, it does not significantly benefit neuropathic pain. In fact, certain nucleoside-analogue HIV reverse transcriptase inhibitors, such as didanosine and stavudine, contribute to the frequent occurrence of painful DSPN, possibly through mitochondrial toxicity. Existing analgesic and adjunctive treatments are inadequate; neuropathic pain in DSPN persists in many cases despite attempts at management with opioids, nonsteroidal anti-inflammatory agents, and adjunctive pain modifying therapies, and patients suffer unfavorable side effects, reducing life quality and socioeconomic productivity.

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Review

Cannabinoids in medicine: A review of their therapeutic potential

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Abstract

In order to assess the current knowledge on the therapeutic potential of cannabinoids, a meta-analysis was performed through Medline and PubMed up to July 1, 2005. The key words used were cannabis, marijuana, marihuana, hashish, hashich, haschich, cannabinoids, tetrahydrocannabinol, THC, dronabinol, nabilone, levonantradol, randomised, randomized, double-blind, simple blind, placebo-controlled, and human. The research also included the reports and reviews published in English, French and Spanish. For the final selection, only properly controlled clinical trials were retained, thus open-label studies were excluded.

Seventy-two controlled studies evaluating the therapeutic effects of cannabinoids were identified. For each clinical trial, the country where the project was held, the number of patients assessed, the type of study and comparisons done, the products and the dosages used, their efficacy and their adverse effects are described. Cannabinoids present an interesting therapeutic potential as antiemetics, appetite stimulants in debilitating diseases (cancer and AIDS), analgesics, and in the treatment of multiple sclerosis, spinal cord injuries, Tourette's syndrome, epilepsy and glaucoma.

Keywords: Cannabinoids; Cannabis; Therapeutic potential; Controlled clinical trials; Efficacy; Safety

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1. Introduction

Originating from Central Asia, cannabis is one of the oldest psychotropic drugs known to humanity. The beginnings of its use by humans are difficult to trace, because it was cultivated and consumed long before the appearance of writing. According to archeological discoveries, it has been known in China at least since the Neolithic period, around 4000 BC (McKim, 2000).

There are several species of cannabis. The most relevant are *Cannabis sativa*, *Cannabis indica* and *Cannabis ruderalis*. *Cannabis sativa*, the largest variety, grows in both tropical and temperate climates. The two main preparations derived from cannabis are marijuana and hashish. Marijuana is a Mexican term initially attributed to cheap tobacco but referring today to the dried leaves and flowers of the hemp plant. Hashish, the Arabic name for Indian hemp, is the viscous resin of the plant (Ben Amar and Léonard, 2002).

The Emperor of China, Shen Nung, also the discoverer of tea and ephedrine, is considered to be the first to have described the properties and therapeutic uses of cannabis in his compendium of Chinese medicinal herbs written in 2737 BC (Li, 1974). Soon afterwards, the plant was cultivated for its fibre, seeds, recreational consumption and use in medicine. It then spread to India from China (Mechoulam, 1986).

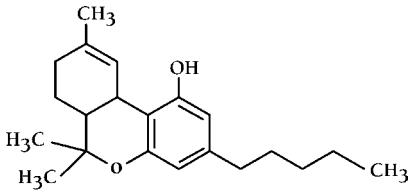
In 1839, William O'Shaughnessy, a British physician and surgeon working in India, discovered the analgesic, appetite stimulant, antiemetic, muscle relaxant and anticonvulsant properties of cannabis. The publication of his observations quickly led to the expansion of the medical use of cannabis (O'Shaugnessy, 1838–1840). It was even prescribed to Queen Victoria for relief of dysmenorrhea (Baker et al., 2003).

In 1854, cannabis is listed in the United States Dispensatory (Robson, 2001). It is sold freely in pharmacies of Western countries. It would be available in the British Pharmacopoeia in extract and tincture form for over 100 years (Iversen, 2000).

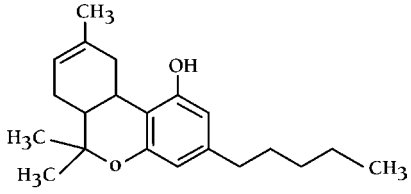
However, after prohibition of alcohol was lifted, the American authorities condemned the use of cannabis, making it responsible for insanity, moral and intellectual deterioration, violence and various crimes. Thus, in 1937, under pressure from the Federal Bureau of Narcotics and against the advice of the American Medical Association, the U.S. Government introduced the *Marihuana Tax Act*: a tax of $1 per ounce was collected when marijuana was used for medical purposes and $100 per ounce when it was used for unapproved purposes (Solomon, 1968; Carter et al., 2004). In 1942, cannabis was removed from the United States Pharmacopoeia, thus losing its therapeutic legitimacy (Fankhauser, 2002).

Great Britain and most European countries banned cannabis by adopting the 1971 Convention on Psychotropic Substances instituted by the United Nations.

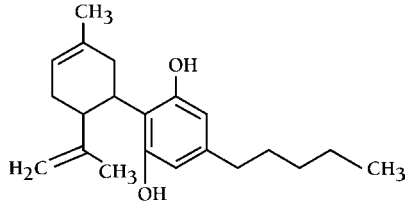
Cannabis contains more than 460 known chemicals, more than 60 of which are grouped under the name cannabinoids (Ben Amar, 2004). The major psychoactive ingredient of cannabis is delta-9-tetrahydrocannabinol, commonly known as THC. Other cannabinoids present in Indian hemp include delta-8-tetrahydrocannabinol (Δ^8THC), cannabinol (CBN), cannabidiol (CBD), cannabicyclol (CBL), cannabichromene (CBC) and cannabigerol (CBG), but they are present in small quantities and have no significant psychotropic effects compared to THC (Smith, 1998; McKim, 2000). However, they may have an impact on the product's overall effect (Ashton, 2001). Cannabinoids exert their actions by binding to specific receptors: the CB_1 cannabinoid receptors, discovered by Devane et al. (1988), then cloned by Matsuda et al. (1990) and the CB_2 cannabinoid receptors, identified by Munro et al. (1993). Both cannabinoid receptors are part of the G-protein coupled class and their activation results in inhibition of adenylate cyclase activity. The identification of agonists (anandamide and 2-arachidonylglycerol, the most studied endocannabinoids, participate in the regulation of neurotransmission) and antagonists of these receptors has stimulated interest in the medical uses of cannabis (Baker et al., 2003; Iversen, 2003; Di Marzo et al., 2004).



Δ^9- tetrahydrocannabinol (THC)



Δ^8- tetrahydrocannabinol



Cannabidiol (CBD)

Despite its illegality, patients have continued to obtain cannabis on the black market for self-medication. In 1978, in response to the success of a lawsuit filed by a glaucoma patient (Robert Randall) who had begun treating himself by smoking marijuana after losing a substantial part of his vision, the U.S. Government created a compassionate program for medical marijuana: 20 people suffering from debilitating diseases legally received marijuana cigarettes from the National Institute on Drug Abuse (NIDA), after approval by the Food and Drug Administration (FDA). This program was closed to new candidates in 1991 by President Bush, but still recently seven people continued to receive their marijuana (Mirken, 2004).

In Canada, 14 years after the 1988 arrest of Terrance Parker (an Ontario patient who had discovered that marijuana con-

sumption relieved his epileptic attacks, contrary to conventional drugs) and 1 year after the Ontario Court of Appeal ruled that discretionary regulation of marijuana use for medical purposes was contrary to the principles of the Canadian Charter of Rights and Freedoms, the Government of Canada decided to draft new regulations (Hoey, 2001). Thus, since July 30, 2001, the *Marihuana Medical Access Regulations* (MMAR) allow Canadian patients suffering from a serious disease to be eligible for therapeutic marijuana consumption. As of April 2005, 821 people were thus authorized to possess marijuana for medical purposes and 363 physicians had supported a request for authorization of possession (Health Canada, 2005).

The therapeutic applications of cannabis and its derivatives have been studied by various world bodies, including the Scientific Committee of the House of Lords in Great Britain (1998), the Institute of Medicine in the United States (1999) and the Senate Special Committee on Illegal Drugs in Canada (Nolin et al., 2002). Since 2003, medicinal cannabis, in standard cannabinoid concentrations, is sold in pharmacies in the Netherlands by medical prescription (Gorter et al., 2005). It is presently available in two dosages: cannabis flos, variety Bedrocan, containing 18% dronabinol and 0.8% cannabidiol and cannabis flos, variety Bedrobinol, containing 13% dronabinol and 0.2% cannabidiol (Office of Medicinal Cannabis, 2005). Various Western countries have authorized and conducted clinical trials on cannabis and its derivatives. Thus, for example, since 1999, Health Canada, in collaboration with the Canadian Institutes of Health Research, has established a Medical Marihuana Research Program (Health Canada/CIHR, 1999).

To date, there are a multitude of anecdotal reports and a certain number of clinical trials evaluating the therapeutic applications of cannabis and its derivatives. This review reports on the most current data available on the therapeutic potential of cannabinoids.

December 3, 2010

New Jersey Closer to Sales of Medical Marijuana

By ANEMONA HARTOCOLLIS

A standoff between Gov. Chris Christie of New Jersey and advocates for medical marijuana has ended in a compromise that could put marijuana on the market for seriously ill patients by next summer.

The new regulations, announced on Friday, would provide for six growing and distribution sites for medical marijuana in various parts of the state. The governor had wanted to limit the number of growers to two and distribution sites to four.

But among the states that allow it, New Jersey would become the only one to limit the amount of psychotropic chemical permitted in the marijuana.

While the Christie administration had pushed to require qualifying patients to exhaust all other treatments before receiving medical marijuana, the compromise applies that restriction to only three nonfatal conditions: seizures, glaucoma and intractable muscle spasms.

Mr. Christie hailed the compromise as “the best way to move forward on a responsible, medically based program that will avoid the significant fraud and criminal diversion that other states have experienced.”

Gov. Jon S. Corzine signed New Jersey’s medical marijuana law as he was leaving office in January, making New Jersey the 14th state to legalize the treatment. New York and Connecticut have not.

Since then, Mr. Christie, who was skeptical of the legalization, has been haggling with lawmakers and advocates over the particulars of how to carry out the law.

Advocates of medical marijuana complained on Friday that despite the compromise, the regulations continued to discourage access to the drug: by forbidding home cultivation or

July 23, 2010

V.A. Easing Rules for Users of Medical Marijuana

By DAN FROSCH

DENVER — The Department of Veterans Affairs will formally allow patients treated at its hospitals and clinics to use medical marijuana in states where it is legal, a policy clarification that veterans have sought for several years.

A department directive, expected to take effect next week, resolves the conflict in veterans facilities between federal law, which outlaws marijuana, and the 14 states that allow medicinal use of the drug, effectively deferring to the states.

The policy will not permit department doctors to prescribe marijuana. But it will address the concern of many patients who use the drug that they could lose access to their prescription pain medication if caught.

Under department rules, veterans can be denied pain medications if they are found to be using illegal drugs. Until now, the department had no written exception for medical marijuana.

This has led many patients to distrust their doctors, veterans say. With doctors and patients pressing the veterans department for formal guidance, agency officials began drafting a policy last fall.

“When states start legalizing marijuana we are put in a bit of a unique position because as a federal agency, we are beholden to federal law,” said Dr. Robert Jesse, the principal deputy under secretary for health in the veterans department.

At the same time, Dr. Jesse said, “We didn’t want patients who were legally using marijuana to be administratively denied access to pain management programs.”

The new, written policy applies only to veterans using medical marijuana in states where it is legal. Doctors may still modify a veteran’s treatment plan if the veteran is using marijuana,

AMA Calls for Feds to Review Marijuana Restrictions

CBS News: November 11, 2009

The American Medical Association on Tuesday adopted a resolution calling for the government to review its classification of marijuana, in order to ease the way for more research into the use of medical marijuana.

While the AMA, the largest physician's organization in the U.S., explicitly states it does not endorse any current state-based medical marijuana programs or the legalization of marijuana, the move is a significant shift that continues a trend toward support for easing restrictions against the drug.

"Our American Medical Association (AMA) urges that marijuana's status as a federal Schedule I controlled substance be reviewed with the goal of facilitating the conduct of clinical research and development of cannabinoid-based medicines," the AMA's statement (PDF) reads. "This should not be viewed as an endorsement of state-based medical cannabis programs, the legalization of marijuana, or that scientific evidence on the therapeutic use of cannabis meets the current standards for a prescription drug product."

Marijuana is currently classified by the federal government as a "Schedule I" controlled substance, the most restrictive of five categories. Schedule I substances are considered to have a high potential for abuse, no accepted medical use and a lack of accepted safety for use of the drug. Other drugs in that category include heroin, LSD and PCP. Less restrictive "Schedule II" substances include cocaine and methamphetamine.

Previously, the AMA recommended marijuana remain a Schedule I controlled substance, but it now believes the substance deserves more clinical research.

"Despite more than 30 years of clinical research, only a small number of randomized, controlled trials have been conducted on smoked cannabis," Dr. Edward Langston, an AMA board member, told the Los Angeles Times. Limited studies, he said, are "insufficient to satisfy the current standards for a prescription drug product."

The White House drug czar's office gave a muted response to the AMA's recommendation, the LA Times reports, saying it would defer to "the FDA's judgment that the raw marijuana plant cannot meet the standards for identity, strength, quality, purity, packaging and labeling required of medicine."

While the Obama administration opposes legalization of marijuana, the Justice Department last month announced it would no longer pursue prosecution for state-sanctioned medical marijuana sales. As many as 13 states now allow the use of medical marijuana.

The debate over whether to legalize marijuana all together seems to be gaining steam. A Gallup poll last month showed a record 44 percent of Americans now support legalizing marijuana. Meanwhile, California residents may get to vote on a 2010 ballot measure to legalize the drug in the state.

Marijuana Use Seldom Associated With Emergency Room Visits, First-Ever National Study

July 20, 2010

Lifetime use of marijuana is rarely associated with emergency room visits, according to an analysis of epidemiologic survey data published online by the American Journal of Emergency Medicine.

Investigators at the University of Michigan reviewed the overall prevalence of drug-related emergency department (ED) visits among lifetime users of illicit substances. Researchers analyzed data from the National Epidemiologic Survey on Alcohol and Related Conditions, which is a nationally representative survey of 43,093 residents age 18 or older. The study is the first to use nationally representative data to examine patterns and correlates of drug-related ED visits.

Among those surveyed, subjects that reported using cannabis were the least likely to report an ED visit (1.71 percent). Respondents who reported lifetime use of heroin, tranquilizers, and inhalants were most likely (18.5 percent, 6.3 percent, and 6.2 percent respectively) to report experiencing one or more ED visits related to their drug use.

Investigators concluded, "[M]arijuana was by far the most commonly used (illicit) drug, but individuals who used marijuana had a low prevalence of drug-related ED visits."

A 2009 Swiss study published in journal BMC Public Health previously reported that the use of cannabis was inversely associated with injuries requiring hospitalization.

A prior case-control study conducted by the University of Missouri also reported an inverse relationship between marijuana use and injury risk, finding, "Self-reported marijuana use in the previous seven days was associated … with a substantially decreased risk of injury."

Most recently, a RAND study published this month reported that fewer than 200 total patients were admitted to California hospitals in 2008 for "marijuana abuse or dependence." By contrast, there are an estimated 73,000 annual hospitalizations in California related to the use of alcohol.

These findings belie the myth that adult marijuana use is a primary cause of hospitalizations or ED visits. The reality is that few if any therapeutic or psychoactive substances possess a safety profile comparable to cannabis.

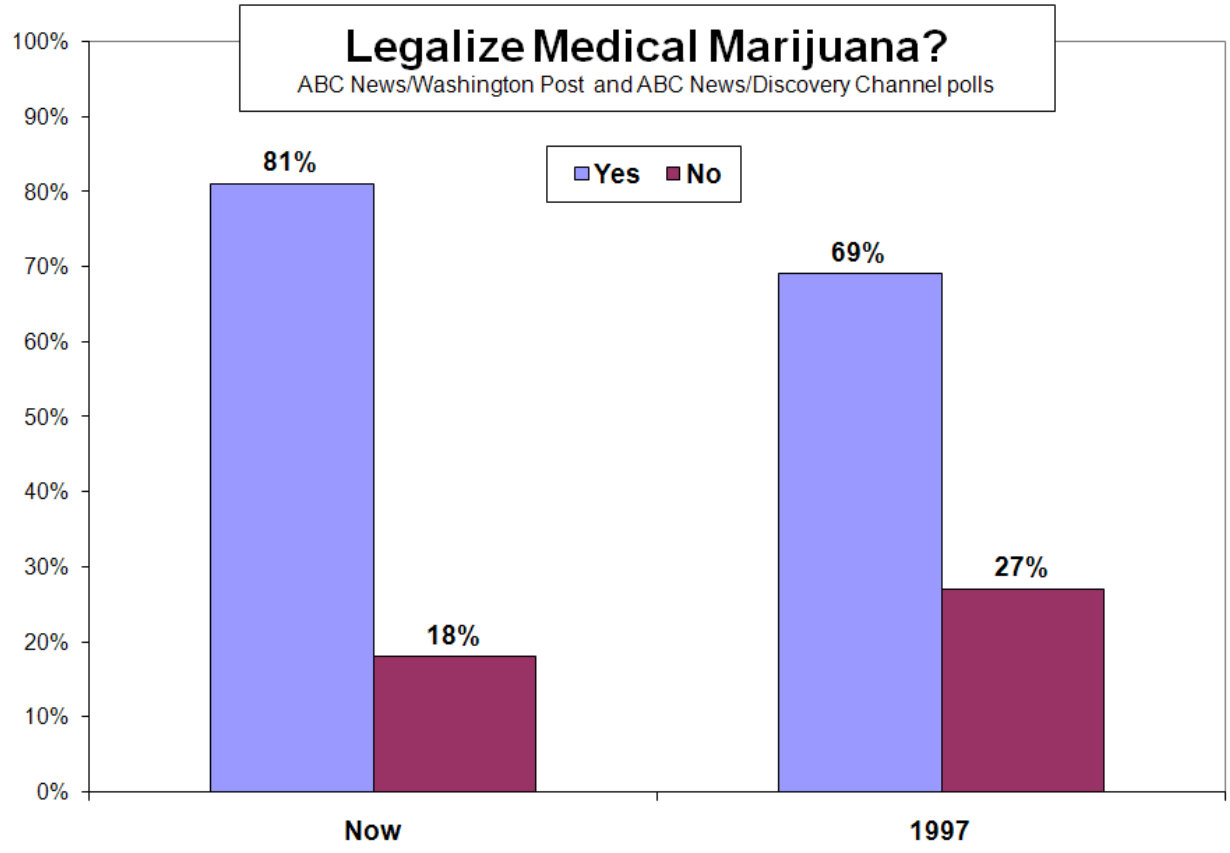
ABC NEWS/WASHINGTON POST POLL: MEDICAL MARIJUANA
EMBARGOED FOR RELEASE AFTER 5 p.m. Monday, Jan. 18, 2010

Poll Shows Widespread Support for Medical Marijuana

Eight in 10 Americans support legalizing marijuana for medical use and nearly half favor decriminalizing the drug more generally, both far higher than a decade ago.

With New Jersey this week poised to become the 14th state to legalize medical marijuana, 81 percent in this national ABC News/Washington Post poll support the idea, up from an already substantial 69 percent in 1997. Indeed the main complaint is with restrictions on access, as in the New Jersey law.

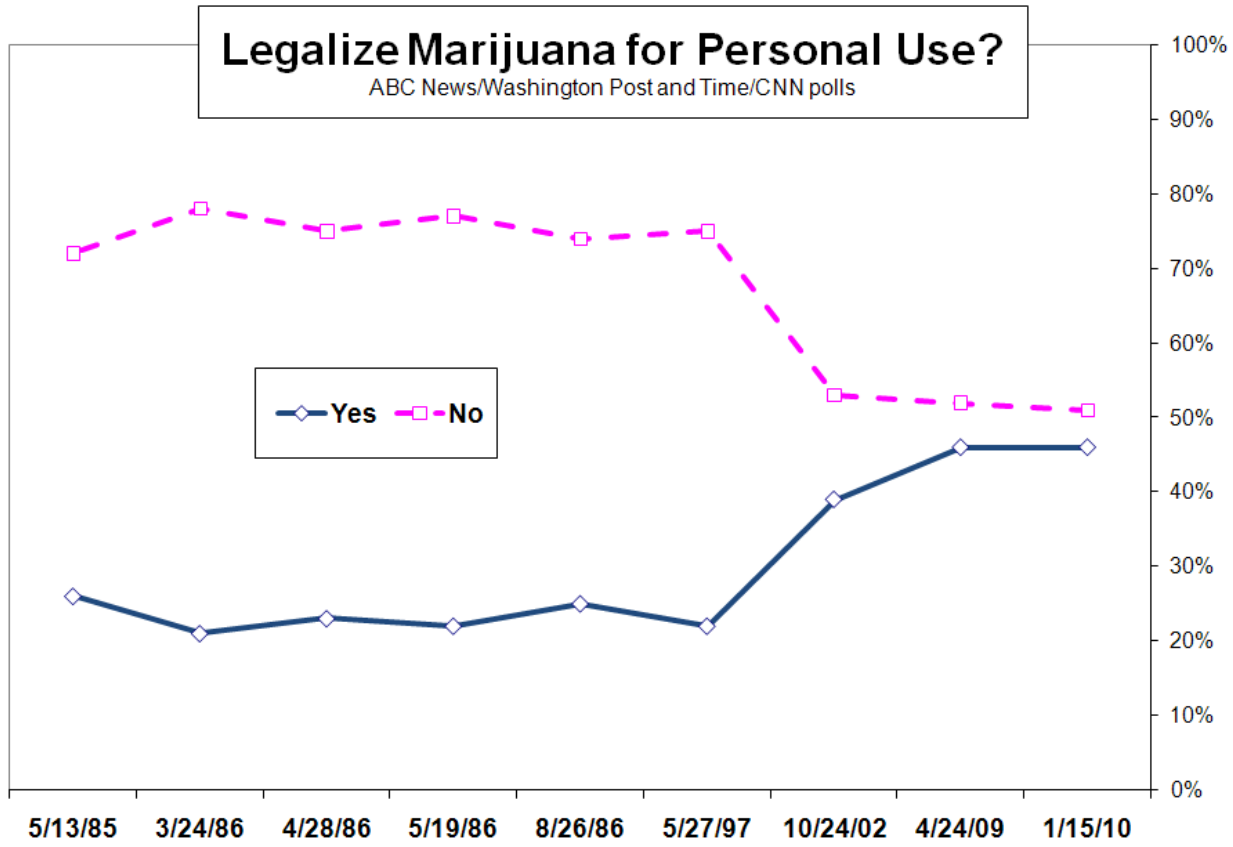
Fifty-six percent say that if it's allowed, doctors should be able to prescribe medical marijuana to anyone they think it can help. New Jersey's measure, which is more restrictive than most, limits prescriptions to people with severe illnesses. State health officials can add to the list.



DECRIMINALIZE? – Apart from medical marijuana, there have been recent efforts to decriminalize marijuana more broadly in some states. A preliminary vote on one such measure is to be held in the Washington state Legislature this week. In California organizers say they've

collected enough signatures to hold a statewide referendum on the issue next fall. And a separate proposal in California to legalize and tax the drug cleared a legislative committee last week. A Field poll there in April found 56 percent support for the idea, which its backers say would raise $1.3 billion a year.

Nationally, this survey finds 46 percent support for legalizing small amounts of marijuana for personal use – the same as it was last spring, and well above its level in past years, for example 39 percent in 2002 and 22 percent in 1997.



GROUPS – Age is a factor. Just 23 percent of senior citizens favor legalizing marijuana for personal use; that jumps to 51 percent of adults under age 65. There are political and ideological differences as well: Thirty percent of conservatives and 32 percent of Republicans favor legalization, compared with 49 percent of independents, 53 percent of Democrats and more than half of moderates and liberals alike (53 and 63 percent, respectively).

Medical marijuana, for its part, receives majority support across the political and ideological spectrum, from 68 percent of conservatives and 72 percent of Republicans as well as 85 percent of Democrats and independents and about nine in 10 liberals and moderates. Support slips to 69 percent among seniors, vs. 83 percent among all adults under age 65.

There are similar divisions on whether medical marijuana should be restricted or made available to anyone a doctor thinks it would help. Overall, 56 percent, as noted, prefer no restrictions, while 21 percent say it should be limited to terminally ill patients and an additional 21 percent say it should be limited to those with serious but not necessarily terminal illnesses.

Liberals are 23 points more apt than conservatives, and Democrats 20 points more likely than Republicans, to oppose restrictions. There's also a difference between the sexes, with men 10 points more likely than women to say the doctor should decide.

But the main difference is whether people think marijuana should be permitted for medical uses in the first place. Among supporters, 63 percent would rely on the doctor's discretion. Among those who oppose medical marijuana, 75 percent say that if it is allowed, it should be limited to seriously or terminally ill patients.

New Jersey passed its medical marijuana law this month and outgoing Gov. Jon Corzine is expected to sign it tomorrow morning, his last day in office. Medical marijuana first became legal in California in 1996, followed by Alaska, Colorado, Hawaii, Maine, Michigan, Montana, Nevada, New Mexico, Oregon, Rhode Island, Vermont and Washington state.

METHODOLOGY – This ABC News/Washington Post poll was conducted by telephone Jan. 12-15, 2010, among a random national sample of 1,083 adults, including landline and cell-phone-only respondents, with an oversample of African Americans (weighted to their correct share of the population) for a total of 153 black respondents. Results for the full sample have a 3.5-point error margin. Click here for a detailed description of sampling error. Sampling, data collection and tabulation by TNS of Horsham, PA.

Analysis by Gary Langer.

ABC News polls can be found at ABCNEWS.com at http://abcnews.com/pollingunit

Media contact: Cathie Levine, (212) 456-4934.

Full results follow (*= less than 0.5 percent).

1-40 previously released or held for release.

41. In general, do you favor or oppose legalizing the possession of small amounts of marijuana for personal use?

	Favor	Oppose	No opinion
1/15/10	46	51	2
4/24/09	46	52	2
10/24/02*	39	53	8
5/27/97	22	75	3
8/26/86	25	74	1
5/19/86	22	77	1
4/28/86	23	75	1
3/24/86	21	78	1
5/13/85	26	72	2

*Time/CNN: "Do you favor or oppose the legalization of marijuana? (IF FAVOR) What about in small amounts, for example three ounces or less? Do you favor or oppose the legalization of marijuana in small amounts?"

42. Regardless of what you think about the personal non-medical use of marijuana, do you think doctors should or should not be allowed to prescribe marijuana for medical purposes to treat their patients?

	Should	Should not	No opinion
1/15/10	81	18	1
5/27/97	69	27	4

43. If doctors are allowed to prescribe marijuana to patients, should it be limited to patients who are terminally ill and near death; or also allowed for patients who have serious but not fatal illnesses; or should it be allowed for any patient the doctor thinks it could help?

	Terminally ill	Serious/ not fatal	Any patient	No opinion
1/15/10	21	21	56	2
5/27/97	29	13	52	6

END