

# Questions about medical marijuana answered by the Institute of Medicine's report.

## *Marijuana and Medicine: Assessing the Science Base*

Copyright 1999 by the National Academy of Sciences (ISBN 0-309-07155-0)

The full report by the National Academy of Sciences can be viewed on-line at

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### **What conditions can marijuana treat?**

"The accumulated data indicate a potential therapeutic value for cannabinoid drugs, particularly for symptoms such as pain relief, control of nausea and vomiting, and appetite stimulation." [p. 3]

"[B]asic biology indicates a role for cannabinoids in pain and control of movement, which is consistent with a possible therapeutic role in these areas. The evidence is relatively strong for the treatment of pain and, intriguing although less well established, for movement disorders." [p. 70]

"For patients such as those with AIDS or who are undergoing chemotherapy and who suffer simultaneously from severe pain, nausea, and appetite loss, cannabinoid drugs might offer broad-

spectrum relief not found in any other single medication. The data are weaker for muscle spasticity but moderately promising." [p. 177]

"Cannabinoids reduce reactivity to acute painful stimuli in laboratory animals. ... Cannabinoids were comparable with opiates in potency and efficacy in these experiments." [p. 54]

"The most encouraging clinical data on the effects of cannabinoids on chronic pain are from three studies of cancer pain." [p. 142]

"In conclusion, the available evidence from animal and human studies indicates that cannabinoids can have a substantial analgesic effect." [p. 145]

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### **Why can't patients use medicines that are already legal?**

"[T]here will likely always be a subpopulation of patients who do not respond well to other medications. The combination of cannabinoid drug effects (anxiety reduction, appetite stimulation, nausea reduction, and pain relief) suggests that cannabinoids would be moderately well suited for certain conditions, such as chemotherapy-induced nausea and vomiting and AIDS wasting." [Pp. 3, 4]

"The critical issue is not whether marijuana or cannabinoid drugs might be superior to the new drugs, but whether some group of patients might obtain added or better relief from marijuana or cannabinoid drugs." [p. 153]

"The profile of cannabinoid drug effects suggests that they are promising for treating wasting syndrome in AIDS patients. Nausea, appetite loss, pain, and anxiety are all afflictions of wasting, and all can be mitigated by marijuana. Although some medications are more effective than marijuana for these problems, they are not equally effective in all patients." [p. 159]

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### **What about Marinol®, the major active ingredient in marijuana in pill form?**

"The poor solubility of Marinol in aqueous solutions and its high first-pass metabolism in the liver account for its poor bioavailability; only 10-20% of an oral dose reaches the systemic circulation. The onset of action is slow; peak plasma concentrations are not attained until two to four hours after dosing. In contrast, inhaled marijuana is rapidly absorbed. ... Variation in individual responses is highest for oral THC and bioavailability is lowest." [p. 203]

"It is well recognized that Marinol's oral route of administration hampers its effectiveness because of slow absorption and patients' desire for more control over dosing." [Pp. 205, 206]

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### **Why not wait for more research before making marijuana legally available as a medicine?**

"[R]esearch funds are limited, and there is a daunting thicket of regulations to be negotiated at the federal level (those of the Food

and Drug Administration, FDA, and the Drug Enforcement Administration, DEA) and state levels." [p. 137]

"Some drugs, such as marijuana, are labeled Schedule I in the Controlled Substance Act, and this adds considerable complexity and expense to their clinical evaluation." [p. 194]

"[O]nly about one in five drugs initially tested in humans successfully secures FDA approval for marketing through a new drug application." [p. 195]

"From a scientific point of view, research is difficult because of the rigors of obtaining an adequate supply of legal, standardized marijuana for study." [p. 217]

"In short, development of the marijuana plant is beset by substantial scientific, regulatory, and commercial obstacles and uncertainties." [p. 218]

"[D]espite the legal, social, and health problems associated with smoking marijuana, it is widely used by certain patient groups." [p. 7]

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## **Do the existing laws really hurt patients?**

"G.S. spoke at the IOM workshop in Louisiana about his use of marijuana first to combat AIDS wasting syndrome and later for relief from the side effects of AIDS medications. ... [He said,] `Every day I risk arrest, property forfeiture, fines, and imprisonment.' " [Pp. 27, 28]

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## Why shouldn't we wait for new drugs based on marijuana's components to be developed, rather than allowing patients to eat or smoke natural marijuana right now?

"Although most scientists who study cannabinoids agree that the pathways to cannabinoid drug development are clearly marked, there is no guarantee that the fruits of scientific research will be made available to the public for medical use." [p. 4]

"[I]t will likely be many years before a safe and effective cannabinoid delivery system, such as an inhaler, is available for patients. In the meantime there are patients with debilitating symptoms for whom smoked marijuana might provide relief." [p. 7]

"[W]hat seems to be clear from the dearth of products in development and the small size of the companies sponsoring them is that cannabinoid development is seen as especially risky."  
[Pp. 211, 212] *[IOM later notes that it could take more than five years and cost \$200-300 million to get new cannabinoid drugs approved -- if ever.]*

"It is too early to forecast the prospects for cannabinoids, other than to note that their development at this point is considered to be especially risky, to judge by the paucity of products in development and the small size of the pharmaceutical firms sponsoring them."  
[p. 219]

"Cannabinoids in the plant are automatically placed in the most restrictive schedule of the Controlled Substances Act, and this is a substantial deterrent to development." [p. 219]

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### **Isn't marijuana too dangerous to be used as a medicine?**

"[E]xcept for the harms associated with smoking, the adverse effects of marijuana use are within the range of effects tolerated for other medications." [p. 5]

"Until the development of rapid-onset antiemetic drug delivery systems, there will likely remain a subpopulation of patients for whom standard antiemetic therapy is ineffective and who suffer from debilitating emesis. It is possible that the harmful effects of smoking marijuana for a limited period of time might be outweighed by the antiemetic benefits of marijuana, at least for patients for whom standard antiemetic therapy is ineffective and who suffer from debilitating emesis. Such patients should be evaluated on a case-by-case basis and treated under close medical supervision." [p. 154]

"Terminal cancer patients pose different issues. For those patients the medical harm associated with smoking is of little consequence. For terminal patients suffering debilitating pain or nausea and for whom all indicated medications have failed to provide relief, the medical benefits of smoked marijuana might outweigh the harm." [p. 159]

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## What should be done to help the patients who already benefit from medical marijuana, prior to the development of new drugs and delivery devices?

"Patients who are currently suffering from debilitating conditions unrelieved by legally available drugs, and who might find relief with smoked marijuana, will find little comfort in a promise of a better drug 10 years from now. In terms of good medicine, marijuana should rarely be recommended unless all reasonable options have been eliminated. But then what? It is conceivable that the medical and scientific opinion might find itself in conflict with drug regulations. This presents a policy issue that must weigh -- at least temporarily -- the needs of individual patients against broader social issues. Our assessment of the scientific data on the medical value of marijuana and its constituent cannabinoids is but one component of attaining that balance." [p. 178]

"Also, although a drug is normally approved for medical use only on proof of its `safety and efficacy,' patients with life-threatening conditions are sometimes (under protocols for `compassionate use') allowed access to unapproved drugs whose benefits and risks are uncertain." [p. 14]

"Until a nonsmoked rapid-onset cannabinoid drug delivery system becomes available, we acknowledge that there is no clear alternative for people suffering from *chronic* conditions that might be relieved by smoking marijuana, such as pain or AIDS wasting. One possible approach is to treat patients as *n*-of-1 clinical trials (single-patient trials), in which patients are fully informed of their status as experimental subjects using a harmful drug delivery system and in which their condition is closely monitored and

documented under medical supervision. ..." [p. 8] *[The federal government's "compassionate use" program, which currently provides marijuana to eight patients nationwide, is an example of an n-of-1 study.]*

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**The IOM report doesn't explicitly endorse state bills and initiatives to simply remove criminal penalties for bona fide medical marijuana users. Does that mean that we should keep the laws exactly as they are and keep arresting patients?**

"This report analyzes science, not the law. As in any policy debate, the value of scientific analysis is that it can provide a foundation for further discussion. Distilling scientific evidence does not in itself solve a policy problem." [p. 14]

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**If patients were allowed to use medical marijuana, wouldn't overall use increase?**

"Finally, there is a broad social concern that sanctioning the medical use of marijuana might increase its use among the general population. At this point there are no convincing data to support this concern. The existing data are consistent with the idea that this would not be a problem if the medical use of marijuana were as closely regulated as other medications with abuse potential. ... [T]his question is beyond the issues normally considered for

medical uses of drugs and should not be a factor in evaluating the therapeutic potential of marijuana or cannabinoids." [Pp. 6, 7]

"No evidence suggests that the use of opiates or cocaine for medical purposes has increased the perception that their illicit use is safe or acceptable." [p. 102]

"Thus, there is little evidence that decriminalization of marijuana use necessarily leads to a substantial increase in marijuana use." [p. 104] *[Decriminalization is defined as the removal of criminal penalties for all uses, even recreational.]*

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### **Doesn't the medical marijuana debate send children the wrong message about marijuana?**

"[T]he perceived risk of marijuana use did not change among California youth between 1996 and 1997. In summary, there is no evidence that the medical marijuana debate has altered adolescents' perceptions of the risks associated with marijuana use." [p. 104]

"Even if there were evidence that the medical use of marijuana would decrease the perception that it can be a harmful substance, this is beyond the scope of laws regulating the approval of therapeutic drugs. Those laws concern scientific data related to the safety and efficacy of drugs for individual use; they do not address perceptions or beliefs of the general population." [p. 126]

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## Isn't marijuana too addictive to be used as a medicine?

"Some controlled substances that are approved medications produce dependence after long-term use; this, however, is a normal part of patient management and does not generally present undue risk to the patient." [p. 98]

"Animal research has shown that the potential for cannabinoid dependence exists, and cannabinoid withdrawal symptoms can be observed. However, both appear to be mild compared to dependence and withdrawal seen with other drugs." [p. 35]

"A distinctive marijuana and THC withdrawal syndrome has been identified, but it is mild and subtle compared with the profound physical syndrome of alcohol or heroin withdrawal." [Pp. 89, 90]

<b>Drug Category</b>	<b>Proportion Of Users That Ever Became Dependent (%)</b>
Alcohol	15
Marijuana (including hashish)	9

[p. 95]

"Compared to most other drugs ... dependence among marijuana users is relatively rare." [p. 94]

"Few marijuana users become dependent. ... Dependence appears to be less severe among people who use only marijuana than among those who abuse cocaine or those who abuse marijuana with other drugs (including alcohol)." [Pp. 96, 97]

"In summary, although few marijuana users develop dependence, some do. But they appear to be less likely to do so than users of other drugs (including alcohol and nicotine), and marijuana dependence appears to be less severe than dependence on other drugs." [p. 98]

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### **Doesn't the use of marijuana cause people to use more dangerous drugs?**

"There is no conclusive evidence that the drug effects of marijuana are causally linked to the subsequent abuse of other illicit drugs. An important caution is that data on drug use progression cannot be assumed to apply to the use of drugs for medical purposes. It does not follow from those data that if marijuana were available by prescription for medical use, the pattern of drug use would remain the same as seen in illicit use." [p. 6]

"There is no evidence that marijuana serves as a stepping stone on the basis of its particular physiological effect." [p. 99]

"Instead, the legal status of marijuana makes it a gateway drug."  
[p. 99]

"[I]t does not appear to be a gateway drug to the extent that it is the *cause* or even that it is the most significant predictor of serious drug abuse; that is, care must be taken not to attribute cause to association." [p. 101]

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## **Shouldn't medical marijuana remain illegal because it is bad for the immune system?**

"The short-term immunosuppressive effects are not well established; if they exist at all, they are probably not great enough to preclude a legitimate medical use. The acute side effects of marijuana use are within the risks tolerated for many medications." [p. 126]

"It appears that marijuana use is associated with intermittent disturbances in T and B cell function, but the magnitude is small and other measures are often normal." [p. 112]

"Despite the many claims that marijuana suppresses the human immune system, the health effects of marijuana-induced immunomodulation are still unclear." [p. 109]

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## **Doesn't marijuana cause brain damage?**

"Earlier studies purporting to show structural changes in the brains of heavy marijuana users have not been replicated with more sophisticated techniques." [p. 106]

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## **Doesn't marijuana cause amotivational syndrome?**

"When heavy marijuana use accompanies these symptoms, the drug is often cited as the cause, but no convincing data

demonstrate a causal relationship between marijuana smoking and these behavioral characteristics." [Pp. 107, 108]

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### **Doesn't marijuana cause health problems that shorten the life span?**

"[E]pidemiological data indicate that in the general population marijuana use is not associated with increased mortality." [p. 109]

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### **Isn't marijuana too dangerous for the respiratory system?**

"Given a cigarette of comparable weight, as much as four times the amount of tar can be deposited in the lungs of marijuana smokers as in the lungs of tobacco smokers." [p. 111]

"However, a marijuana cigarette smoked recreationally typically is not packed as tightly as a tobacco cigarette, and the smokable substance is about half that in a tobacco cigarette. In addition, tobacco smokers generally smoke considerably more cigarettes per day than do marijuana smokers." [Pp. 111, 112]

"There is no conclusive evidence that marijuana causes cancer in humans, including cancers usually related to tobacco use. ... More definitive evidence that habitual marijuana smoking leads or does not lead to respiratory cancer awaits the results of well-designed case control epidemiological studies." [p. 119]

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## **Doesn't marijuana cause fertility problems?**

"[T]he effect of cannabinoids on the capacity of sperm to fertilize eggs is reversible and is observed at [concentrations] which are higher than those likely to be experienced by marijuana smokers." [p. 122]

"The well-documented inhibition of reproductive functions by THC is thus not a serious concern for evaluating the short-term medical use of marijuana or specific cannabinoids." [p. 123]

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## **Doesn't marijuana use cause people to become rebellious and anti-social?**

"Although parents often state that marijuana caused their children to be rebellious, the troubled adolescents in the study by Crowley and coworkers developed conduct disorders *before* marijuana abuse." [p. 97]

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## **Don't the euphoric side effects diminish marijuana's value as a medicine?**

"The high associated with marijuana is not generally claimed to be integral to its therapeutic value. But mood enhancement, anxiety reduction, and mild sedation can be desirable qualities in medications -- particularly for patients suffering pain and anxiety. Thus, although the psychological effects of marijuana are merely

side effects in the treatment of some symptoms, they might contribute directly to relief of other symptoms." [p. 84]

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### **How bad is it for pregnant women to use marijuana?**

"Several studies of women who smoked marijuana regularly during pregnancy show that they tend to give birth to lower weight babies. Mothers who smoke tobacco also give birth to lower weight babies, and the relative contributions of smoking versus THC are not known from these studies. ... Babies born to mothers who smoked marijuana during pregnancy weighed an average of 3.4 ounces less than babies born to a control group of mothers who did not smoke marijuana; there was no statistically significant difference in either gestational age or frequency of congenital abnormalities. ... However, Jamaican women who use marijuana rarely smoke it, but instead prepare it as tea. In a study of neonates born to Jamaican women who did or did not ingest marijuana during pregnancy, there was no difference in neurobehavioral assessments made at three days after birth and at one month." [Pp. 123, 124]

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### **What other therapeutic potential does marijuana have?**

"[B]oth THC and CBD [two of marijuana's main ingredients] can be neuroprotective through their antioxidative activity; that is, they can reduce the toxic forms of oxygen that are released when cells are under stress." [p. 47]

"One of the most prominent new applications of cannabinoids is for 'neuroprotection,' the rescue of neurons from cell death associated with trauma, ischemia, and neurological diseases." [p. 211]

"There are numerous anecdotal reports that marijuana can relieve the spasticity associated with multiple sclerosis or spinal cord injury, and animal studies have shown that cannabinoids affect motor areas in the brain -- areas that might influence spasticity." [p. 160]

<b>Drug and Dose</b>	<b>Study Design</b>	<b>Results</b>	<b>Reference</b>
Oral THC 5 and 10 mg, single doses	Double-blind, placebo controlled 9 MS patients	Spasticity was improved based on examiner ratings	Petro and Ellenberger (1981)

[p. 163]

"Many spinal cord injury patients report that marijuana reduces their muscle spasms. Twenty-two of 43 respondents to a 1982 survey of people with spinal cord injuries reported that marijuana reduced their spasticity." [Pp. 163, 164]

"[I]n rats with autoimmune encephalomyelitis (an experimental model used to study multiple sclerosis), cannabinoids were shown to attenuate the signs and the symptoms of central nervous system damage." [p. 67]

"There is clearly a need for improved migraine medications. Sumatriptan (Imitrex) is the best available medication for migraine headaches, but it fails to abolish migraine symptoms in about 30% of migraine patients. ... However, a possible link between cannabinoids and migraine is suggested by the abundance of

cannabinoid receptors in the periaqueductal gray (PAG) region of the brain. The PAG region is part of the neural system that suppresses pain and is thought to be involved in the generation of migraine headaches." [Pp. 143, 144]

"High intraocular pressure (IOP) is a known risk factor for glaucoma and can, indeed, be reduced by cannabinoids and marijuana. However, the effect is too and [sic] short lived and requires too high doses, and there are too many side effects to recommend lifelong use in the treatment of glaucoma. The potential harmful effects of chronic marijuana smoking outweigh its modest benefits in the treatment of glaucoma. Clinical studies on the effects of smoked marijuana are unlikely to result in improved treatment for glaucoma." [p. 177] *[Note that IOM found that marijuana does work for glaucoma, but was uncomfortable with the amount that a person needs to smoke. Presumably, it would be an acceptable treatment for glaucoma patients to eat marijuana. Additionally, MPP believes that IOM would not support arresting patients who choose to smoke marijuana to treat glaucoma.]*

"POAG [the most common form of glaucoma] is most prevalent among the elderly, with 1% affected in those over 60 years old and more than 9% in those over 80. In African Americans over 80, there is more than a 10% chance of having the disease, and older African Caribbeans (who are less racially mixed than African Americans) have a 20-25% chance of having the disease." [p. 173]

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**Do the American people really support legal access to medical marijuana, or were voters simply tricked into passing medical marijuana ballot initiatives?**

"Public support for patient access to marijuana for medical use appears substantial; public opinion polls taken during 1997 and 1998 generally report 60-70 percent of respondents in favor of allowing medical uses of marijuana." [p. 18]

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**But shouldn't we keep medical marijuana illegal because some advocates want to "legalize" marijuana for all uses?**

"[I]t is not relevant to scientific validity whether an argument is put forth by someone who believes that all marijuana use should be legal or by someone who believes that any marijuana use is highly damaging to individual users and to society as a whole." [p. 14]