



HUMAN
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NUMBER OF PAGES: 3
(including cover)

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News Release

FOR IMMEDIATE RELEASE

Thursday, March 18, 1999

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HRC SAYS MCCAFFREY'S POSITION ON MEDICAL MARIJUANA STUDY DIRECTLY CONTRADICTS HIS POSITION ON NEEDLE EXCHANGE PROGRAMS

WASHINGTON -- The Human Rights Campaign strongly criticized General Barry McCaffrey, Director of the Office of National Drug Control Policy today for touting "science" in his reaction to a medical marijuana study, but refusing to consider "science" in his position on needle exchange programs last Spring.

"We are pleased that General McCaffrey has found science," said Winnie Stachelberg, HRC's political director. "We hope his new found confidence in science will lead him to reconsider his opposition to needle exchange programs, which the science concludes saves lives."

A statement released yesterday by the ONDCP in response to a study by the Institute of Medicine on the use of medical marijuana, says "We are delighted that science is the basis of the discussion of this issue." The statement concluded by saying "We will continue to rely on the professional judgement of the Secretary of Health and Human Services, the Director of the National Institute of Health, and the Surgeon General on all issues related to the medical value of marijuana...."

Yet General McCaffrey refused to listen to the same government officials who all concluded that needle exchange programs are effective in the battle against HIV and AIDS.

"After reviewing all of the research, we have unanimously agreed that there is conclusive scientific evidence that needle exchange programs, as part of a comprehensive HIV prevention strategy, are an effective public health intervention that reduces the transmission of HIV and does not encourage the use of illegal drugs," said the heads of the National Institute of Health, Centers for Disease Control and Prevention, National Institute of Allergy and Infectious Diseases, and the Surgeon General among others. The statement was made in an April 20, 1998 memorandum to Health and Human Services Secretary Donna Shalala urging her to certify the effectiveness of needle exchange programs which she did the same day.

By certifying the scientific evidence in support of needle exchange, the Secretary could have allowed local communities to use federal funds to support these life saving programs. However, due in large part to Gen. McCaffrey's opposition, the Clinton Administration decided to maintain the federal funding ban despite the Secretary's action. According to a Washington Times report a week after the Secretary's certification of the science, it was McCaffrey who convinced President Clinton that the opinions of the country's preeminent scientists and public health officials were wrong and that the science on needle exchange was still uncertain. "[The President] and I are happy [with] the way this came out," he is quoted as saying.

Despite the continued prohibition on the use of federal funds, the debate continues. Congress last year prohibited the District of Columbia from using their own local funds for needle exchange and cut off all federal funds to individual organizations which use private funds to do so. Similar bills have already been introduced to apply similar prohibitions across the country.

"Our hope is that General McCaffrey will apply his new found confidence in science to this debate" says Stachelberg. "His words can actually save lives if he choose to oppose further Congressional involvement in this issue."

The Human Rights Campaign is the largest national lesbian and gay political organization, on with members throughout the country. It effectively lobbies Congress, provides campaign support and educates the public to ensure that lesbian and gay Americans can be open, honest and safe at home, at work and in the community.

Devakul -

FYI. I put a
copy of this in
Cmt's box as well.

This full report is
coming out on
Wednesday.

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MARIJUANA AND MEDICINE: ASSESSING THE SCIENCE BASE

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«11 a.m. EST»

PLEASE CITE AS A REPORT OF THE
INSTITUTE OF MEDICINE

Janet E. Joy, Stanley J. Watson, Jr., and John A. Benson, Jr., *Editors*

Division of Neuroscience and Behavioral Health

INSTITUTE OF MEDICINE

NATIONAL ACADEMY PRESS
Washington, D.C. 1999

EXECUTIVE SUMMARY

Public opinion on the medical value of marijuana has been sharply divided. Some dismiss medical marijuana as a hoax that exploits our natural compassion for the sick; others claim it is a uniquely soothing medicine that has been withheld from patients through regulations based on false claims. Proponents of both views cite 'scientific evidence' to support their views and have expressed those views at the ballot box in recent state elections. In January 1997, the White House Office of National Drug Control Policy (ONDCP) asked the Institute of Medicine to conduct a review of the scientific evidence to assess the potential health benefits and risks of marijuana and its constituent cannabinoids (see box: *Statement of Task*). That review began in August 1997 and culminates with this report.

The ONDCP request came in the wake of state "medical marijuana" initiatives. In November 1996, voters in California and Arizona passed referenda designed to permit the use of marijuana as medicine. Although Arizona's referendum was invalidated five months later, the referenda galvanized a national response. In November 1998, voters in six states (Alaska, Arizona, Colorado, Nevada, Oregon, and Washington) passed ballot initiatives in support of medical marijuana. (The Colorado vote will not count, however, because after the vote was taken a court ruling determined there had not been enough valid signatures to place the initiative on the ballot.)

Can marijuana relieve health problems? Is it safe for medical use? Those straightforward questions are embedded in a web of social concerns, most of which lie outside the scope of this report. Controversies concerning the nonmedical use of marijuana spill over onto the medical marijuana debate and obscure the real state of scientific knowledge. In contrast with the many disagreements bearing on social issues, the study team found substantial consensus among experts in the relevant disciplines on the scientific evidence about potential medical uses of marijuana.

This report summarizes and analyzes what is known about the medical use of marijuana; it emphasizes evidence-based medicine (derived from knowledge and experience informed by rigorous scientific analysis), as opposed to belief-based medicine (derived from judgment, intuition, and beliefs untested by rigorous science).

Throughout this report, *marijuana* refers to unpurified plant substances, including leaves or flower tops whether consumed by ingestion or smoking. References to "the effects of marijuana" should be understood to include the composite effects of its various components; that is, the effects of THC, the primary psychoactive ingredient in marijuana, are included among its effects, but not all the effects of marijuana are necessarily due to THC. *Cannabinoids* are the group of compounds related to THC, whether found in the marijuana plant, in animals, or synthesized in chemistry laboratories.

Three focal concerns in evaluating the medical use of marijuana are:

- Evaluation of the effects of isolated cannabinoids.
- Evaluation of the health risks associated with the medical use of marijuana.
- Evaluation of the efficacy of marijuana.

EFFECTS OF ISOLATED CANNABINOID

Cannabinoid Biology

Much has been learned since a 1982 IOM *Marijuana and Health* report. Although it was clear then that most of the effects of marijuana were due to its actions on the brain, there was little information about how THC acted on brain cells (neurons), which cells were affected by THC, or even what general areas of the brain were most affected by THC. Additionally, too little was known about cannabinoid physiology to offer any scientific insights into the harmful or therapeutic effects of marijuana. That all changed with the identification and characterization of cannabinoid receptors in the 1980s and 1990s. During the last 16 years, science has advanced greatly and can tell us much more about the potential medical benefits of cannabinoids.

CONCLUSION: At this point, our knowledge about the biology of marijuana and cannabinoids allows us to make some general conclusions:

- Cannabinoids likely have a natural role in pain modulation, control of movement, and memory.
- The natural role of cannabinoids in immune systems is likely multifaceted and remains unclear.
- The brain develops tolerance to cannabinoids.
- Animal research demonstrates the potential for dependence, but this potential is observed under a narrower range of conditions than with benzodiazepines, opiates, cocaine, or nicotine.
- Withdrawal symptoms can be observed in animals, but appear to be mild compared to opiates or benzodiazepines, such as diazepam (Valium®).

CONCLUSION: The different cannabinoid receptor types found in the body appear to play different roles in normal human physiology. In addition, some effects of cannabinoids appear to be independent of those receptors. The variety of mechanisms through which cannabinoids can influence human physiology underlies the variety of potential therapeutic uses for drugs that might act selectively on different cannabinoid systems.

RECOMMENDATION 1: Research should continue into the physiological effects of synthetic and plant-derived cannabinoids and the natural function of cannabinoids found in the body. Because different cannabinoids appear to have different effects, cannabinoid research should include, but not be restricted to, effects attributable to THC alone.

Efficacy Of Cannabinoid Drugs

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. The therapeutic effects of cannabinoids are best established for THC, which is generally one of the two most abundant of the cannabinoids in marijuana. (Cannabidiol, the precursor of THC, is generally the other most abundant cannabinoid.)

The effects of cannabinoids on the symptoms studied are generally modest, and in most cases, there are more effective medications. However, people vary in their responses to medications and there 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.

Defined substances, such as purified cannabinoid compounds, are preferable to plant products which are of variable and uncertain composition. Use of defined cannabinoids permits a more precise evaluation of their effects, whether in combination or alone. Medications that can maximize the desired effects of cannabinoids and minimize the undesired effects can very likely be identified.

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. Cannabinoid-based drugs will only become available if public investment in cannabinoid drug research is sustained, and if there is enough incentive for private enterprise to develop and market such drugs.

CONCLUSION: Scientific data indicate the potential therapeutic value of cannabinoid drugs, primarily THC, for pain relief, control of nausea and vomiting, and appetite stimulation; smoked marijuana, however, is a crude THC delivery system that also delivers harmful substances.

RECOMMENDATION 2: Clinical trials of cannabinoid drugs for symptom management should be conducted with the goal of developing rapid-onset, reliable, and safe delivery systems.

Influence Of Psychological Effects On Therapeutic Effects

The psychological effects of THC and similar cannabinoids pose three issues for the therapeutic use of cannabinoid drugs. First, for some patients—particularly older patients with no previous marijuana experience—the psychological effects are disturbing. Those patients report experiencing unpleasant feelings and disorientation after being treated with THC, generally more severe for oral THC than for smoked marijuana. Second, for conditions such as movement disorders or nausea, in which anxiety exacerbates the symptoms, the anti-anxiety effects of cannabinoid drugs can influence symptoms indirectly. This can be beneficial or can create false impressions of the drug effect. Third, in cases where symptoms are multifaceted, the combination of THC effects might provide a form of adjunctive therapy; for example, AIDS wasting patients would likely benefit from a medication that simultaneously reduces anxiety, pain, and nausea while stimulating appetite.

CONCLUSION: The psychological effects of cannabinoids, such as anxiety reduction, sedation, and euphoria can influence their potential therapeutic value. Those effects are potentially undesirable for certain patients and situations, and beneficial for others. In addition, psychological effects can complicate the interpretation of other aspects of the drug effect.

RECOMMENDATION 3: Psychological effects of cannabinoids such as anxiety reduction and sedation, which can influence medical benefits, should be evaluated in clinical trials.

RISKS ASSOCIATED WITH MEDICAL USE OF MARIJUANA

Physiological Risks

Marijuana is not a completely benign substance. It is a powerful drug with a variety of effects. However, except for the harms associated with smoking, the adverse effects of marijuana use are within the range of effects tolerated for other medications. The harmful effects to individuals from the perspective of possible medical use of marijuana are not necessarily the same as the harmful physical effects of drug abuse. When interpreting studies purporting to show the harmful effects of marijuana, it is important to keep in mind that the majority of those studies are based on *smoked* marijuana, and cannabinoid effects cannot be separated from the effects of inhaling smoke of burning plant material and contaminants.

For most people, the primary adverse effect of *acute* marijuana use is diminished psychomotor performance. It is, therefore, inadvisable to operate any vehicle or potentially dangerous equipment while under the influence of marijuana, THC, or any cannabinoid drug with comparable effects. In addition, a minority of marijuana users experience dysphoria, or unpleasant feelings. Finally, the short-term immunosuppressive effects are not well established but, if they exist, are not likely great enough to preclude a legitimate medical use.

The *chronic* effects of marijuana are of greater concern for medical use and fall into two categories: the effects of chronic smoking, and the effects of THC. Marijuana smoking is associated with abnormalities of cells lining the human respiratory tract. Marijuana smoke, like tobacco smoke, is associated with increased risk of cancer, lung damage, and poor pregnancy outcomes. Although cellular, genetic, and human studies all suggest that marijuana smoke is an important risk factor for the development of respiratory cancer, proof that habitual marijuana smoking does or does not cause cancer awaits the results of well-designed studies.

CONCLUSION: Numerous studies suggest that marijuana smoke is an important risk factor in the development of respiratory disease.

RECOMMENDATION 4: Studies to define the individual health risks of smoking marijuana should be conducted, particularly among populations in which marijuana use is prevalent.

Marijuana Dependence And Withdrawal

A second concern associated with chronic marijuana use is dependence on the psychoactive effects of THC. Although few marijuana users develop dependence, some do. Risk factors for marijuana dependence are similar to those for other forms of substance abuse. In particular, antisocial personality and conduct disorders are closely associated with substance abuse.

CONCLUSION: A distinctive marijuana withdrawal syndrome has been identified, but it is mild and short-lived. The syndrome includes restlessness, irritability, mild agitation, insomnia, sleep EEG disturbance, nausea, and cramping.

Marijuana As A "Gateway" Drug

Patterns in progression of drug use from adolescence to adulthood are strikingly regular. Because it is the most widely used illicit drug, marijuana is predictably the first illicit drug most people encounter. Not surprisingly, most users of other illicit drugs have used marijuana first. In fact, most drug users begin with alcohol and nicotine before marijuana—usually before they are of legal age.

In the sense that marijuana use typically precedes rather than follows initiation of other illicit drug use, it is indeed a "gateway" drug. But because underage smoking and alcohol use typically precede marijuana use, marijuana is not the most common, and is rarely the first, "gateway" to illicit drug use. 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.

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.

CONCLUSION: Present data on drug use progression neither support nor ref the suggestion that medical availability would increase drug abuse. However this question is beyond the issues normally considered for medical uses drugs, and should not be a factor in evaluating the therapeutic potential of marijuana or cannabinoids.

USE OF SMOKED MARIJUANA

Because of the health risks associated with smoking, smoked marijuana should generally not be recommended for long-term medical use. Nonetheless, for certain patients, such as the terminally ill or those with debilitating symptoms, the long-term risks are not of great concern. Further, despite the legal, social, and health problems associated with smoking marijuana, it is widely used by certain patient groups.

RECOMMENDATION 5: Clinical trials of marijuana use for medical purposes should be conducted under the following limited circumstances: trials should involve only short-term marijuana use (less than six months); be conducted in patients with conditions for which there is reasonable expectation of efficacy; be approved by institutional review boards; and collect data about efficacy.

The goal of clinical trials of smoked marijuana would not be to develop marijuana as a licensed drug, but rather as a first step towards the possible development of non-smoked, rapid-onset cannabinoid delivery systems. However, it will likely be many years before a safe and effective cannabinoid delivery system, such as an inhaler, will be available for patients. In the meantime, there are patients with debilitating symptoms for whom smoked marijuana might provide relief. The use of smoked marijuana for those patients should weigh both the expected efficacy of marijuana and ethical issues in patient care, including providing information about the known and suspected risks of smoked marijuana use.

EXECUTIVE SUMMARY

RECOMMENDATION 6: Short-term use of smoked marijuana (less than six months) for patients with debilitating symptoms (such as intractable pain or vomiting) must meet the following conditions:

- failure of all approved medications to provide relief has been documented;
- the symptoms can reasonably be expected to be relieved by rapid-onset cannabinoid drugs;
- such treatment is administered under medical supervision in a manner that allows for assessment of treatment effectiveness;
- and involves an oversight strategy comparable to an institutional review board process that could provide guidance within 24 hours of a submission by a physician to provide marijuana to a patient for a specified use.

Until a non-smoked, 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, 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, thereby increasing the knowledge base of the risks and benefits of marijuana use under such conditions.