

CSAM NEWS

Newsletter of the California Society of Addiction Medicine Spring 1997 Vol. 24, No. 1

A WATCHDOG OVER
PEER REVIEW BODIES

New Reporting Requirement

When a hospital medical staff initiates a formal investigation of a physician's ability to practice medicine safely based on information that the physician may be suffering from "a disabling mental or physical condition that poses a threat to patient care," a report must be sent to the Medical Board's Diversion Program within 15 days. Because any peer review body defined in Section 805 of California's Business and Professions Code is required to report, Medical Society committees and some others are included in the requirement. Another report must be filed when the peer review body closes its investigation. The reports must be made even though the investigation may show that the physician does not have a problem.

The reports go to the Medical Board's Diversion Program. All correspondence should be addressed to the MBC Diversion Program, 1430 Howe Avenue, Sacramento 95825.

The information is not reported to the Medical Board's Enforcement arm unless the Administrator of the Diversion Program determines that the peer review body is not acting quickly enough to protect the public. If, at any time, the Diversion Program determines that the progress of the formal peer review investigation is not adequate to protect the public, it will notify the Board's Chief of Enforcement. However, prior to referring any case to the Chief of

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Cannabis and Medical Marijuana

PREPARED BY
TIMMEN L. CERMAK, MD
AND THE CSAM TASK FORCE ON MEDICAL MARIJUANA

Since the central purpose of CSAM is to advance the understanding of addiction medicine, our contribution to the medical marijuana debate should strive to embody this defining framework. In other words, *CSAM should assume primary responsibility for clarifying and promulgating the unique and critically important perspectives which addiction medicine has to offer regarding the medicalization of marijuana in California.* While all California physicians are faced with a host of important questions, ranging from whether marijuana possesses therapeutic efficacy to what rights physicians have to discuss patient care in confidentiality without intrusions by the federal or state government, the members of CSAM are no more qualified than most physicians to answer these questions. Since the California Medical Association is actively involved in pursuing many of these issues, CSAM should concentrate primarily on issues directly related to our specific specialty - addiction medicine.

It is CSAM's opportunity and challenge to provide substantive, constructive input first to the physician's role in implementing California Health and Safety Code 11362.5, and then to the wider implications for all psychoactive chemicals. Our responsibility begins with asserting that passage of Proposition 215 into law does not negate the fact that *marijuana is a psychoactive substance with significant potential for physiological and psychological dependence.* While the

CSAM Actions on Medical Marijuana

**Over-the-counter Test for Drugs of
Abuse Approved**

Acamprosate Studies

potential for marijuana to be addictive and/or to serve as a gateway to use of more destructive psychoactive substances should not exclude it from medical usage, the known hazards of marijuana use do require that thoughtful safeguards be considered to minimize potential negative effects on individuals for whom medical use is justified and to satisfy the dictates of good public health policy. It is CSAM's responsibility both to document the addictive qualities of cannabis for the rest of California's physicians, state and federal officials as well as to help everyone keep this potential for addiction in proper perspective by challenging exaggerated claims of harmfulness. The foundation for our perspective should be the scientific and clinical facts. The following White Paper was designed to summarize documented information regarding cannabis that has the most direct relevance to addiction medicine.

It is CSAM's responsibility to document the addictive qualities of cannabis and to keep them in proper perspective by challenging exaggerated claims of harmfulness.

Historical Context

Cannabis has a long history of therapeutic use, with references from the 6th century BC found in the Middle East and Asia. William Brooke O'Shaughnessey, an Irish physician serving in the British Army in India, reviewed the literature and researched the usefulness and safety of cannabis, leading to a monograph in 1839 noting its use in the treatment of seizures and spasticity. In 1894, the Indian Hemp Drugs Commission reviewed the literature and listed cramps, convulsions, neuralgia and tetanus as indications for cannabis. Medical use of cannabis in the U.S. was consistent with the rest of the English speaking world prior to its prohibition. At the turn of the century, its use waned in response to the development of synthetic medications. Rising fear about the recreational use of cannabis, mixed with undertones of racial prejudice, led to the Marijuana Tax Act of 1937, abolishing all cannabis use. Despite occasional efforts to reintroduce the medical use of cannabis (e.g., the California Research Advisory Panel in 1970 recommended decriminalization; Judge Francis Young, following hearings and testimony in a suit brought against the Drug Enforcement Agency by the National Organization for the Reform of Marijuana Laws, recommended down-scheduling cannabis; and brief compassionate use as an Investigative New Drug (IND) until 1991), the federal government has taken a leading role in preventing any effective exploration

of the potential medical value of cannabinoids other than dronabinol, which was made available in 1985.

Basic Pharmacology

Marijuana refers to the flowering tops and leaves of *Cannabis sativa*, subspecies *indica* - a hemp plant that secretes a resin containing psychoactive compounds called cannabinoids. This immediately raises the issue of whether the medicalization of "marijuana" is a red herring, since medicine is ultimately interested in the biochemical essence of the cannabis plant, as opposed to the flowering tops and leaves per se.

Research findings regarding cannabis have closely recapitulated the opiate story. Following initial observations of the plant's significant psychoactive properties in humans, we have isolated the essential biochemistry producing that psychoactivity, found receptor sites for these exogenous molecules, and then discovered endogenous ligands for those receptor sites. Therefore, we now know that the ingestion of cannabis leads to alterations in an entire cannabinoid neurotransmitter system (consisting of neural pathways, neurotransmitters/modulators, and receptor sites), although the normal physiological functions of this entire system have not yet been well delineated.

The cannabis plant contains over 400 chemical compounds, approximately 60 of which are cannabinoids (a class of C-21 compounds), which possess high lipophilicity, allowing passage through the blood brain barrier and storage in fat cells. Delta-9-tetrahydrocannabinol (THC), first isolated in the 1960s, has been found to be primarily responsible for the psychoactive properties of cannabis. Delta-9-THC is stereoselective. Other compounds, such as delta-8-THC are also psychoactive, though less potent. The Delta-9-THC content of marijuana is reported to have risen from 1.5% in the late 60s, to 3.0-3.5% in the mid 80s, to as high as 20% in current sinsemilla (unfertilized flowering tops from the female cannabis plant).

Potent agonists of THC have recently become available, including CP-55,940 (4-25 times the potency of delta-9-THC) and 11-OH-delta-8-THC-DMH (300-400 times more potent). The characteristics of these agonists stimulated a search for an endogenous cannabinoid ligand, resulting in the discovery in 1992 of anandamide (arachidonylethanolamide), a name derived from the Sanskrit word for "bliss." Recently, a selective and highly potent cannabinoid antagonist, SR 141716A, has been developed.

Radiolabeling of CP-55,940 permitted identification of cannabinoid specific receptors, both centrally and peripherally (especially in macrophages in the spleen and the cortex of lymph nodes). The human cannabinoid receptor has been cloned and found to exist in two subtypes (CB1 and CB2), corresponding to central and

peripheral sites. Pharmacologic potency of the different cannabinoid agonists correlates well with their affinity for the cannabinoid binding site. Evidence suggests that CB1 receptors mediate most of the central cannabinoid effects. There is wide phylogenetic distribution of the cannabinoid receptor, suggesting that the gene governing its structure must have been present early in evolution, and its conservation implies that the receptor serves an important biological function.

The densest binding of radiolabeled cannabinoids occurs in the basal ganglia (substantia nigra, globus pallidus, entopeduncular nucleus, and lateral caudate) and the molecular layer of the cerebellum. Intermediate levels of binding occur in the hippocampus, dentate gyrus and selected layers of the cortex. The effects of cannabinoids generally correspond with the neuroanatomic distribution of cannabinoid receptor sites (e.g., effects of learning and memory are consistent with receptor localization in the hippocampus).

The federal prohibitions against cannabis use have grossly affected the quality of information regarding its medical usefulness.

Current research demonstrating cannabinoid receptors and an endogenous ligand, with associated pathways for biosynthesis and degradation, has therefore conclusively established the existence of a distinct neurochemical system.

Despite the fact that the number of cannabinoid receptors in the brain may outstrip any other neurotransmitter, the physiological role of this system still lacks clarification. Until we understand the function of the cannabinoid neurotransmitter system, we are limited in our ability to predict or recognize the physical and psychological manifestations of imbalance in this system. However, it should be clearly understood that THC is not a naturally occurring substance in the brain; it merely possesses psychoactive properties by mimicking the naturally occurring neurotransmitter anandamide.

Medical Uses of Marijuana/Cannabis

CAVEATS: The federal prohibitions against cannabis use, in place since passage of the Marijuana Tax Act in 1937, have grossly affected the quality of information available regarding the medical usefulness of cannabis. The primary

sources of information are historical (both ancient/global and during the preceding century in the U.S.), anecdotal and/or illegal. The lack of academically sanctioned, controlled research should neither aggravate nor mitigate a dispassionate investigation of cannabis's medical uses. In other words, cannabis may be medically useful, despite the lack of research confirming this fact. On the other hand, the absence of research data should not lead to a decrease in our critical faculties regarding its usefulness or promote its acceptance. The prudent perspective would be an open, but discerning approach. The following information should be viewed as a provisional indication of potentially valuable medical uses for cannabis, each requiring critical evaluation by research that still largely remains to be undertaken. Those who espouse the following medical uses of cannabis should not be penalized or judged because of a lack of traditional research underpinning their assertions.

Emphasis for the therapeutic effects of cannabis have usually been placed on the following conditions: allergies, migraines, analgesia, glaucoma, convulsions, muscle spasticity, bronchial asthma, nausea and vomiting (especially secondary to chemotherapy), anorexia and wasting (e.g., AIDS related). The Australian National Task Force on Cannabis reviewed literature on the anti-emetic effects of THC and found it superior to placebo and equivalent in effectiveness to other widely used anti-emetics. The role for cannabis in treating glaucoma is unclear, since the body develops tolerance to its decrease in intra-ocular pressure, but the side effects are deemed less onerous by some patients than the side effects of other glaucoma drugs. Animal studies have provided some evidence of the efficacy of cannabis in preventing seizures. Evidence of anti-spasmodic effects on both voluntary and smooth muscles in multiple sclerosis and post spinal injury are largely anecdotal; but reports continue to appear with regularity. There is evidence from animals for an analgesic effect which operates outside the opiate mechanism (i.e., not blocked by naloxone) as well as evidence of synthetic cannabinoids which appear to separate analgesia from mood-altering effects. Analgesic effects in humans have most often been reported for arthritic conditions.

The Australian National Task Force on Cannabis ended its review of the medical uses with the following important quote: *"The application of the same demanding standards to existing agents for the candidate diseases, and more generally, to existing psychoactive drugs that are widely used in medical practice, would denude the pharmacopoeia."* This is an important political statement vis-a-vis the U. S. government's intransigence regarding funding for cannabis research.

The first available data from a survey of members of Cannabis Buyers Clubs in California, obtained by Tod

Mikuriya, CSAM member, found that the most common reasons given for medicinal use of cannabis include anorexia/N/V/diarrhea, insomnia/depression, anxiety/panic attacks, AIDS related illness, arthritis/other pain, muscle spasm, and harm reduction. Underlying this survey is Mikuriya's framework for organizing the medical uses for cannabis into five categories: (1) psychotherapeutic - antidepressant/anxiolytic (decreasing emotional reactivity, sedating), (2) anticonvulsant-antispasmodic, (3) analgesic immunomodulator (particularly useful in the discomfort of autoimmune disorders), (4) harm reduction, and (5) appetite stimulant.

Marijuana's physiological effects have been demonstrated, but their clinical significance is generally unclear.

Adverse Medical Effects

Cannabinoids affect a variety of organ systems, often in highly complex ways, and readily cross the placenta. Although multiple physiological effects have been demonstrated, their ultimate clinical significance is generally unclear.

Studies of health care use by marijuana smokers document some increased incidence of respiratory problems, even in those who do not smoke tobacco. Although acute exposure to marijuana smoke causes bronchodilation, chronic use causes inflammatory and pre-neoplastic changes. Marijuana smokers report more symptoms of acute and chronic bronchitis than nonsmokers of either tobacco or marijuana. Squamous metaplasia and bronchial tumors can be induced by marijuana smoking. Until proven otherwise, it is prudent to assume that chronic marijuana smoking leads to the same panoply of illnesses as chronic tobacco smoking, including respiratory cancers.

There is, as yet, little evidence that chronic cannabis use causes irreversible brain injury. However, SPECT scans show hypoperfusion in the frontal and temporal lobes and EEG studies show chronic changes in long-term smokers, especially in the frontal lobes. Although there is no conclusive evidence that these EEG changes correlate with neuropsychological impairment, the subtle cognitive changes documented by Solowij are highly suggestive of frontal lobe dysfunction. In addition, cannabis has clearly been demonstrated to affect fine perceptual and motor functions, theoretically putting users at risk of accidents, especially auto accidents. However, tests of actual driving behavior and motor vehicle accident victims have not borne this out as a practical reality.

Although it is not at all clear that marijuana smoking causes psychiatric illness, there is considerable evidence that pre-existing psychiatric conditions, including psychotic episodes in schizophrenics, can be triggered by ingestion of cannabinoids. The relative risk of developing psychiatric problems appears to be very small among the general population of cannabis users. On the other hand, marijuana does appear to play a significant role in complicating the care for the chronically mentally ill, including contributing to a patient's failure to comply with prescribed medication regimens.

Cannabis ingestion has an effect on the cardiovascular system, causing tachycardia, orthostatic hypotension and EKG changes. Chronic conditions such as angina or congestive heart failure may be aggravated by cannabis, especially when smoked. However, the role of cannabis as an etiologic factor in heart disease has not been established.

Cannabinoids interact in multiple and complex ways with the immune and endocrine systems, leading to alterations in gonadotropin, prostaglandin, cortisol and sperm levels, and may affect ovulation in humans as it has been proven to in other primates. To date, studies of the effect of cannabinoids on immunity have been contradictory and, when viewed in the aggregate, difficult to interpret, especially in regard to their clinical significance to humans. This is an area in special need of further research, as HIV+ patients are frequent requesters of marijuana for medicinal purposes.

There is little evidence of teratogenic effects of cannabis. However, smoking marijuana leads to the same effects as tobacco by lowering birth weight and shortening gestation. Evidence for post-natal developmental difficulties is suggestive, but far from definitive. A 10-fold increase in the relative risk of childhood leukemia in children exposed to cannabinoids during gestation has been reported.

The conclusion of the Addiction Research Foundation kept the known and potential adverse physical effects of cannabis in perspective when it stated that, "By any accounting, the impact of health problems linked to cannabis is much less than that resulting from alcohol or tobacco use."

Psychopharmacology

While recreational users specifically seek the psychoactive properties of cannabis, psychological effects are more likely to be seen as side effects by people seeking relief from a medical condition (except perhaps for those who are attempting to alleviate anxiety or depression). From the perspective of addiction medicine, therefore, our interest lies in two areas: understanding the psychopharmacology of cannabis in order to educate medical patients about its

potential "side effects" and developing criteria to help physicians determine whether cannabis use is truly treating anxiety and depression or providing short term palliation while simultaneously exacerbating the problems in the long run (the hallmark of many drugs of abuse and dependence).

Delineation of the psychological effects of cannabis is complicated by the fact that its impact on mental functions varies in response to set and setting. Set refers to the subject's psychological expectations of a drug's impact and varies widely depending on whether the user is naive or experienced with cannabis, and especially whether the user is an adult, adolescent or child. Setting refers to the total environment in which the drug is taken. Set and setting regarding cannabis have continuously and substantially evolved within American culture over the past century as perceptions of both the drug's value and dangers changed. Since both set and setting are known to affect response to opiates in post-operative situations, where physical dependence can develop in the absence of psychological dependence, it is quite likely that the new set and setting

created by society's recent sanctioning of medicinal use of cannabis, including the fact that patients will be ingesting the drug for the primary purpose of alleviating symptoms of serious physical illness, will significantly impact perceptions of its side effects. The practical consequences of this new set and setting will need to be discovered empirically, since it is impossible to predict human behavior of such complexity.

Research studies of cannabis have documented three categories of psychoactive effects:

Sensory

Time perception is altered, producing an overestimation of elapsed time. Users consistently describe a "heightened sensitivity" to sensory input, leading to greater appreciation of colors, patterns and music, for example.

Cognitive

Early studies established that cannabis does not grossly affect cognitive functions, although suggestions of subtle impairments remained.

Is Cannabis a gateway drug?

It is not proven that use of cannabis "causes" the use of other, more acutely dangerous drugs (alcohol, opiates, cocaine, speed, LSD), and many proponents of harm reduction argue that the availability of marijuana can decrease the use of more dangerously addictive drugs. However, many others believe that marijuana, alcohol and tobacco are often the first drugs experienced by children and adolescents who do slide into harmful addiction, and that marijuana is often the first drug used by people addicted to more acutely dangerous drugs as they begin to relapse. Very different social policy perspectives and considerable scientific ignorance combine to make this an extremely difficult question to address.

Is there an "amotivational syndrome?"

Clinical reports of an "amotivational syndrome" typically have described a state among chronic, heavy cannabis users in which the user's focus of interest narrowed, they became apathetic, withdrawn, lethargic, unmotivated, and showed evidence of impaired memory, concentration and judgment. To date, all of these studies have been uncontrolled and impossible to disentangle the effects of chronic cannabis use from those of poverty, low socioeconomic status, and pre-existing psychiatric disorders. Despite clinical observations conforming to descriptions of an amotivational syndrome, research evidence is quite equivocal, and perhaps the entire phenomenon is more related to a depressive syndrome. Such a depressive syndrome could either be independent from the cannabis use, or secondary to its use, although there is no way of knowing currently whether any causative relationship would be primarily psychological or pharmacological. The Addiction Research Foundation (Toronto) concludes that "While there is reasonable evidence that heavy use of cannabis can affect motivation, the existence of a syndrome with identifiable symptoms outlasting the drug use and withdrawal has not been demonstrated."

Can cannabis cause psychosis?

There is reasonable evidence that heavy cannabis use can precipitate a toxic psychosis in which confusion, amnesia, delusions, hallucinations, anxiety, agitation and hypomanic symptoms occur. More common, perhaps, is the strong possibility that cannabis can precipitate a latent psychosis in vulnerable individuals.

Improvements in neuropsychological and electrophysiological testing methodology during the late 1980s and through the 1990s have now permitted more sensitive studies of specific stages of information processing. Using these new tools, Solowij et al. have demonstrated that heavy frequency of cannabis use prolongs stimulus evaluation time (measured by P300 latency) while long duration use impairs the ability to focus attention effectively and to reject irrelevant information (evidenced by increased processing negativity to irrelevant stimuli). These results suggest that different mechanisms underlie the different cognitive impairments caused by cannabis, with the slowing of information processing perhaps reflecting a buildup of cannabinoids and the inability to focus attention and reject irrelevant information possibly reflecting changes at the level of cannabinoid receptor sites. Therefore, although no gross cognitive impairments occur with long-term use, very sensitive measurements do reveal impairments specific to the organization and integration of complex information, involving various mechanisms of attention and memory. It is not known to what extent such impairment may recover with prolonged abstinence. Wayne Hall, of the National Drug and Alcohol Research Centre at the University of New South Wales, proposes that multiple lines of evidence now point to frontal lobe dysfunction as the underlying cause of these subtle impairments. His hypothesis is consistent with the facts that the frontal lobes are responsible for the temporal organization of behavior necessary for memory and planning (one well-recognized effect of cannabis intoxication being altered time perception), cerebral blood flow studies demonstrate the greatest alterations in the frontal lobes, and EEG power is most altered over the frontal lobes in long-term cannabis users.

Motor

Cannabis produces a dose-dependent impairment of specific motor skills and attentional mechanisms underlying motor behaviors tested in laboratory studies, particularly tracking, divided attention and vigilance tests. However, the extent to which cannabis contributes to traffic accidents is unknown, and driving simulator tests reveal relatively small effects. "Drivers under the influence of marijuana tend to overestimate the level of impairment and compensate by concentrating on driving and/or slowing down. In contrast, drivers under the influence of alcohol tend to underestimate the effects of alcohol and not make allowances for impairment." (Adams and Martin, p. 1602)

When patients use cannabis for medical purposes, the psychological effects outlined above are likely to be experienced as undesirable. The adverse effects of cannabis can be either acute or chronic.

Adverse *acute* effects of cannabis ingestion include

- anxiety, dysphoria, panic and paranoia
- sedation and drowsiness
- cognitive impairment, especially attention and memory, during intoxication
- psychomotor impairment
- exacerbation of pre-existing or latent psychiatric symptoms
- relapse of chemical dependence

Adverse *chronic* effects of cannabis may include

- cannabis dependence
- subtle cognitive impairment characteristic of frontal lobe dysfunction
- impaired educational performance in adolescents and professional performance in adults
- exacerbation of pre-existing or latent psychiatric symptoms

As with most medications, specific populations can be identified as being at higher risk of adverse effects. In the case of cannabis, high risk populations include

- children and adolescents - developmental delays and disturbances
- women of childbearing age - no dose of cannabis is known to be safe during pregnancy
- chemical dependence - latent or pre-existing
- psychiatric illness - latent or pre-existing

Cannabis Abuse and Dependence

The hallmark neurophysiologic effect of psychoactive drugs of abuse lies in their interaction with the brain's reward mechanisms. Cannabinoids have been shown to stimulate the release of dopamine in the nucleus accumbens, which is the benchmark measure of such interaction.

Tolerance and withdrawal have long served as the grossest, and surest, markers for an organism's physical dependence on an ingested substance. Neither are obvious features in most human use of cannabis.

However, much research evidence for tolerance does exist. Various animal models have demonstrated tolerance to analgesic effects, catalepsy, depression of locomotor activity, hypothermia, hypotension, corticosteroid release, and ataxia, for examples. Tolerance does not occur to all cannabinoid effects, such as ACTH secretion. Cultured cells also display tolerance in various biochemical activities. Humans on high doses of marijuana have convincingly been shown to develop tolerance to a variety of its effects, including

intoxication (the "high"). Several groups have demonstrated cannabinoid receptor downregulation in animals after tolerance develops.

Withdrawal can be demonstrated by ceasing the administration of cannabinoids or precipitated by administering an antagonist. Rats chronically infused with delta-9-THC for four days demonstrate behavioral signs of withdrawal ten minutes after intraperitoneal injection of the antagonist SR 141716A, including head shakes, facial tremors, tongue rolling, biting, wet-dog shakes, eyelid ptosis, facial rubbing, arched back. Withdrawal in humans chronically using large amounts of cannabis has been described as involving primarily irritability and restlessness, but also insomnia, anorexia, mild nausea, increased body temperature and hand tremor (all alleviated by re-administration of delta-9-THC). Even in cases where there is no clinically evident withdrawal syndrome, cessation of chronic cannabis use would, at a minimum, lead to a situation in which the cannabinoid receptors are in a down-regulated state compared to normal.

The actual clinical significance of tolerance and withdrawal in humans is, however, by no means clear. The fact that withdrawal is so minor as to be rarely observed in humans has not prevented cannabis abuse and dependence from being included within DSM-IV as recognizable syndromes falling into the same category as other substance abuse/dependence disorders. The incidence of cannabis abuse or dependence, either alone or in association (co-temporaneously or antedating) with other drugs is quite unknown. However, according to T. A. Constantine of the Drug Enforcement Agency, in 1993, marijuana was the primary drug of abuse in 119,444 treatment center admissions in the United States. Among those seeking primary treatment for cannabis dependence, the major complaints have been the loss of control over their drug use, cognitive and motivational impairments which interfere with occupational performance, lowered self-esteem and depression, and the complaints of partners.

The acute effects considered desirable and sought by recreational users include an intoxicating sense of euphoria and relaxation (which can meld into sedation and drowsiness), perceptual alterations and intensification of sensory experience, an altered "state of consciousness" that enables a range of phenomena, such as greater sociability and/or a perception of greater introspection and creativity, and an enhanced sense of wonder, often in matters that are otherwise habituated to as mundane. In some cultures cannabis intoxication is an integral part of spiritual life. For many chronic users, the experience is often an antidote to tension and integral to an unconventional, alternative lifestyle that can either be quite encompassing or contained to evenings and weekends. As with alcohol, many people

ingest cannabis as a reward, solace, or simply an announcement to oneself that the day is over and you are temporarily "off duty."

When use becomes compulsive, when the drug user's behavioral and psychological repertoire is narrowed in order to safeguard cannabis use, and when cannabis use takes on a high enough salience in a person's life that problems are created in relationships, finances, employment, etc., then it can be said that psychological dependence has developed.

CSAM should be guided in large part by the public health model

Wider and Deeper Implications of Proposition 215

The California public's passage of Proposition 215 into law as Health and Safety Code Section 11362.5 calls into question more than the medical use of cannabis. If, for example, "It is time for physicians to acknowledge more openly that the present classification is scientifically, legally, and morally wrong," it is at least as important to acknowledge more openly that the present approach to public drug policy (summarized in the phrase "War on Drugs") is bankrupt. It has failed us. Canadian experience presents a parallel story, with the Le Dain Commission's recommendation in 1973 for the gradual withdrawal of criminal sanctions against cannabis being ignored in favor of more harsh approaches. In contrast, the Addiction Research Foundation of Toronto concludes that "...the justifiable concern with the health effects of cannabis is not incompatible with a less punitive legal response to the user."

Also called into question is the entire drug evaluation process involving the complex tapestry of pharmaceutical companies, the Food and Drug Administration, and the Drug Enforcement Agency. This complex has been driven by economic and political forces, as well as more scientific forces, and the public is beginning to recognize that their interests are not always being adequately served. Furthermore, forces favoring medical approaches deemed to be alternatives to the traditional allopathic perspective are likely to be strengthened by recent events. It is unclear whether all these challenges to the status quo will have beneficial effects; but it is certainly clear that the medical field will not be well served, nor will it serve its patients well, if we hold back and remain behind the curve of change.

Ultimately, CSAM should be guided in large part by the public health model, exemplified by the following quote from the Addiction Research Foundation's *Cannabis, Health*

and Public Policy: "...the use of alcohol, tobacco and other drugs should be seen primarily as a public health issue rather than one dominated by moral or legal principles. The main goal of public policy and practice should be twofold: to reduce harm and cost from drug use, and to minimize the harms and costs of drug policy [and drug treatment]."

The author acknowledges particular indebtedness to two excellent review articles by Adams and Martin (Addiction, 1996) and Hall, Solowij, and Lemon (Australian Government Publishing Service, 1995) which provided the backbone of this paper.

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David L. Breithaupt, MD

ASAM Statement on Marijuana

Marijuana is a mood-altering drug capable of producing dependency. Its chief active ingredient is delta-9-tetrahydrocannabinol.

Marijuana has been shown to have adverse effects on various organ systems, on perception, behavior and functioning, and on fetal development. Because of the widespread use of this drug, its effects on mind and body, and the increasing potency of available supplies, ASAM strongly recommends:

1. Education about drugs, beginning in the earliest grades of elementary school and continuing through university level. Drug education should contain scientifically accurate information on the dangers and harmful effects of marijuana, and on the disease of marijuana dependence.
2. Health and human service professionals should be educated about marijuana and marijuana dependence as a required part of their curriculum.
3. Persons suffering from alcoholism and other drug dependencies should be educated about the need for abstinence from marijuana and its role in precipitating relapse, even if their original drug of choice is other than marijuana.
4. Marijuana dependent persons, like other drug dependent people, should be offered treatment rather than punishment for their illness. Treatment of marijuana dependence should be part of the plan for rehabilitation of any person convicted of a drug-related offense, including driving under the influence of alcohol and/or drugs, who is found to be marijuana dependent.
5. Approved medical use of marijuana or delta-9-tetrahydrocannabinol for treatment of glaucoma, illnesses associated with wasting such as AIDS, the emesis associated with chemotherapy, or other uses should be carefully controlled. The drug should be administered only under the supervision of a knowledgeable physician.
6. Research on marijuana, including both basic science and applied clinical studies, should receive increased funding and appropriate access to marijuana for study. The mechanisms of action of marijuana, its effect on the human body, its addictive properties, and any appropriate medical applications should be investigated, and the results made known for clinical and policy applications. In addition, ASAM strongly encourages research related to the potential and actual effects of marijuana-related public policy.
7. ASAM encourages the study of the potential impact of making cannabis available for approved medical uses, and the consideration of what changes might result from moving cannabis from Schedule I to another Schedule.
8. Physicians should be free to discuss the risks and benefits of medical use of marijuana, as they are free to discuss any other health-related matters.

Passed by ASAM Board of Directors on 4/16/97

CSAM Position on Medical Use of Marijuana in California

The CSAM Task Force on Medical Marijuana prepared a series of recommendations for CSAM positions and actions about the medical use of marijuana in California which were adopted by the Executive Council in May. CSAM's position is based on three core beliefs and one prediction:

1. **Marijuana is a mood-altering drug capable of producing dependency.** This basic assertion, which begins the American Society of Addiction Medicine's 1987 Public Policy Statement on Marijuana, has not been altered by recent passage of California's Proposition 215 - the Compassionate Use Act of 1996.

2. **"Compassionate use" of marijuana is accepted by a majority of the voting segment of California's population.** Physician support for the concept of compassionate use of cannabis and physician opposition to the unwarranted intrusion of governmental control into the practice of medicine and the doctor-patient relationship are both strong, as reflected in a quote from the JAMA Commentary published June 21, 1995: "It is time for physicians to acknowledge more openly that the present [Schedule I] classification [of marijuana] is scientifically, legally, and morally wrong."

3. **Proposition 215, which became Health and Safety Code 11362.5, is poorly written and unimplementable without further enabling and clarifying legislation.** Implementing legislation and regulatory changes creating appropriate safeguards (both for physicians and patients) are required on both the state and federal levels.

4. **The use of marijuana, as opposed to the therapeutic value of the cannabinoids it contains, is likely to be a time-limited issue.** "While there may be some merit in legalization arguments [for medical purposes], the development of a potent and selective cannabinoid possessing greater efficacy than current drugs [and disconnecting the medically valuable effects from psychoactive effects] would, of course, end the ongoing debate." Adams, Irma and Martin, Billy, "Cannabis: pharmacology and toxicology in animals and humans," *Addiction* (1996) 91(11), 1585-1614.

"Because marijuana and delta-9-THC often produce troublesome psychotropic or cardiovascular side-effects that limit their therapeutic usefulness, particularly in older patients, the greatest therapeutic potential probably lies in the use of synthetic analogues of marijuana derivatives with higher ratios of therapeutic to undesirable effects." *Marijuana and Health*, Report of a Study by a Committee of the Institute of Medicine, National Academy Press, Washington, D.C., 1982.

The following CSAM actions have as their goal to provide California physicians who are recommending cannabis for medical reasons appropriate practice guidelines and to

identify enabling legislation and regulatory changes required to implement such legislation.

CSAM Actions:

CSAM urges the Medical Board of California to take formal action to adopt the position that all physicians who recommend cannabis should be held to the accepted standards of practice for prescribing as they were cited in an article in the January 1997 issue of *Action Report*: "history and physical examination of the patient; development of a treatment plan with objectives; provision of informed consent, including discussion of side effects; periodic review of the treatment's efficacy and, of critical importance especially during this period of uncertainty, proper record keeping that supports the decision to recommend the use of marijuana."

CSAM suggests that the statement be expanded to include a requirement for notation of a diagnosis, or differential diagnosis, which can be coded according to ICD10 or DSMIV, or a notation of the specific symptoms being addressed.

CSAM urges all California physicians to adhere voluntarily to these standards until such time as the Medical Board takes formal action.

CSAM supports controlled studies of the medical usefulness of marijuana, including all routes of administration, and especially supports studies of the therapeutic effects of the essential ingredients and the congeners of cannabis sativa.

CSAM urges immediate funding for research directed towards understanding the populations seeking medical use of marijuana at cannabis centers and the impact of marijuana's medicalization on the general public's attitudes toward and use of marijuana and other psychoactive drugs, with special emphasis on minors, the mentally ill, the chemically dependent, and women of childbearing age.

CSAM urges the DEA to remove cannabis from Schedule I and move it to an appropriate Schedule, below Schedule I, as determined by what is known about its therapeutic benefit and its potential for abuse in proportion to other drugs of abuse.

Regarding the way in which marijuana is distributed, the Task Force on Medical Marijuana expressed some concern about the unregulated nature of the practices in use now and the lack of standardization from locale to locale. The members of the Task Force agreed to continue to gather information and consider if a CSAM position seems appropriate.

CSAM plans to publish guidelines outlining the information which should be given to patients in order for them to give a truly informed consent regarding medical use of cannabis, and to urge the Medical Board of California to publish them. □

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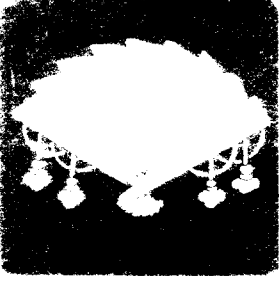
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510/428-9091 FAX 510/653-7052.