

THE LINDESMITH CENTER

Therapeutic Potential and Medical Uses of Marijuana

Milksripe, Tod. "Critique: Marijuana and Health, Report of a Study by a Committee of The Institute of Medicine Division of Health Sciences Policy, National Academy of Science Washington, D.C. (National Academy Press, 1982). 108 PP. Chapter 7 (PP. 139-155), Therapeutic Potential and Medical Uses of Marijuana." Journal of Psychoactive Drugs 14 (1982): 339-341.

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*War Is Peace
Freedom Is Slavery
Ignorance Is Strength*

- George Orwell, 1984

Inscribed on the facade of the Ministry of Truth, these words summarize the federal medical and scientific policies in the field of moral pharmacology. With this most recent groupthink revision of scientific newspeak, cannabis history now starts in 1981 in response to the introduction of a bill in Congress (H.R. 4498) "to provide for the therapeutic use of marijuana in situations involving life-threatening or sense-threatening illness and to provide adequate supplies of marijuana for such use," and promises a review of the literature, which, except for one citation in 1889, one in 1947 and one in 1953, the expunged literature is now comprised mostly of research conducted in the 1970's. Thus, the perspective of the Committee is based on minimal experience in therapeutic applications, deprived of the practical experience from clinical access enjoyed by their colleagues of half a century ago when cannabis was available by prescription.

Most important in therapeutic potential and medical uses of marijuana are the omissions. Left out was the fact that cannabis presentations were widely used in Western medicine from 1839 to the early 1940's. Omitted: concise and accurate descriptions of the medicinal applications of cannabis that appeared in the *U.S. Pharmacopoeia* and Goodman and Gilman's textbook of pharmacology, second edition (1955). Forgotten: primary scientific, structure-activity and pharmacologic studies by Professor S. Loewe (1950) in the 1940's and early 1950's. Neglected: comprehensive clinical research by the Mayor's Committee on Marijuana in 1944.

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GLAUCOMA

A reasonably fair assessment of variable results with different varieties of the illness. Indeed, topical application would be desirable in nonneurogenic glaucoma, but solubility characteristics of cannabinoids would appear to be intrinsically irritating. It would appear that slow titration with natural or synthetic cannabinoids orally (Reynolds 1890) would enhance the possibility of favorable results with the greatest medical safety.

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ANTIEMETIC ACTION

Indeed, the discovery of cannabis as an antiemetic is a most important and truly new discovery that was not known to medicine when it was available. It is exciting to learn of the positive results, and one can only wonder why an inhalant cannot be developed to deliver purified natural and synthetic cannabinoids. The inhaled route is inherently preferable especially when nausea and vomiting are inhibiting gastrointestinal retention and absorption. Autotitration is also made possible because of this comparatively short latency period after administration by this route.

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ANTICONVULSANT ACTION

Medical practitioners of more than a century ago (e.g., McMeens 1856, O' Shaughnessy 1839) would turn over in their graves to read that a major drug for certain nervous disorders had retrogressed to a preclinical status of "showing promise" in a 15-subject seizure disorder study in 1980.

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MUSCLE RELAXANT ACTION

As described in the context of utility in spasticity, this delineation being centrally mediated would correctly fall within the domain of the anticonvulsant activity.

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ANTIASTHMATIC

It is encouraging to see cannabis rediscovered as an antiasthmatic agent. McMeens (1860) and Waring (1874) noted cannabis to be useful in some cases of asthma and hay fever where an "irritable nervous system" seemed to be involved. Cannabis as a treatment for asthma was mentioned in India in 1954.

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ANTIANKXIETY-ANTIDEPRESSANT EFFECT

This section by the Committee demonstrates the methodological problems involved in translating commonly observed cannabis-use behavior into a scientific presentation that is oriented to therapeutic utilization. This author's personal observations of chronic users clearly show cannabis' applications to closely approximate those of the benzodiazepines or alcohol. Like other sedatives, the onset of effects may be an initial stimulation. Alcohol and cannabis share this property. After the stimulation phase there is a calming effect. The intensity of the stimulation (and sedation) is directly dose-related. Low dose (two or fewer joints/day) chronic use of cannabis appears to have an effect comparable to five mg of diazepam (Valium®) twice a day. Chronic cannabis users also show a slight stimulant effect with a mental lift and an EEG shift from predominantly alpha/theta (four to 13 Hz) to mostly beta waves (>14 Hz).

Low and moderate dose cannabis use appears to decrease affectual reactivity and subjective sense of pressure with reduction of concomitant multisystem stress. The site of activity is probably at the thalamo-cortical level, as postulated by Walton

(1938). The reddened eyes of cannabis users reflect an apparent specific meningeal/vasomotor response. Cannabis, as compared with other psychotropics, has remarkably minimal brain stem and other peripheral effects.

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ANALGESIC ACTION

Not referenced nor mentioned: Animal models showing analgesic effects for cannabis and its derivatives starting as far back as Hare (1887) and Marshall (1898), as well as overlooking the extensive bioassay protocol utilized by the pharmaceutical industry to standardize the strength of cannabis preparations in reference to U.S.P. standard preparations available from the U.S. Food and Drug Administration until 1938.

The "mental clouding" side effect reported in 1976 when using THC as an analgesic for cancer pain control might have been avoided by emulating Dr. J. Russell Reynold's protocol of gradual upward titration of cannabis tincture, as described in *Lancet* in 1890. (Perhaps, using a U.S.P. standard cannabis tincture might have been more effective than THC.)

Ignored: Numerous descriptions of cannabis as the treatment of choice for migraine headache, as listed in materia medica, journals and texts with the latest (and unfortunately last) in the *Journal of the American Medical Association* by Morris Fishbein (1942) 40 years, ago.

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ALCOHOLISM

In this author's limited clinical and social experience, the substitution of cannabis as a euphoriant/sedative is possible in some cases. The success of substitution depends on support groups of other cannabis users. Failure is usually due to denial and rigidly habituated behavior patterns usually involving other alcoholics or alcohol abusers. Another significant source of failure is the deterrence by its illegal status and uncertain supply of the drug.

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OPIATE WITHDRAWAL

It should be said that the reason there are no efforts to follow up on Birch's (1889) and Mattison's (1891) early clinical experiences is because of the excessively restrictive multiagency federal involvement. In the moral pharmacologic regulatory reality, the treatment of discomfort brought on by the abuse of another illegal drug is low priority.

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ANTITUMOR ACTION

It might be construed to be antitumor in the enhancement of appetite and suppression of nausea, but, as such, specific antioncologic activity seems unlikely.

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SUMMARY

The lack of clinical experience is a serious impediment to a realistic appraisal of the therapeutic potential of cannabinoids. The federal bias toward pushing THC for scientific "purity" and the inability to grow or process cannabis would appear to constitute another negative influence. It is gratifying that despite these difficulties the Committee is in favor of further research into the medicinal applications of cannabis.

There is sufficient clinical data, both recently and historically, to warrant the restoration of cannabis products for general prescribing. The Committee is generally correct in their favorable findings in glaucoma and antiemetic applications, but grossly underestimates the utility of cannabinoids as sedative, anticonvulsant and antimigraine agents because of inadequate experimental protocol, a less than thorough review of the medical literature and dog-in-the-manger interagency conflict-based

federal policy.

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RECOMMENDATIONS FOR RESEARCH

The development of nonirritating purified natural cannabinoid aerosol preparations should be a top priority effort. The reality is that because the smoked route is used, there will be huge numbers of chronic cannabis smokers subjecting their tracheobronchial trees to irritation from pyrolyzed impurities that technology could prevent. Precisely how much morbidity and mortality, which could have been prevented through appropriate research and development, remains to be answered in the distant future.

Cannabis homologues have been studied since the late 1930's. The compounds synthesized and studied by Loewe (1950) have yet to be adequately reevaluated and would be of potential benefit to the present knowledge of chemical structure-activity relationships in cannabinoids - the only complex nonnitrogenous water insoluble psychotropic agents known.

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conclusive evidence

This response submitted by zake on 9/23/96.

Author's Email:

Niaamas asked about conclusive evidence.

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Also consider the following comments from a commentary from the Journal of the American Medical Association:

Marijuana as Medicine - A Plea for Reconsideration

Lester Grinspoon, MD James B. Bakalar, JD
Department of Psychiatry, Harvard Medical School

European and American medical journals published more than 100 articles on the therapeutic use of the drug known then as *Cannabis indica* (or Indian hemp) and now as marihuana. **It was recommended as an appetite stimulant, muscle relaxant, analgesic, hypnotic, and anticonvulsant.**

And yet physicians and patients in increasing numbers continue to relearn through personal experience the lessons of the 19th century. Many people know that marihuana is now being used illegally for the nausea and vomiting induced by chemotherapy. Some know that it lowers intraocular pressure in glaucoma. **Patients have found it useful as an anticonvulsant**, as a muscle relaxant in spastic disorders, and as an appetite stimulant in the wasting syndrome of human immunodeficiency virus infection.

Physicians have both a right and a duty to be skeptical about therapeutic claims for any substance, but only after putting aside fears and doubts connected with the stigma of illicit nonmedical drug use. Advocates of medical use of marihuana are sometimes charged with using medicine as a wedge to open a way for "recreational" use. The accusation is false as applied to its target, but expresses in a distorted form a

truth about some opponents of medical marihuana; they will not admit that it can be a safe and effective medicine largely because they are stubbornly committed to exaggerating its dangers when used for nonmedical purposes.

[Link to JAMA Article quoted above](#)

BTW niahmas, amphetamines also have an anti-seizure effect. Look at the indications for dextroamphetamine sulfate [HERE](#).

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Speaking from experience....

This response submitted by Sarah K. Rossi on 9/11/96.

Author's Email: SPEK123@aol.com

I am a 25 yr. old female and I've had Grand Mal seizures since I was 17. I usually have one every few months. I'm taking 400mgs. of Dilantin every night, which made it almost impossible for me to drink alcohol. Anything beyond two beers gives me hangover type symptoms an hour after I've started drinking.

I have been a pot smoker long before seizures were ever a part of my life and will probably continue to be one well into my old age. The only problems I have experienced with it is the drowsiness. My medication already causes me to be tired all the time, so when I smoke pot, it's got to be when I'm at home near my bed.

I even asked one of my doctors quite a few years ago if smoking pot would have any adverse effects on my seizures, and he told me that if anything, it may help (if done in moderation). It helps ease the symptoms of stress, eliminating one of the major causes of seizures.

If you're interested about the effects of any other drugs on the condition, let me know because I can give you first hand information on quite a few of them. And it's not some theory from a medical journal and it may not be the same for someone else as it was for me, so take it with a grain of salt.

Hope I was of help...

Sarah K. Rossi

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Marijuana... Cause or Cure?

This article submitted by John Cillhup on 11/11/95.

I have heard of marijuana being used to control siezures and some say it can cause it. I've read that before it was illegal it was tested once on 5 severe grand mal epileptics who still had seizures while on Dilantin, Phenobarbital or Mesatoin, the result was that 3 responded at least as well and the other 2 were seizure free!!! (This was done by J.P. Davis and H.H. Ramsey in 1949 "Antiepileptic Action of Marijuana-Active Substances" Fed.Proc.,8(1949),284-285) Is anyone controlling their seizures with it or does anyone have any experiences of it causing their seizures. It seems as if the side effects are far less, and I couldn't see it causing depression, (maybe quite the opposite!) if it were legal, I wonder what I would say if I was given the choice of Tegretol or Marijuana. Open minds open doors. Why has research stopped?

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Who can prescribe it?

This response submitted by Candace Parsley on 7/15/96.

Author's Email:

I was wondering if any neurologist can prescribe marijuana or is it only a choice few? I have a feeling my neurologist might be a tad closed minded about it. Also, how much do you use? I have never been a big supporter of drugs, but my meds don't work when I get stressed, and it seems that marijuana would calm me down. Does it effect hormones in any way? my seizures are very tied to my hormones, and the pill has stopped working. I have juvenile myoclonic epilepsy and am on Neurontin and Zerontin. Both have pretty evil side effects. I am a sophomore in college so I need my mind in good order. Would the marijuana effect my memory in a negative way? I have lots of questions about this. Who can I ask that has a well rounded knowledge of the subject.

Please e-mail any info to
cparsley@skidmore.edu
Thank you

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marijuana-does it help?

This response submitted by Duke Doyun on 10/13/97.

As an epileptic who has responded very poorly to the "normal" drugs, I can attest to the help MJ has been in my life. I've got Juvenile Myoclonic Epilepsy (JME) and the MJ has helped me calm down when I was on my way to serious trouble, as it were.. T.C. sz; myoclonic clusters can control my life, IF they're not stopped a.s.a.p. Some how that isn't an attractive idea. Lorzapam works about 40% of the time, if I'm lucky and take alot in an hour [4mgs. minimum] Depression? No. This is from an expert with serious depression, I've been that way the majority of my life. It really does help some of us.

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marijuana-does it help?

This response submitted by P. Murphy, M.D. on 11/14/97.

I have a 26 year old brother that suffers from seizures who was on Valproic Acid for 3 years and now is on Tegretol. he has also used Dilantin. He says the use of pot helps him through the headaches and easier to sleep. I would like to find out more info on resaerch for this.

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it works for me

This response submitted by luvnwm on 10/16/96.

Author's Email:

I am 25 years old and developed temporal lobe epilepsy causing complex partial seizures 18 months ago. At the time I was smoking marijuana a couple of times a week. I immediately ceased smoking as I assumed it would be having a negative effect on my condition. Treatment for my seizures was difficult as I was allergic to most medications. 1995 was a nightmare.

January this year things began to improve as I found a drug combination that seemed to work (I was on sodium valproate, lamictal and a common sedative). As I was feeling a little better I thought I might try smoking pot again. When I did I noticed that the occurrence of seizures actually improved. This seemed to make sense to me as marijuana is a form of sedative (has a calming effect). As such I managed to take myself off my highly addictive prescription sedative with a long half-life.

I have been smoking pot again regularly ever since. I have also noticed that when I don't smoke for a period of time my seizures get worse again. Recently I found the courage to mention this to my neurologist. His reply was that he could not recommend that I smoke an illegal drug, but that neurologically it made sense and that it is better for you than cigarettes. (I have also found other references on the net indicating the same.)

I would never advise someone how much marijuana they should take and how often as it really is an individual thing, and I do acknowledge that it is not for everyone. However it honestly does work for me.

P. S. As for how to administer it - I usually smoke it or sometimes bake it into cookies, either way it is fun!

good luck and I hope this has been of some assistance!

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Database Record

Record: 35378

Accession Number: AD35378

Author:

Corporate Source: American Medical Association,

Corporate Source: Department of Science News

Corporate Source: Chicago, Illinois, USA

Title: Marijuana should be legally available as medicine

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Abstract: It is contended that the treatment of a number of illnesses, including AIDS, cancer, glaucoma, and migraine headaches, would be furthered greatly by the legalization of marijuana. According to a physician and an attorney from the Massachusetts Mental Health Center in Boston, a multitude of research has refuted claims that marijuana is either dangerous or addictive, and, in fact, researchers have more knowledge of the effects of marijuana than of most prescription drugs; yet, it remains illegal. Its legal status forces those who are in need of its therapeutic effects to turn to drug dealers and to leave themselves open to possible criminal prosecution. Marijuana has been found effective in reducing the nausea induced by chemotherapy, lowering the intraocular pressure caused by glaucoma, as an anticonvulsant for spastic disorders, as an appetite stimulant for those suffering from AIDS, and in relieving such chronic pain disorders as migraine headaches, menstrual cramps, and phantom limb pain. It is suggested that its one legitimate drawback, the introduction of high levels of tar into the lungs when smoked, could be controlled by the smaller doses used for medicinal purposes and by refinement of procedures as use was allowed. The American Medical Association (AMA) opposed the Marijuana Tax Act of 1937, which made marijuana difficult to obtain and removed it from the pharmacopeia. Physicians are urged to acknowledge that the current classification of marijuana by the Drug Enforcement Administration (DEA) as a Schedule I drug -- indicating it is a substance with a high potential for abuse, no accepted medical use, and is unsafe for use under medical supervision -- is scientifically, legally, and morally wrong. It is hoped that further research into marijuana's potential as a medical therapy will lead to its rescheduling by the DEA as a Schedule II drug, making it available by physician prescription. The AMA does not condone the production, sale, or use of marijuana, and its current position is that the sale and possession of marijuana should not be

legalized for recreational public use; however, it does assert that research into marijuana's potential usefulness in the treatment of medical conditions should continue.

Term Descriptors: Marijuana in any form

Term Descriptors: Drug therapy

Term Descriptors: Neoplastic disease

Term Descriptors: Acquired immunodeficiency syndrome

Term Descriptors: Migraine headache

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BMA To Lobby For Legalization Of Marijuana For Medicinal Use

LONDON, Jul 3 (Reuters) - Members of the British Medical Association (BMA) voted unanimously at their annual meeting to lobby Parliament for legislation to allow the use of marijuana for management of a number of clinical conditions. The vote took place during the third day of the BMA's 4-day convention in Edinburgh.

"We don't want our patients to use unlicensed cannabinoids that could be dangerous," a spokeswoman for the BMA said, quoting Dr. Upendra Pati, author of a motion to legalize marijuana for therapeutic use.

Currently, British physicians are allowed to prescribe two cannabis derivatives to inpatients for the single indication of chemotherapy-induced nausea.

A spokeswoman for the AMA said that the physicians' group was not interested in decriminalizing the drug for general public use. The BMA is preparing a report on the possible medical uses of marijuana, which will be published in the autumn, she added.

Britain's physicians are not alone in investigating the possible medicinal value of marijuana. A research panel advising the National Institutes of Health also has been looking at therapeutic applications associated with its use such as management of iatrogenic anorexia and glaucoma.

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Pharmacologists Call For Revamping Of Drug Laws

SAN DIEGO, Mar 11 (Reuters) - At their annual meeting, members of the American Society for Pharmacology and Experimental Therapeutics overwhelmingly approved a resolution calling for an overhaul of the

nation's drug laws.

The resolution, which originated at the Hoover Institute at Stanford University, criticizes today's emphasis on the legal system and its "...cottage industry of prisons..." to combat the nation's drug problems.

The Resolution for a Federal Commission on Drug Policy, which is commonly known as the Hoover Resolution, has been signed by, among others, editors of some of the major medical journals. However, a number of medical groups, including the American Medical Association, have not endorsed the resolution, which states that society's efforts to punish drug abusers have had an unwanted effect in that "...legitimate medical uses for the relief of pain and suffering of patients have been suppressed."

The professional association intends to mail a copy of the resolution to every member for his or her signature.

"The vote was a very pleasant and wonderful surprise," said Dr. G. Alan Robison, of the University of Texas Health Science Center at Houston. One year ago, the Hoover resolution was considered to be too controversial to be put on the agenda, but this year it passed. "It sort of reflects society at large," said Dr. Robison, referring to voters' recent approval of medical marijuana use in California and Arizona.

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Marijuana Should Be Allowed As Therapy, NEJM Editor Says

WESTPORT, Jan 30 (Reuters) - Dr. Jerome P. Kassirer, editor-in-chief of The New England Journal of Medicine, argues in an editorial in the January 30 issue of the journal that the government should allow the use of marijuana to relieve the pain, nausea and vomiting experienced by patients being treated for advanced stages of cancer, AIDS and other diseases.

In his editorial "Federal Foolishness and Marijuana," Dr. Kassirer says the government should move marijuana from a Schedule 1 drug, which is considered potentially addictive with no medical use, to a Schedule 2 drug, which is considered potentially addictive with some accepted medical use. Dr. Kassirer writes, "I believe that a federal policy that prohibits physicians from alleviating suffering by prescribing marijuana for seriously ill patients is misguided, heavy-handed and inhumane. Marijuana may have long-term adverse effects and its use may presage

serious addictions, but neither long-term side effects nor addiction is a relevant issue in such patients."

Dr. Kassirer says it is hypocritical to allow doctors to prescribe morphine and meperidine but not marijuana. He says it is also hypocritical to demand evidence of therapeutic efficacy because it is extremely difficult to quantify the noxious sensations felt by such patients.

Dr. Kassirer concludes: "Some physicians will have the courage to challenge the continued proscription of marijuana for the sick. Eventually, their actions will force the courts to adjudicate between the rights of those at death's door and the absolute power of bureaucrats whose decisions are based more on reflexive ideology and political correctness than on compassion."

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Unpublished Federal Study Shows Marijuana Doesn't Cause Cancer

WESTPORT, Jan 31 (Reuters) - An unpublished federal study which was completed more than 2 years ago showed that tetrahydrocannabinol (THC) didn't cause cancer in laboratory animals.

The 126-page draft of the unpublished study was leaked to AIDS Treatment News, which discusses the study in its January 17 issue. The author of the article, John S. James, suggested that the study may have been suppressed "...because its findings are not what the drug-war industry would want." John Bucher, deputy director of the National Toxicology Program, which conducted the study, said his agency had not been pressured to keep the study quiet. He blamed the delay on a personnel shortage, according to the Associated Press.

In the study, THC was put directly into the stomachs of rats and mice daily for two years. According to AIDS Treatment News, the rats that were given THC displayed a clear survival advantage over those in the untreated control group, while among the mice there was no survival difference between the treated and control group.

The researchers in the study discovered that the more THC given to the mice and the rats, the fewer tumors the animals developed. Because the animals that were given the THC weighed less than those in the control group, "...the researchers speculated that the lower body weight may

have partly accounted for the increased survival and reduced tumors in the THC-treated animals," according to AIDS Treatment News.

Although, the study did not assess the effects of marijuana smoke, it provided evidence that there is no significant cancer risk from THC. However, the author cautioned, "It would be wrong to interpret this study as showing a beneficial or protective effect of marijuana."

Mr. James commented, "The literature review on the effects of THC and marijuana shows how medical research has been politically skewed (although the paper itself does not state this point). There are almost no studies of possible medical uses of marijuana, but many studies looking for possible harm."

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Physician-Assisted Suicide, Managed Care Top Agenda At AMA Annual Meeting

CHICAGO, Jun 25 (Reuters) - A wide range of issues, from physician-assisted suicide to managed care, were debated on opening day at this week's annual AMA House of Delegates meeting. Some 430 delegates will consider close to 200 resolutions during this week's meeting to establish future AMA policies. Voting will begin during today's sessions.

The meeting finds the AMA coming off its "...most successful season of Washington lobbying in more than 20 years," noted AMA President Dr. Lonnie R. Bristow in his opening remarks Sunday. Among 10 key medicine-related votes in Congress this year, said Dr. Bristow, 8 were favorable to organized medicine. "As a result, no new regulatory restrictions are being placed on our profession," he said. "Not one."

Ethical dilemmas and managed care constraints remain troublesome, however, Dr. Bristow said. While acknowledging that the issue of physician-assisted suicide is a highly emotional one, Dr. Bristow staunchly opposes it. He stated that doctors "...must never prescribe a deliberately deadly therapy, even if asked...What is there to trust about a profession which would say it can as easily kill you as save you?" he asked. But the Chicago contingent also heard from supporters of physician-assisted suicide. "What business is it of organized medicine to require the continuation of agony when the result is imminent and inevitable?" Dr. David P. Carter, a family physician in Pawtucket, Rhode

Island asked, as quoted in yesterday's Los Angeles Times. A proposal supporting physician-assisted suicide submitted by an Illinois delegate received lukewarm support at a committee hearing Sunday.

In other Sunday meeting actions:

- The AMA's Council on Ethical and Judicial Affairs conducted an open forum to hear comment on capitation, multiplex genetic testing, quality care at end of life, organ donation, HIV confidentiality and confidentiality of patient records. "None of these are easy issues," said Dr. Charles W. Plows, council chairperson.

- A study of management services organizations released at the meeting found that physician input and involvement in treatment decisions and quality of care were key factors in the success of such organizations.

- AMA member physicians of the Oklahoma County Medical Society received the AMA Medal of Valor for their heroic actions following the April 1995 bombing of the Oklahoma City Federal Building. The award recognized all the society's members, who provided volunteer emergency care to survivors and their family members and rescue workers.

Not on this year's agenda is legislation supporting the legalization of marijuana. The AMA's Scientific Council withdrew their report in the face of strong opposition and "outrage" expressed by the American Psychiatric Association, the American Society of Addiction Medicine and the American Academy of Addiction Psychiatry. AMA spokesman Mark Stuart said that he expects a "...revised version of the report to be submitted at the group's interim meeting in December."

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REUTERS [H: PLCY][MANC]

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Marijuana Use Changes Brain Chemistry

NEW YORK, June 26 (Reuters) -- Many people view marijuana as a relatively harmless drug, probably because it doesn't prompt the severe and frightening withdrawal symptoms seen in heroin-users and

alcohol-abusers.

Now, two new studies in rats suggest that marijuana causes changes in the brain similar to those seen with other drugs, such as nicotine, alcohol, cocaine or heroin. And such changes may "prime" the brain -- making marijuana-users more susceptible to the action of other drugs.

"The finding from this and other studies, that long-term exposure to cannabinoids (the active ingredient in marijuana) can produce changes in the brain that resemble those associated with other major drugs of abuse, suggests that addiction to one drug may make a person more vulnerable to abuse and addiction to other drugs," said study co-author Dr. George Koob in a release from the National Institute on Drug Abuse. Cannabinoids are compounds that include tetrahydrocannabinol (THC), the active ingredient in marijuana.

"Cannabinoid abuse, by activating corticotropin-releasing factor (CRF) mechanisms, may lead to subtle disruption of brain processes that are then "primed" for further and easier disruption by other drugs of abuse," said Koob, of the Scripps Research Institute in La Jolla, California.

Corticotropin-releasing factor is a substance that increases in the brain during stress or withdrawal from cocaine, alcohol or opiates (such as heroin), and is thought to cause depression, anguish, and anxiety.

In the new study, researchers found that when rats were exposed to a synthetic cannabinoid for two weeks, they had a reduction in CRF in the amygdala, the part of the brain dealing with emotions. When the cannabinoid was abruptly blocked with a second agent, CRF levels increased and the rats exhibited withdrawal symptoms, while at the same time, stress-related regions of the brain were activated -- similar to that seen in rats withdrawing from cocaine, alcohol, or other drugs.

These changes in the brain may explain why long-term marijuana users may experience irritability and discomfort when they stop using the drug, according to Koob and colleagues at the Universidad Complutense de Madrid in Spain. Marijuana tends to linger in the body, which may explain why withdrawal symptoms are not as intense as those with other drugs.

The study also provides scientific support for the gateway hypothesis -- that marijuana-users are at risk for abusing other illegal or legal drugs, according to the report.

In the second study, researchers exposed rats to THC and heroin, and found that both drugs increased the neurotransmitter dopamine in the nucleus accumbens, a region of the brain linked to addiction and

drug-seeking behavior. Morphine, cocaine, amphetamine and nicotine are all thought to increase dopamine release in this way, according to the researchers from the University of Cagliari in Italy.

A cannabinoid-blocking agent stopped the effect of THC, but not heroin. However, a heroin-blocking agent, called naloxone, halted both the effect of THC and the heroin -- suggesting they had a similar brain-stimulating mechanism.

"Together, the two sets of experiments suggest that marijuana manipulates the brain's stress and reward systems in the same way as more potent drugs, to keep users coming back for more," wrote Ingrid Wickelgren in a Science commentary.

SOURCE: Science (1997;276: 1967-1968, 2048-2049, 2050-2053)

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De Bellis MD, Gold PW, Geraciotti TD Jr, Listwak SJ, Kling MA: ASSOCIATION OF FLUOXETINE TREATMENT WITH REDUCTIONS IN CSF CONCENTRATIONS OF CORTICOTROPIN-RELEASING HORMONE AND ARGININE VASOPRESSIN IN PATIENTS WITH MAJOR DEPRESSION. American Journal of Psychiatry 1993; 150(4):656-7. Summary: The authors measured CSF concentrations of corticotropin-releasing hormone (CRH) and arginine vasopressin in nine depressed patients before and after fluoxetine treatment. They found significant decreases in CSF CRH, CSF arginine vasopressin, and Hamilton depression ratings. Thus, the therapeutic effect of this serotonin-uptake inhibitor may be related to diminution of these arousal-promoting neuropeptides.

Messiha FS: FLUOXETINE: ADVERSE EFFECTS AND DRUG-DRUG INTERACTIONS. [REVIEW]. Journal of Toxicology - Clinical Toxicology 1993; 31(4):603-30. Summary: This overview summarizes the major and minor side effects and drug interactions of fluoxetine. The adverse reactions include the "serotonin syndrome", cardiovascular complications, extrapyramidal side effects such as akathisia, dyskinesias, and parkinsonian-like syndromes and an apparently increased risk of suicidality. Fluoxetine-induced mania and hypomania, seizures and sexual disorders are evaluated along with minor symptoms of allergic reactions, stuttering, hematological changes, psoriasis, and inappropriate

secretion of the antidiuretic hormone. The major fluoxetine-drug interactions involve the amino acids L-dopa and L-tryptophan, anorexiant, anticonvulsants, antidepressants, anxiolytics, calcium channel blockers, cyproheptadine, lithium salts, and drugs of abuse. The underlying mechanism and the paradoxical effects of fluoxetine are addressed. [References: 251]

Gigli GL, Diomedì M, Troisi A, Baldinetti F, Marciani MG, Girolami E, Pasini A: LACK OF POTENTIATION OF ANTICONVULSANT EFFECT BY FLUOXETINE IN DRUG-RESISTANT EPILEPSY. *Seizure* 1994; 3(3):221-4. Summary: To test the hypothesis that fluoxetine may be a useful adjunct to antiepileptic therapy, we treated with fluoxetine (20-40 mg/day) nine patients suffering from medically intractable epilepsy with daily seizures. Five patients remained unchanged and four worsened. Worsening was more evident at 40 mg/day. One patient improved when receiving the lower dose (20 mg/day) and worsened with the higher dose (40 mg/day). These data suggest: (1) that fluoxetine is not effective as add-on antiepileptic treatment; (2) that caution should be exerted when using fluoxetine as an antidepressive treatment in epileptic patients.

Tueth MJ: REVISITING FLUOXETINE (PROXAC) AND SUICIDAL PREOCCUPATIONS. *Journal of Emergency Medicine* 1994; 12(5):685-7. Summary: Several reports were published in the psychiatric literature in 1990 and 1991 documenting fluoxetine (Prozac) causing patients to consider or attempt suicide. During the following 2 years, retrospective studies appeared in the medical literature that seemed to indicate that suicidal preoccupation was not related to the antidepressant fluoxetine (Prozac) but was probably a symptom of the depressive illness. Recent studies have suggested, however, that fluoxetine (Prozac) may in fact lead to suicidal behavior because the drug appears to adversely affect serotonergic neuronal discharge and induce an akathisia-like extrapyramidal reaction. While fluoxetine (Prozac) has a very favorable side effect profile compared to the tricyclic antidepressants, it may cause akathisia and induce a small subset of patients to consider or attempt suicide.

<<http://www.mentalhealth.com/drug/p30-p05.html>>

Fluoxetine

Brand name: Prozac

Drug monograph

Contents

*@Pharmacology
*@Indications
*@Contraindications
*@Warnings
*@Precautions
*@Adverse Effects
*@Overdose
*@Dosage
*@Supplied
*@Research

Precautions

Anxiety and Insomnia:

During premarketing clinical trials, anxiety, nervousness and insomnia were reported by 10 to 15% of patients treated with fluoxetine. These symptoms led to discontinuation of the drug in 5% of the patients.

Weight Change:

Significant weight loss, especially in underweight depressed patients, may be an undesirable result of treatment with fluoxetine.

Mania/Hypomania:

During premarketing clinical trials in a patient population comprised primarily of unipolar depressives, hypomania or mania occurred in approximately 1% of fluoxetine treated patients. The incidence in a general patient population which might also include bipolar depressives is unknown. The likelihood of hypomanic or manic episodes may be increased at the higher dosage levels. Such reactions require a reduction in dosage or discontinuation of the drug.

Seizures:

Fluoxetine should be used with caution in patients with a history of convulsive disorders. The incidence of seizures associated with fluoxetine during clinical trials did not appear to differ from that reported with other marketed antidepressants; however, patients with a history of convulsive disorders were excluded from these trials.

Concurrent administration with electroshock therapy should be avoided because of the absence of experience in this area. There have been rare reports of a prolonged seizure in patients on fluoxetine receiving ECT treatment.

Hypokalemia:

Self-induced vomiting often leads to hypokalemia which may lower seizure

threshold and/or may lead to cardiac conduction abnormalities. Electrolyte levels of bulimic patients should be assessed prior to initiation of treatment.

Suicide:

The possibility of a suicide attempt is inherent in depression and may persist until significant remission occurs. Therefore, high risk patients should be closely supervised throughout therapy and consideration should be given to the possible need for hospitalization. In order to minimize the opportunity for overdosage, prescriptions for fluoxetine should be written for the smallest quantity of drug consistent with good patient management.

Pleasant, Unpleasant Effects Of Marijuana Use Related In Part To Genetics

WESTPORT, Apr 07 (Reuters) - Genetics appear to play a role in marijuana use, according to a report in the current journal *Addiction*.

Dr. Michael J. Lyons, an investigator at Harvard University Medical School in Boston, Massachusetts, and colleagues there and at other U.S. sites evaluated the response to smoking marijuana in more than 8,000 male twins registered with the Vietnam Era Twin Registry. Pairs of twins who reported using marijuana at least 5 times completed a subjective questionnaire assessing their "positive" and "negative" responses to the drug.

"Identical male twins were more likely than nonidentical male twins to report similar responses to marijuana use," according to an NIH press release.

Although positive subjective responses to marijuana use were correlated with an increased frequency and duration of drug use, this association was not strong. Dr. Lyons explains that the team "...did not get information about the frequency, or strength of the [positive or negative] reaction, which may have had an influence on frequency of use that we could not detect."

"Genetic influence on subjective effects is probably one of several genetically influenced mechanisms that mediate the association between the genotype and the phenotype of drug-using behavior," the investigators conclude. "Environmental factors are also very likely to influence drug use via mechanisms in addition to learned beliefs and expectations."

Addiction 1997;92:000-000.

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AMA Delegates Vote To Continue To Oppose Physician-Assisted Suicide

CHICAGO, Jun 26 (Reuters)

Gen. Barry McCaffrey, director of National Drug Control Policy, who is known as the "drug czar," addressed a special session of the AMA House of Delegates Tuesday afternoon. He said of the drug problem that "...this is not that tough an issue. It's not AIDS. It's not racism... One of the biggest problems I face is apathy and the attitude that it is somebody else's problem." Dr. McCaffrey does not support the legalization of marijuana and says that arguments in favor of legalization are those of "...bright but frustrated people."

<http://www.pantless.com/~pdxnorml/091296.html>

The Nation's Correctional Population Reaches 5.4 Million

As noted previously in the Aug. 22 Portland NORML Weekly News Release, the United States' "Prison Population Climb[ed] To 1.6 Million Nationwide" in 1995, up 100 percent in the past decade. Also noted Aug. 22 was the omission from this year's Justice Department press release of the number of people serving parole or probation in 1995. The latest government press releases with those numbers have now been located, and it turns out America's total correctional population reached about 5.4 million in 1995 compared to 5.1 million the year before, including "almost 3.8 million adult men and women on probation or parole at the end of 1995, an increase of about 119,000 during the year." ("Probation and Parole Population Reaches Almost 3.8 Million," June 30, 1996, posted at gopher://www.ojp.usdoj.gov:70/00/bjs/press/pap95.pr). The Justice Department's Aug. 18, 1996 press release headed "Almost 1.6 million men and women in the Nation's Prisons and Jails," is posted at gopher://www.ojp.usdoj.gov:70/00/bjs/press/pji95.pr.

The Justice Department press release for 1994, headed "The Nation's Correctional Population Tops 5 Million," dated Aug. 27, 1995 and posted

at <http://www.pantless.com/~pdxnorm1/dojpr3.html>, states there were "More than 5.1 million Americans - or almost 2.7 percent of the adult population ... under some form of correctional supervision" in 1994, including 2,962,000 adults on probation and 690,000 adults on parole. While last year's Justice Department press release did not state the actual number of people incarcerated in 1994, the number can be deduced easily enough, starting with the Department of Justice's statement that "Almost three-quarters of these [5.1 million] men and women were being supervised in the community on probation or parole. The others were confined in jail or prison." If one starts with 5.1 million and subtracts 2,962,000 probationers [= 2,138,000] and then 690,000 parolees [= 1,448,000], the resulting number of prisoners is consistent with the statement that "almost three-quarters ... were ... on probation or parole" [$4 \times 1,448,000 = 5,792,000$].

Currently, about 70 percent of all federal prisoners are drug offenders - almost 20 percent of them marijuana POWs. If Multnomah County court records for 1996 are indicative (see "Body Count," above), more than 55 percent of all felons sentenced locally to county jails or state prisons are also drug offenders, though the county doesn't separate the marijuana tally.

Illegal Drug Users - Helping Make America Strong

Prohibitionists are fond of citing bogus statistics purporting to show that cannabis consumers and other illegal-drug users are, on the whole, a drag on business productivity. In fact, however, there is little credible evidence on the subject, and what good evidence there is suggests that the only drug whose use significantly correlates with lower productivity and higher workplace accidents is alcohol, and even then only among heavy drinkers. *

As documented below, the 1995 National Household Survey on Drug Abuse and the August 1996 statistics from the U.S. Department of Labor state that 71 percent of cannabis consumers and other illegal drug users are gainfully employed, compared to just 63.3 percent of the general population. So let the prohibitionists explain, in view of the government's own figures, just how locking up illegal-drug users is going to improve the productivity of Americans (who are already the most productive workers in the world - as well as the biggest illicit-drug consumers).

As noted in the "Science & the Citizen" column in the March 1990 Scientific American, the myth that illegal-drug users impair overall business productivity was first put forth by President Bush and the U.S. Chamber of Commerce as recently as 1989 ("Test Negative -- A look at the 'evidence' justifying illicit-drug tests," pp. 18 & 22, posted at

<http://www.pantless.com/~pdxnorm1/test.html>). However, when Scientific American examined the evidence cited by Bush and the Chamber of Commerce, the research showed that workers who tested positive only for marijuana: 1) cost less in health insurance benefits; 2) had a higher than average rate of promotion; 3) exhibited less absenteeism; and 4) were fired for cause less often than workers who did not test positive. The article specifically states:

Yet according to [White House drug-policy official Henrick J.] Harwood there was no significant difference between the income of households with current users of any illegal drug - including marijuana, cocaine and heroin - and the income of otherwise similar households. Does this mean that current use of even hard drugs - as opposed to perhaps a single marijuana binge in the distant past - does not lead to any "loss"? "You would be on safe ground saying that," Harwood replies.

<http://www.pantless.com/~pdxnorm1/7_presidents.html>

from Hemp: Lifeline to the Future, by Chris Conrad, 1994, pp. 192-193, part of Chapter 16, "A World of Cannabis Cultures." Creative Xpressions Publications, Los Angeles, ISBN 0-9639754-1-2, \$12.95 from FS Book Company, Sacramento, 1-800-635-8883 credit cards, 916-771-4203 customer service.

American High Society

The extent of cannabis smoking during the Colonial era is still subject to debate. President George Washington wrote a letter that contained an oblique reference to what may have been hashish. "The artificial preparation of hemp, from Silesia, is really a curiosity." (38) Washington made specific written references to Indian hemp, or cannabis indica, and hoped to "have disseminated the seed to others." (39) His August 7, 1765 diary entry, "began to separate the male from the female (hemp) plants," describes a harvesting technique favored to enhance the potency of smoking cannabis, among other reasons. (40) Hemp farmer Thomas Jefferson and paper maker Ben Franklin were ambassadors to France during the initial surge of the hashish vogue. Their celebrity status and progressive revolutionary image afforded them ample opportunities to try new experiences. Jefferson smuggled Chinese hemp seeds to America and is credited with the phrase in the Declaration of Independence, "Life, liberty and the pursuit of happiness."

Did the Founding Fathers of the United States of America smoke cannabis? Some researchers think so. Dr. Burke, president of the American Historical Reference Society and a consultant for the Smithsonian

Institute, counted seven early presidents as cannabis smokers: George Washington, Thomas Jefferson, James Madison, James Monroe, Andrew Jackson, Zachary Taylor and Franklin Pierce. (41) "Early letters from our founding fathers refer to the pleasures of hemp smoking," said Burke. Pierce, Taylor and Jackson, all military men, smoked it with their troops. Cannabis was twice as popular among American soldiers in the Mexican War as in Vietnam: Pierce wrote to his family that it was "about the only good thing" about that war.

Central and Western African natives were farming and harvesting cannabis sativa in North America as slaves. If they did smoke on the plantations, that would be kept secret. (42) By the time of the Louisiana purchase in 1803, New Orleans had a mixed Spanish, French, Creole, Cajun, Mexican and Black population. The city teemed with adventurers and sailors, wise to the ways of cannabis. It was mixed with tobacco or smoked alone, used to season food (43), to treat insomnia and impotence, and so on.

Cannabis was mentioned as a medicinal agent in a formal American medical text as early as 1843. (44)

38 A region now shared by Germany & Poland. Letter to Dr. James Anderson, May 26, 1794. in Writings of George Washington. Washington DC. vol. 33. p. 384.

39 Ibid. vol. 35. p. 72

40 Such as creating more space for females to flower for seed production, or to take advantage of the male fiber before it overmatures in the field.

41 Burke asserted that Washington & Jefferson were said to exchange smoking blends as personal gifts. Washington reportedly preferred a pipe full of "the leaves of hemp" to alcohol, & wrote in his diaries that he enjoyed the fragrance of hemp flowers. Madison once remarked that hemp gave him insight to create a new & democratic nation. Monroe, creator of the Monroe Doctrine, began smoking it as Ambassador to France & continued to the age of 73. Burke. "Pot & Presidents." in Green Egg. CA. June 21, 1975

42 "That might explain some cultural differences." Aldrich, Michael, Ph.D. 'On use of marijuana by slaves in colonial times.' in Best of High Times. vol. 10. 1991. p. 61