

TESTIMONY OF JON HAUXWELL, MD
BEFORE THE SENATE HEALTH CARE STRATEGIES COMMITTEE
CONCERNING THE MEDICAL MARIJUANA DEFENSE ACT

Mr. Chairman and members of the Committee, I appreciate the opportunity to share with you my perspectives on the Medical Marijuana Defense Act.

I am a retired family physician from Stockton, now living in Hays. For fifteen years I chaired a multidisciplinary chemical dependence recovery team on the Northern Cheyenne Reservation in Montana. I have maintained longstanding interests in clinical pharmacology and medicinal ethnobotany, as well as the management of chronic pain.

HUMAN PHYSIOLOGY AND MEDICINAL CANNABIS

I consider whole-plant cannabis to be both a drug and a medicine. By “medicine,” I mean any substance or combination of substances which, when administered to a human, can influence human physiology and pathology in a beneficial manner.

We are just beginning to understand how and why cannabis has medicinal properties. Tiny structures termed “cannabinoid receptors” are widely distributed throughout the body, in such diverse tissues as brain, muscles, heart, and immune system. Nature is thrifty; we may safely assume that this extensive distribution of cannabinoid receptors reflects their versatile role in the regulation of human health.

Nature did not create these with any “intent” of accommodating exogenous medicines; the receptors evolved in tandem with chemicals the body itself makes, termed endocannabinoids. When patients administer cannabis as a medicine, they are simply taking advantage of the body’s pre-existing apparatus, much as happens when we use morphine to utilize our system of opiate receptors.

If the therapeutic claims advanced on behalf of cannabis seem suspiciously close to those of a panacea, we must only consider the distribution of those cannabinoid receptors throughout such a host of different tissues. It is apparent that the effects of a given cannabinoid receptor are expressed by virtue of its tissue context. Receptors found in peripheral nerve tissue are likely to influence peripheral nerve function, and the same may be inferred for receptors located in skeletal muscle, bladder wall, brain, blood, bone, intestines, pancreas, and liver. Such versatile effects of limited receptor types on multiple tissue functions are already well known - for example, the alpha and beta adrenergic complexes.

DRUG DEPENDENCE ISSUES

Cannabis has been used medicinally worldwide for thousands of years safely and effectively. But like many other medicines we routinely use, it has abuse potential. Around 9% (depending on one’s definitions) of frequent users subsequently develop an addiction syndrome - the persistent obsessive repetition of a behavior despite adverse consequences. This is a far lower percentage than we see in other medicinal or social drugs such as opiates, stimulants, sedatives, alcohol and tobacco, but it still warrants our attention and

concern. Upon stopping use of the substance, heavy cannabis users can experience an abstinence syndrome, commonly termed “withdrawal,” although withdrawal from cannabis is itself benign when contrasted with the potentially fatal outcomes seen in withdrawal from drugs like opiates, alcohol, barbiturates, and Valium.

Evidence shows the potential for cannabis dependence is greatest among the young, before and during adolescence. Health care providers must exercise caution prescribing any medicine with abuse potential, especially when the young are receiving treatment.

“EXCUSES” AND REASONS - DRUG ABUSE AND DIVERSION

Professional debunkers on the lecture circuit get a lot of mileage from a favorite catch phrase, “medical *excuse* marijuana.” People are just using their cancer or multiple sclerosis as an *excuse* to get high. Never mind that hundreds of thousands of people are getting high without feeling it necessary to offer an excuse at all. When patients use cannabis as medicine, they are at best deluded, and at worse just faking.

Not only is this charge largely inaccurate, it is cruel and monstrously unfair.

Any physician who has prescribed controlled substances knows that there is a subset of the population which will indeed try to obtain prescriptions through deceit. Despite our vigilance, we’ve all been fooled. But society has made an important decision: we will accept the risk of drug diversion and abuse in order to provide genuine patients with humane treatment and relief of suffering. This has its parallel in jurisprudence - better to free nine guilty men than to execute one innocent one. Or in the case of medicines, we must not allow a small group of abusers to call the shots, to deny treatment to the large group of legitimate patients.

Drug diversion of medical cannabis would not pose the problem we see with, say, Oxy-contin. Marijuana is readily available through an extensive and lucrative black market, and any contribution to the supply from medical sources would be minimal; illicit Oxy, on the other hand, is obtained almost entirely by diversion from medical sources.

Cannabis debunkers often state that medicinal cannabis is just a strategy to poise us on a slippery slope leading to full legalization of marijuana. Now that’s just silly. We all know Kansas is not about to legalize marijuana. Ironically, this is one area where workers in the recovery community and blackmarket profiteers agree. Counselors fear that legalization would tempt people who have never tried recreational marijuana to do so; pushers and dealers fear that legal marijuana would put them out of business.

Approving the medical use of controlled substances - opiates, stimulants, sedatives, etc - has not led to their sale in 7-11's. Just because something is abusable doesn't mean that abusers should dictate to real sufferers whether or not they should get relief. And if someone I find generally misguided were to advocate the legalization of drugstore opium, I would still support morphine for medical use.

SAFETY ISSUES

Pharmacologic safety remains a concern, however, as it is for virtually all medicines. Aspirin causes a thousand deaths a year, mainly due to bleeding; thinning the blood is a known, and sometimes sought, action of aspirin. Aspirin is lethal in overdose. Cannabis, by contrast, has no known lethal dosage, and deaths attributable solely to the pharmacologic effects of cannabis are extremely rare if they can be found at all. Our challenge is to identify, understand, and minimize any toxicity associated with cannabis, as we must do with any other medication.

In the laboratory, potentially adverse effects of cannabis have been discovered. For example, interference with immune function has been detected. What has not been shown is that such immune compromise is clinically significant in patients; that is, modest and inconsistent evidence of reduced immune system components' function does not equate with actual compromise of human health, even in AIDS patients. There is evidence that cannabinoids can weaken or even destroy some types of brain cancer, but we don't know yet if that's clinically significant either.

Two types of adverse effects are currently of greatest concern: impairment of mental function, and lung damage.

Unquestionably acute cannabis effects include reduced short-term memory, distractability, reduced vigilance, etc. This would make cannabis, as is the case with Valium, Benadryl, many other medications (and of course alcohol), inappropriate for use during or immediately before driving or operating dangerous machinery. There is little if any evidence of long-term brain damage. In fact, evidence suggests that cannabinoids can exert a neuroprotective effect in the setting of spinal cord injury or stroke, reducing damage resulting from the injury. Some studies have shown no impairment of work performance among long-term users. Because of the phenomenon of "tolerance," the attrition of effect seen with ongoing use of some drugs, activities of daily living such as cooking, dressing, communication, self-care, etc. do not appear to suffer. Tolerance to side effects occurs faster than tolerance to therapeutic effects.

Still, effects of cannabis on cognition are among those that must be weighed in any decision regarding using cannabis as medicine.

The presence in cannabis smoke of carcinogens deserves scrutiny. Unlike tobacco, in which carcinogens are produced by fermentation and curing prior to use, cannabis is simply dried. Carcinogens are produced primarily by combustion itself, in cannabis and in almost any burning plant substance. The presence of carcinogens is of relatively little concern to someone already suffering from terminal lung cancer or end-stage AIDS, but they are worrisome for someone who might profit from using cannabis for years, like an MS patient.

Studies of populations with a high prevalence of cannabis use, such as Rastafarians, have not shown increased rates of lung cancer due to cannabis use alone. A recent retrospective New Zealand study of people who already had lung cancer indicated that volume for volume, cannabis smoke carried a higher risk of lung cancer than tobacco smoke. However, a study on emphysema

showed that when cannabis was smoked in the absence of tobacco use, it did not cause emphysema. But when tobacco was also used, cannabis contributed to emphysema risk, with one cannabis cigarette the equivalent of five tobacco cigarettes. This is noteworthy for two reasons. One is that for emphysema, cannabis risk must be triggered by tobacco or it doesn't occur. Also, testing equal *volumes* of smoke is not the same as testing equal *doses*.

That is, with today's extremely potent cannabis varieties, a patient might actually stop after three or four puffs of cannabis smoke, not inhaling the smoke produced by an entire cigarette. We often hear cannabis compared to tobacco, primarily because both are plants, both can be smoked, and both can lead to chemical dependence; in terms of addiction potential, proven toxicity, and chemical makeup, though, the two are very different. However, some studies simply fail to consider the different usage patterns between the two. While it's true that cannabis smokers inhale smoke more deeply and retain it longer, only the most dedicated chronic users do this more than once or twice a day. The most common dose of smoked tobacco is one cigarette, but today's cannabis is so potent that most cannabis patients, even those who have become tolerant, do not consume more than a few puffs per dose. Some use pipes so they don't "waste" the scarce commodity, and so they don't have to smoke burnt paper.

So cannabis smoke's higher carcinogen concentration, inhaled deeply and held longer but in more limited quantities, might still require concomitant tobacco use to trigger its contribution to cancer risk.

MEDICATION DELIVERY METHODS

Such considerations are of lesser import when we realize that from a medical perspective, cannabis smoking is simply unnecessary. Many drugs are inhaled (though few are burned first!) because this allows a rapid onset of action, and the ability to titrate, or adjust, the dosage very precisely. These same assets can be achieved without combustion of medicinal cannabis, now that low-temperature vaporization apparatus is available.

Furthermore, in many situations cannabis can simply be eaten. The effects take longer to manifest, but they last much longer than inhaled cannabis, reducing the number of doses needed in a day. The proper dose can be determined only after investing several days in an upward titration, beginning with small amounts and gradually increasing until the optimal effect is reached. Today's potent varieties can be pulverized, encapsulated, and swallowed like any other pill.

Debunkers like to display a list of "contaminants" present in some illicit cannabis preparations, micro-organisms and chemicals among them. These contaminants can also be found in many home gardens. We have not seen that the presence of such contaminants has actually been linked to clinical disease among users. An exception might be the presence of an herbicide, Paraquat, which has been sprayed on illicit cannabis crops in eradication attempts.

RELATIVE RISKS

We have seen that there are potential side effects to cannabis use, and these must be considered and managed as they are for any other drugs. In fact, the hazards of cannabis are often much smaller than those of the drugs they supplant or replace. Furthermore, the versatility of those cannabinoid receptors can mean that cannabis can replace several drugs at once - for example, cannabis use can simultaneously reduce or eliminate the use of anti-nauseants, anti-anxiety drugs, sleep aids, antidepressants, and appetite stimulants in some cancer patients, and might enhance the effects of chemotherapy or radiation by inhibiting the growth of new blood vessels upon which the tumor relies for nourishment.

CONSISTENCY OF DOSING

With any medication, we want assurance that today's dose is identical to yesterday's and tomorrow's. Cannabis reproduces sexually, giving rise to new generations combining both parents' genes. There is as much genetic diversity among cannabis cultivars as there is among dogs. This is not only significant when it comes to consistency of the medicine, but it also means that one variety might have very different effects on one disease versus another. (This is of paramount importance, but widely ignored, during the testing of cannabis' therapeutic potential for specific diseases. More on this later.)

This problem can be addressed quite simply - by cloning, or as we more commonly term it, propagation from cuttings. Once a given variety of cannabis has been determined to be effective for a given condition, the plant can be trimmed and the cuttings grown into genetically identical daughter plants; this is the primary determinant of potency and specificity, provided growing conditions are roughly comparable.

Hypothetical concerns regarding cannabis' safety will be an ongoing issue. Cannabis is the most commonly-used plant-derived recreational drug in the world, and has been for a long time - more than enough time for major hazards to have become visible, a la Vioxx, Bextra, or tobacco. But these uncertainties fully warrant limiting use of cannabis to treatment of disabling or debilitating conditions, as we do drugs actually known to possess serious liabilities.

DATA, RESEARCH, AND THE FDA

Clearly research must continue into the nature of cannabis and its interactions with human physiology. This is no simple matter, at least in this country. It can take years for a researcher to even obtain permission to study cannabis, much less the funding needed to do it. Because of social opprobrium attached to any illegal drug, researchers are reluctant to be associated with legitimate studies of cannabis, fearing it would stigmatize them and jeopardize future research funding. Profit-oriented drug companies have no incentive to try to validate the effectiveness of a medication they can't manufacture, sell, or patent.

Proponents of using medical illness as a defense against possession charges have been accused of wanting to "bypass" or circumvent the FDA.

The FDA, DEA, and NIDA have become entangled in politics, leading to their diversion, among other things, into carrying out the “War on Drugs.” As a result of this compromise of its original mission, the FDA has arguably become derelict in its duty. The persistence of widespread unrelieved suffering, and the compelling evidence for cannabis’ safety and effectiveness, leave no compassionate choice other than bypassing or preempting the FDA when it specifically comes to cannabis.

However, we do not fail to recognize that savvy but unsavory entrepreneurs continue to endorse a host of bogus nostrums that are neither safe nor effective, ranging from “Natural” remedies to “supplements” which are all marketed in ways that to any sensible person represent therapeutic claims. Recall also the laetrile debacle. If we sanction overriding the FDA on behalf of one unusually promising medicine, we could be mistakenly seen as opening the door for a deluge of worthless or harmful product purveyors to do the same, citing fervent public support as a sufficient justification for foregoing the lengthy FDA-approval process. Pandora’s box. Even though we must acknowledge the system’s other problems, and must be informed by them, we cannot afford to be intimidated by them; the problems that cannabis can potentially alleviate are real and present, and they demand we act to overcome hurdles both social and political. It is simply not necessary to accept snake oil sales in order to profit from the application of cannabis’ uniquely compelling volume of evidence.

National administrations do not want to become vulnerable to charges of being “soft on drugs.” Many in the recovery community feel threatened by the prospect of acknowledging that there could conceivably be anything good to be said about any drug they combat daily in their professional roles.

When researchers do succeed in obtaining permission and funding to study cannabis itself, they are limited to a single monopolized strain grown by the National Institute on Drug Abuse (NIDA). This is an inferior, low-potency cultivar, “your grandfather’s cannabis.” And this product is denied by NIDA even to FDA-approved protocols if NIDA disagrees with them; its bias is apparent in NIDA’s name – they are predisposed to consider cannabis only in light of its potential for abuse.

Alternatively, researchers can examine a synthetic version of THC now approved, but little used, as an anti-nauseant; THC is the most psychoactive of cannabis’ 60 or so cannabinoids. Being limited to studying THC in isolation, or to one strain of cannabis, is akin to trying to characterize a Pizza Supreme by a cursory examination of an anchovy fragment.

ISOLATION AND POTENTIATION, THE WHOLE-PLANT ISSUE

Pharmacologists are familiar with the phenomenon of “potentiation.” Essentially, two or more drugs used together reinforce, or potentiate, each other’s effects, so that their combined effect is greater than the sum of their individual effects: one plus one equals three.

Whole-plant cannabis can have effects differing markedly from one or two of its ingredients used alone. Add to this the enormous genetic variation among cannabis strains - the difference between a St. Bernard and a chihuahua - and it

is no surprise that studies have often failed to discern a therapeutic benefit of one particular cannabis product on a given disease. Cannabis users themselves have long ago learned to distinguish one cultivar from another, based on the net effect of a number of active ingredients. A strain that helps muscle spasticity might not have much effect on pain; one strain may enhance alertness, while another has relaxing or sedating properties.

ANECDOTES AND CONTROLLED STUDIES

Still, we needn't reinvent the wheel, or pretend that we have no information to allow us to make plausible choices in matching the most promising cultivar with an appropriate disease for research purposes.

As the International Journal of Clinical Practice put it, "patients' reports could serve as a valid indicator of target diseases and symptoms for cannabinoid drug development."

Modern science properly looks askance at non-controlled or "anecdotal" reports. Although it was anecdotes that led to the discovery of AIDS, anecdotes, being inherently vulnerable to subjectivity, are granted almost no evidentiary value. Medical scientists are reluctant to support any assertion based primarily on anecdotal evidence.

However, there is a very large volume of such reports when it comes to the therapeutic effects of cannabis, and there is a great deal of consistency among them. Some of the claimed benefits involve the sustained ability to relieve severe symptoms; although any of us are susceptible to the placebo effect, placebo effects on severe symptoms such as chemo-induced nausea or intractable pain tend to attenuate fairly rapidly. Initially a gratifying response does not exclude placebo origin, but a "placebo" that continues to work for months is highly likely to involve a genuine pharmacologic and physiologic phenomenon.

We face an uphill battle convincing politicians, doctors, and researchers to take the enormous volume of experiential data seriously enough to loosen the strictures on cannabis research or on individual cannabis utilization.

TWO CASE STUDIES

I won't try to present a detailed review of all the potential forms of therapeutic response to cannabis; those data are already available from other sources. Let me mention the experiences related to me by a couple of patients, before I list some of the other areas in which both anecdotal and experimental evidence suggest the safe efficacy of cannabis use.

Both of these patients had briefly used marijuana recreationally years before, but had only recently tried it again in a recreational setting. The medical effects of the experience were neither sought nor anticipated, but appeared gratuitously.

One man suffered debilitating back pain which both restricted his mobility and caused a lot of pain even at rest. To his surprise, for nearly a day after he used marijuana, his back pain was markedly reduced, as was his stiffness. He was able to ambulate with much greater ease.

When he mentioned this to me, I explored alternative explanations - maybe he was just distracted from his pain by the psychotropic effects, simply wasn't paying as much attention to it as usual. He assured me that once he noticed what was happening, and paid explicit attention to it, the pain was still far less perceptible than usual; furthermore, the pain decrease persisted for hours after the euphoriant effect had disappeared. I suggested that maybe he found it easier to ambulate because his *fear* of pain normally prevented him from even *trying* to get around much, and that while distracted, he "forgot" to worry about pain, and discovered he had more ambulatory capability than he'd realized. Not so, he said. He has steadfastly refused to be intimidated by pain, or to let it dictate what he can or can't do, and he forces himself to go for walks and do exercises on a regular basis. The difference was that he could do with ease the same things that he usually must force himself to endure out of principle. This does not sound like a simple placebo effect, which requires at the least an expectation of relief.

While his pain decreased substantially, his ability to experience other sensation was not dulled. This is consistent with what we know about the function of cannabinoid receptors along nerve fibers. They depress the reactivity of spinal neurons which conduct pain sensation to the brain, but have no effect on other neurons responsible for non-pain sensation. This contrasts with other pain relievers such as opiates which not only have a pain-suppressant effect on sensation, but can depress the sense of needing to breathe - respiratory drive - leading to respiratory depression and even asphyxiation.

Another patient similarly was not totally unfamiliar with marijuana, but had not used it for years. An old friend came to visit, and convinced her to share some marijuana before walking around the zoo. She had interstitial cystitis, involving pronounced bladder irritability with urgency and incontinence, problems which had not responded to commonly-used "bladder sedatives" or even to surgery. The first thing she did on entering the zoo was get a map and locate all the rest rooms on the grounds, anticipating the usual sequence of sudden dashes to the nearest stall.

To her surprise, she only had to pause once for a bathroom break, and this was only because she felt like she was soon going to need to urinate, as opposed to the usual abrupt overwhelming demand. Although she is accustomed to urinary frequency, she can't avoid it simply by refusing to obsess about it; when it comes, it comes, and it brooks no delays or procrastination.

The effect of cannabis on bladder irritability, spasm, and incontinence has surfaced in more formal studies. This condition is common to many different types of disorder, including multiple sclerosis, inflammatory cystitis, and anatomical distortions such as pelvic relaxation due to multiple childbirth. Related medicines currently available are ineffective for many people, and have the potential to cause serious side effects.

In the case of neither patient could I legally advise them to repeat or continue the use of cannabis despite its seemingly obvious benefits for them as individuals. Instead, I could listen non-judgmentally and empathetically, and note

that I “could understand if you were to resort to cannabis to control this problem.” And I could add an exhortation to be wary of legal penalties.

SPECTRUM OF THERAPEUTIC VERSATILITY

Again, there is plausible evidence in both animal and human studies, and unstructured human usage, that many disease states respond favorably to cannabis, without the degree of side-effects found among currently-available alternative surgical and medical therapies. Cannabis constituents might help prevent diabetes, osteoporosis, Alzheimer’s, and certain cancers. It can slow progress or alleviate symptoms of fibromyalgia, dystonias, arthritis, intestinal disorders, hypertension, Tourette’s Syndrome, ALS (Lou Gehrig’s Disease), sleep apnea, AIDS, inanition, and Hepatitis C.

Of particular interest is the effect of cannabis on a specific type of pain – neuropathic pain. A complex, lancinating pain due to diseased nerve trunks and fibers, and often associated with common diseases such as diabetes, or less common ones like multiple sclerosis, neuropathic pain has proved frustrating, resistant to even the strongest pain relievers, the opiates. Anticonvulsant drugs such as gabapentin and pregabalin have been used with some success to treat neuropathic pain, but their side-effects can prove intolerable. The same is true for another class of drugs, the tricyclics.

But as we learn more about the function of cannabinoid receptors in the nervous system, we are coming to understand why cannabis seems to have a unique, and in some cases remarkable, ability to alleviate this challenging disorder.

It is a travesty and a tragedy that patients who have been unable to safely achieve relief or remission using available therapeutic modalities must risk criminal prosecution for attempting to control their diseases using cannabis.

Debunkers put forth the notion that cannabis use, whatever its side-effects, is simply unnecessary – that there are always currently-available alternatives that adequately relieve symptoms without any adverse effects. If you have a friend or relative who has dealt with cancer treatments, or the chemicals used to fight Hepatitis C or multiple sclerosis, you will have noticed that this assertion is bogus. Even today some patients elect to just “die and get it over with,” rather than endure the side-effects of chemo- and radiotherapy.

It is common knowledge that the effects of any medical therapy can be “idiosyncratic.” A given medicine will work better than another for a given patient, or worse; one person may experience debilitating side-effects from a medicine that someone else tolerates without any problem. There is often no way to predict such idiosyncrasies in advance; only trial and error reveal the best choice, if indeed any such choice is available. The more options available, the better the chances that we can find the drug that is ideal, or least problematic, for a given patient.

THE UPSIDE OF EUPHORIA

I suspect that many opponents’ stance on cannabis arises in some part from their concern over therapeutic cannabis’ potential to cause concomitant

euphoria - that people will continue to use it because it makes them feel good when it really isn't doing anything to alter their diseases' manifestations. Chemical dependence is always an issue that must be considered, and it is not mere Puritanism reverberating through such attitudes. However, I'm reminded of a statement made by the late Peter McWilliams: "I had forgotten how healing enjoyment can be. Pleasure as therapy. Ease to unravel disease. A deep appreciation of life as an answer to death." We must not trivialize or dismiss the role of a positive outlook, or the responsiveness of the mind-body unit to optimism and to an ability to take pleasure in daily life's variety of sensations and experiences. For many sick people, cannabis enhances these dimensions of their lives.

CONCLUSION

There is abundant evidence that in many cases, the administration of cannabis can provide safe and effective relief of a spectrum of human discomfort and disease. Side effects exist, and they must be balanced against the degree of efficacy when a person decides to try, or to continue, using cannabis as a medicinal agent. Currently, among the most devastating side effects of the medicinal therapeutic use of cannabis is its legal status, and the potential for life-disrupting legal penalties.

We need to educate patients about responsible decision-making and proper self-care, about weighing the potential benefits and liabilities of using cannabis as a medication. To punish as criminals those who, with the approval of a licensed physician, elect to use it, does nothing to discourage others' illicit recreational and abusive use. So long as charges relate to simple possession or production of small quantities of cannabis for personal medicinal use, and not to illicit commercial enterprises, a medical defense does not give comfort or assistance to drug dealers, nor does it urge healthy persons to adopt its use. There are already many societal forces at work which unfortunately encourage marijuana experimentation, principally the reports of others' experiences; but medical use as a defense will impact these other factors not at all. Necessitating a medical evaluation and recommendation, as this bill does, precludes the gratuitous and frivolous use of this defense, as it also requires consideration of currently-available therapeutic alternatives to cannabis as a prerequisite to cannabis therapy.

Research needs to continue - indeed, to progress to a higher level - to explore the mechanisms of cannabis' therapeutic actions as well as its liabilities for adverse reactions. But the need is now, and thousands of sufferers for whom existing interventions are either ineffective or intolerable cannot afford to wait for social biases and political infighting to cease their intrusion into the therapeutic alliance among doctors, patients, and medication.

Cannabis is not now, nor is it likely to soon become, the sole or the initial therapeutic option for most of the conditions in which it has already demonstrated its capacity to aid healing. But it should be an option, and those genuine, sincere sufferers who turn to it as a last resort should not be dealt with in the same fashion as career criminals who prey on society through the production and sale

of harmful substances. These patients are sick, not criminal, and we should acknowledge this reality.

Please lend your support to the Medical Marijuana Defense Act.