NORML's Testimony on Medical Marijuana Before Congress (1997) Lester Grinspoon, MD

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Mr. Chairman and members of the subcommittee, I appreciate the opportunity to appear before you this morning to share my views on the use of marihuana as a medicine.

In September 1928 Alexander Fleming returned from vacation to his laboratory and discovered that one of the petri dishes he had inadvertently left out over the summer was overgrown with staphylococci except for the area surrounding a mold colony. That mold contained a substance he later named penicillin. He published his finding in 1929, but the discovery was ignored by the medical establishment, and bacterial infections continued to be a leading cause of death. Had it aroused the interest of a pharmaceutical firm, its development might not have been delayed. More than 10 years later, under wartime pressure to develop antibiotic substances to supplement sulfonamide, Howard Florey and Ernst Chain initiated the first clinical trial of penicillin (with six patients) and began the systematic investigations that might have been conducted a decade earlier.[1]

After its debut in 1941, penicillin rapidly earned a reputation as "the wonder drug of the '40s." There were three major reasons for that reputation: it was remarkably non-toxic, even at high doses; it was inexpensive to produce on a large scale; and it was extremely versatile, acting against the microorganisms that caused a great variety of diseases, from pneumonia to syphilis. In all three respects *cannabis* suggests parallels:

(1) *cannabis* is remarkably safe. Although not harmless, it is surely less toxic than most of the conventional medicines it could replace if it were legally available. Despite its use by millions of people over thousands of years, *cannabis* has never caused an overdose death. The most serious concern is respiratory system damage from smoking, but that can easily be addressed by increasing the potency of *cannabis* and by developing the technology to separate the particulate matter in marihuana smoke from its active ingredients, the cannabinoids (prohibition, incidentally, has prevented this technology from flourishing). Once *cannabis* regains the place in the U.S. Pharmacopoeia that it lost in 1941 after the passage of the Marihuana Tax Act (1937), it will be among the least toxic substances in that compendium. Right now the greatest danger in using marihuana medically is the illegality that imposes a great deal of anxiety and expense on people who are already suffering.

(2) Medical *cannabis* would be extremely inexpensive. Street marihuana today costs $200 to $400 an ounce, but the prohibition tariff accounts for most of that. A reasonable estimate of the cost of *cannabis* as a medicine is $20 to $30 an ounce, or about 30 to 40 cents per marihuana cigarette. As an example of what this means in practice, consider the following. Both the

marihuana cigarette and an 8 mg ondansetron pill -- cost to the patient, $30 to $40 -- are effective in most cases for the nausea and vomiting of cancer chemotherapy (although many patients find less than one marihuana cigarette to be more useful, and they often require several ondansetron pills). Thus *cannabis* would be at least 100 times less expensive than the best present treatment for this symptom.

(3) *Cannabis* is remarkably versatile. Let me review briefly some of the symptoms and syndromes for which it is useful.

Cancer Treatment

Cannabis has several uses in the treatment of cancer. As an appetite stimulant, it can help to slow weight loss in cancer patients.[2] It may also act as a mood elevator. But the most common use is the prevention of nausea and vomiting of cancer chemotherapy. About half of patients treated with anticancer drugs suffer from severe nausea and vomiting, which are not only unpleasant but a threat to the effectiveness of the therapy. Retching can cause tears of the esophagus and rib fractures, prevent adequate nutrition, and lead to fluid loss. Some patients find the nausea so intolerable they say they would rather die than go on. The antiemetics most commonly used in chemotherapy are metoclopramide (*Reglan*), the relatively new ondansetron (*Zofran*), and the newer granisetron (*Kytril*). Unfortunately, for many cancer patients these conventional antiemetics do not work at all or provide little relief.

The suggestion that *cannabis* might be useful arose in the early 1970s when some young patients receiving cancer chemotherapy found that marihuana smoking reduced their nausea and vomiting. In one study of 56 patients who got no relief from standard antiemetic agents, 78% became symptom-free when they smoked marihuana.[3] Oral tetrahydrocannabinol (THC) has proved effective where the standard drugs were not. [4, 5] but smoking generates faster and more predictable results because it raises THC concentration in the blood more easily to the needed level. Also, it may be hard for a nauseated patient to take oral medicine. In fact, there is strong evidence that most patients suffering from nausea and vomiting prefer smoked marihuana to oral THC.[2]

Oncologists may be ahead of other physicians in recognizing the therapeutic potential of *cannabis*. In the spring of 1990, two investigators randomly selected more than 2,000 members of the American Society of Clinical Oncology (one-third of the membership) and mailed them an anonymous questionnaire to learn their views on the use of *cannabis* in cancer chemotherapy. Almost half of the recipients responded. Although the investigators acknowledge that this group was self-selected and that there might be a response bias, their results provide a rough estimate of the views of specialists on the use of *Marinol* (dronabinol, oral synthetic THC) and smoked marihuana.

Only 43% said the available legal antiemetic drugs (including *Marinol*) provided adequate relief to all or most of their patients, and only 46% said the side effects of these drugs were rarely a serious problem. Forty-four percent had recommended the illegal use of marihuana to at least one patient, and half would prescribe it to some patients if it were legal. On average, they considered smoked marihuana more effective than Marinol and roughly as safe.[6]

Glaucoma

Cannabis may also be useful in the treatment of glaucoma, the second leading cause of blindness in the United States. In this disease, fluid pressure within the eyeball increases until it damages the optic nerve. About a million Americans suffer from the form of glaucoma (open angle) treatable with *cannabis*. Marihuana causes a dose-related, clinically significant drop in intraocular pressure that lasts several hours in both normal subjects and those with the abnormally high ocular tension produced by glaucoma. Oral or intravenous THC has the same effect, which seems to be specific to *cannabis* derivatives rather than simply a result of sedation. *Cannabis* does not cure the disease, but it can retard the progressive loss of sight when conventional medication fails and surgery is too dangerous.[7]

Seizures

About 20% of epileptic patients do not get much relief from conventional anticonvulsant medications. *Cannabis* has been explored as an alternative at least since 1975 when a case was reported in which marihuana smoking, together with the standard anticonvulsants phenobarbital and diphenylhydantoin, was apparently necessary to control seizures in a young epileptic man.[8] The *cannabis* derivative that is most promising as an anticonvulsant is cannabidiol. In one controlled study, cannabidiol in addition to prescribed anticonvulsants produced improvement in seven patients with grand mal convulsions; three showed great improvement. Of eight patients who received a placebo instead, only one improved.[9] There are patients suffering from both grand mal and partial seizure disorders who find that smoked marihuana allows them to lower the doses of conventional anticonvulsant medications or dispense with them altogether. [2]

Pain

There are many case reports of marihuana smokers using the drug to reduce pain: post-surgery pain, headache, migraine, menstrual cramps, and so on. Ironically, the best alternative analgesics are the potentially addictive and lethal opioids. In particular, marihuana is becoming increasingly recognized as a drug of choice for the pain that accompanies muscle spasm, which is often chronic and debilitating, especially in paraplegics, quadriplegics, other victims of traumatic nerve injury, and people suffering from multiple sclerosis or cerebral palsy. Many of them have discovered that *cannabis* not only allows them to avoid the risks of other drugs, but also reduces muscle spasms and tremors; sometimes they are even able to leave their wheelchairs.[10]

One of the most common causes of chronic pain is osteoarthritis, which is usually treated with synthetic analgesics. The most widely used of these drugs -- aspirin, acetaminophen (*Tylenol*), and nonsteroidal antiinflammatory drugs (NSAIDs) like ibuprofen and naproxen -- are not addictive, but they are often insufficiently powerful. Furthermore, they have serious side effects. Stomach bleeding and ulcer induced by aspirin and NSAIDs are the most common serious adverse drug reactions reported in the United States, causing an estimated 7,000 deaths each year. Acetaminophen can cause liver damage or kidney failure when used regularly for long periods of time; a recent study suggests it may account for 10% of all cases of end-stage renal disease, a condition that requires dialysis or a kidney transplant. [11,12] Marihuana, as I pointed out earlier, has never been shown to cause death or serious illness.

AIDS

More than 300,000 Americans have died of AIDS. Nearly a million are infected with HIV, and at least a quarter of a million have AIDS. Although the spread of AIDS has slowed among homosexual men, the reservoir is so huge that the number of cases is sure to grow. Women and children as well as both heterosexual and homosexual men are now being affected; the disease is spreading most rapidly among intravenous drug abusers and their sexual partners. The disease can be attacked with anti-viral drugs, of which the best known are zidovudine (AZT) and protease inhibitors. Unfortunately, these drugs sometimes cause severe nausea that heightens the danger of semi-starvation for patients who are already suffering from nausea and losing weight because of the illness -- a condition sometimes called the AIDS wasting syndrome.

Marihuana is particularly useful for patients who suffer from AIDS because it not only relieves the nausea but retards weight loss by enhancing appetite. When it helps patients regain lost weight, it can prolong life. Marinol has been shown to relieve nausea and retard or reverse weight loss in patients with HIV infection, but most patients prefer smoked *cannabis* for the same reasons that cancer chemotherapy patients prefer it: it is more effective and has fewer unpleasant side effects, and the dosage is easier to adjust.

These are the symptoms and syndromes for which *cannabis* is most commonly used today, but there are others for which clinical experience provides compelling evidence. It is distressing to consider how many lives might have been saved if penicillin had been developed as a medicine immediately after Fleming's discovery. It is equally frustrating to consider how much suffering might have been avoided if *cannabis* had been available as a medicine for the last 60 years. Initial enthusiasm for drugs is often disappointed after further investigation, but this is hardly likely in the case of *cannabis*, since it is not a new medicine at all. Its long medical history began 5,000 years ago in China and extended well into the twentieth century. Between 1840 and 1900, more than one hundred papers on its therapeutic uses were published in American and European medical journals. It was recommended as an appetite stimulant, muscle relaxant, analgesic, sedative, anticonvulsant, and treatment for opium addiction. As late as 1913, the great Sir William Osler cited it as the best remedy for migraine in a standard medical textbook.

In the United States, what remained of marihuana's medical use was effectively eliminated by the *Marihuana Tax Act of 1937*, which was ostensibly designed to prevent nonmedical use but made *cannabis* so difficult to obtain that it was removed from standard pharmaceutical references. When the present comprehensive federal drug law was passed in 1970, marihuana was officially classified as a Schedule I drug: a high potential for abuse, no accepted medical use, and lack of safety for use under medical supervision.

But in the 1970s the public began to rediscover its medical value, as letters appeared in lay publications from people who had learned that it could relieve their asthma, nausea, muscle spasms, or pain and wanted to shared that knowledge with readers who were familiar with the drug. The most effective spur to the movement for medical marihuana came from the discovery that it could prevent the AIDS wasting syndrome. It is not surprising that the Physicians Association for AIDS Care was one of the medical organizations that endorsed the California initiative prohibiting criminal prosecution of medical marihuana users. The mid-1980s had already seen the establishment, often by people with AIDS, of *cannabis* buyers' clubs, organizations that distribute medical marihuana in open defiance of the law. These clubs buy marihuana wholesale

and provide it to patients at or near cost, usually on the written recommendation of a physician. Although a few of the clubs have been raided and closed, most are still flourishing, and new ones are being organized. Some of them may gain legal status as a result of the initiative.

Until the recent vote in California, efforts to change the laws had been futile. In 1972 the National Organization for the Reform of Marijuana Laws (NORML) entered a petition to move marihuana out of Schedule I under federal law so that it could become a prescription drug. It was not until 1986 that the Drug Enforcement Administration (DEA) finally agreed to the public hearings required by law. During two years of hearings, many patients and physicians testified and thousands of pages of documentation were introduced. In 1988 the DEA's Administrative Law Judge, Francis L. Young, declared that marihuana fulfilled the requirement for transfer to Schedule II. In his opinion he described it as "one of the safest therapeutically active substances known to man." His order was overruled by the DEA.

Nevertheless, a few patients have been able to obtain medical marihuana legally in the last twenty years. Beginning in the 1970s, thirty-five states passed legislation that would have permitted medical use of *cannabis* but for the federal law. Several of those states actually established special research programs, with the permission of the federal government, under which patients who were receiving cancer chemotherapy would be allowed to use *cannabis*. These projects demonstrated the value of both smoked marihuana and oral THC. The FDA then approved oral THC as a prescription medicine, but ignored the data that suggested that smoked marihuana was more useful than oral THC for some patients. With the approval of *Marinol*, this research came to an end. In 1976, the federal government introduced the Individual Treatment Investigational New Drug program (commonly referred to as the Compassionate IND), which provided marihuana to a few patients whose doctors were willing to undergo the paperwork-burdened and time-consuming application process. About three dozen patients eventually received marihuana before the program was discontinued in 1992, and eight survivors are still receiving it -- the only persons in the country for whom it is not a forbidden medicine. It is safe to say that a significant number of the more than ten million American citizens arrested on marihuana charges in the last thirty years were using the drug therapeutically. The Schedule I classification persists, although in my view and the view of millions of other Americans, it is medically absurd, legally questionable, and morally wrong.

Opponents of medical marihuana often object that the evidence of its usefulness, although strong, comes only from case reports and clinical experience. It is true that there are no double-blind controlled studies meeting the standards of the Food and Drug Administration, chiefly because legal, bureaucratic, and financial obstacles have been constantly put in the way. The situation is ironical, since so much research has been done on marihuana, often in unsuccessful efforts to show health hazards and addictive potential, that we know more about it than about most prescription drugs. In any case, individual therapeutic responses are often obscured in group experiments, and case reports and clinical experience are the source of much of our knowledge of drugs. As Dr. Louis Lasagna has pointed out, controlled experiments were not needed to recognize the therapeutic potential of chloral hydrate, barbiturates, aspirin, insulin, or penicillin.[13] Nor was that the way we learned about the use of propranolol for hypertension, diazepam for status epilepticus, and imipramine for enuresis. All these drugs had originally been approved for other purposes.

In the experimental method known as the single patient randomized trial, active and placebo treatments are administered randomly in alternation or succession. The method is often used when large-scale controlled studies are inappropriate because the disorder is rare, the patient is atypical, or the response to treatment is idiosyncratic.[14] Several patients have told me that they assured themselves of marihuana's effectiveness by carrying out such experiments on themselves, alternating periods of *cannabis* use with periods of abstention. I am convinced that the medical reputation of *cannabis* is derived partly from similar experiments conducted by many other patients.

Some physicians may regard it as irresponsible to advocate use of a medicine on the basis of case reports, which are sometimes disparaged as merely "anecdotal" evidence which counts apparent successes and ignore apparent failures. That would be a serious problem only if *cannabis* were a dangerous drug. The years of effort devoted to showing that marihuana is exceedingly dangerous have proved the opposite. It is safer, with fewer serious side effects, than most prescription medicines, and far less addictive or subject to abuse than many drugs now used as muscle relaxants, hypnotics, and analgesics.

Thus *cannabis* should be made available even if only a few patients could get relief from it, because the risks would be so small. For example, as I mentioned, many patients with multiple sclerosis find that *cannabis* reduces their muscle spasms and pain. A physician may not be sure that such a patient will get more relief from marihuana than from the standard drugs baclofen, dantrolene, and diazepam -- all of which are potentially dangerous or addictive -- but it is almost certain that a serious toxic reaction to marihuana will not occur. Therefore the potential benefit is much greater than any potential risk.

During the past few years, the medical uses of marihuana have become increasingly clear to many physicians and patients, and the number of people with direct experience of these uses has been growing. Therefore the discussion is now turning from whether *cannabis* is an effective medicine to how it should be made available. It is essential to relax legal restrictions that prevent physicians and patients from achieving a workable accommodation that takes into account the needs of suffering people. H.R. 1782 (the Medical Use of Marihuana Act) is a worthwhile move in that direction because it gets the federal government out of the way and allows the states to experiment with their own solutions to the problem. I strongly urge that you pass this law.

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