Lester Grinspoon

Cannabis: Wonder Drug of the '90s

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. 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 (Hayes, *et al*., 1993).

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 a death. The most serious concern is lung 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 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 Marijuana Tax Act (1937), it will be among the least toxic substances in that compendium.

(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 $10 to $20 an ounce, or about 25 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, $20 -- are effective in most cases for the nausea and vomiting of cancer chemotherapy (although many patients find cannabis to be more useful). Thus cannabis would be nearly 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.

Pain

There are many anecdotal reports of marihuana smokers using the drug to reduce pain: post-surgery pain, headache, migraine, menstrual cramps, and so on. In particular, marihuana is becoming increasingly recognized as a drug of choice for pain that accompanies muscle spasm. This kind of pain 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 these sufferers have discovered that cannabis not only allows them to avoid the risks of opioids for pain relief, but also reduces muscle spasms and tremors, sometimes allowing them to leave their wheelchairs (Petro, 1980). Cannabis may act by mechanisms different from those of other analgesics. Some new synthetic cannabinoids might prove to be especially effective as an analgesic -- a possibility implied by the recent discovery of cannabinoid nerve receptor sites in the brain and other organs (Matsuda, *et al*., 1990; Munro, *et al*., 1993).

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 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 (Consroe, *et al*., 1975). 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 (whole body) convulsions; three showed great improvement. Of eight patients who received a placebo instead, only one improved (Cunha, *et al*., 1980). While again the evidence is anecdotal, 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 (Grinspoon and Bakalar, 1993).

Asthma

Asthma is a breathing disorder that arises when bronchial muscles go into spasm and the pathway to the lungs is blocked by mucus and swelling. A number of antiasthmatic drugs are available, but they all have drawbacks -- limited effectiveness or side effects. Because marihuana dilates the bronchi and reverses bronchial spasm, cannabis derivatives have been tested as antiasthmatic drugs. Smoking marihuana would probably not be a good way to treat asthma because of chronic irritation of the bronchial tract by tars and other substances in marihuana smoke, so recent researchers have sought a better means of administration. THC in the form of an aerosol spray has been investigated extensively (Tashkin, *et al*., 1975; Tashkin, *et al*., 1977). Other cannabinoids such as cannabinol and cannabidiol may be preferable to THC for this purpose. An interesting finding for future research is that cannabinoids may affect the bronchi by a different mechanism from that of the familiar antiasthmatic drugs.

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 (Hepler, *et al*., 1976).

It remains to be seen whether topical use of THC or a synthetic cannabinoid in the form of eyedrops will be preferable to smoking marihuana for this purpose. So far THC eyedrops have not proved effective, and in 1981 the National Eye Institute announced that it would no longer approve human research using these eyedrops

(Roffman, 1982). Other natural cannabinoids and certain synthetic cannabis derivatives are still being studied. But smoking marihuana (six to ten times a day) seems to be a better way of titrating the dose than taking an oral cannabinoid, and most patients apparently prefer it.

Cancer Treatment

Cannabis derivatives have several minor or speculative uses in the treatment of cancer, and one major use. As appetite stimulants, marihuana and THC may help to slow weight loss in cancer patients (Regelson, *et al*., 1976). THC has also retarded the growth of tumor cells in some animal studies, but results are inconclusive, and another cannabis derivative, cannabidiol, seems to increase tumor growth (White, *et al*., 1976). Possibly cannabinoids in combination with other drugs will turn out to have some use in preventing tumor growth.

But the most promising use of cannabis in cancer treatment is the prevention of nausea and vomiting in patients undergoing chemotherapy. About half of patients treated with anticancer drugs suffer from severe nausea and vomiting, and for 30% to 40% of them, the commonly used antiemetics do not work (Roffman, *op. cit*., pp. 82-83). The nausea and vomiting 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 phenothiazines like prochlorperzine (Compazine) and the relatively new ondansetron (Zofran). The suggestion that cannabis might be useful arose in the early 1970s when some young patients receiving cancer chemotherapy found that marihuana smoking, which was of course illegal, 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 (Vinciguerra, *et al*., 1988). Oral THC has proved effective where the standard drugs were not (Lucas and Laszlo, 1980; Sallan, *et al*., 1975.). But smoking generates faster and more predictable results in both glaucoma and cancer treatment, because it raises THC concentration in the blood more easily to the needed level (Chang, *et al*., 1979). 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 (Grinspoon and Bakalar, *op. cit*., 1993).

Oncologists may be ahead of other physicians in recognizing the therapeutic potential of cannabis. In the spring of 1900, 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 dronabinol (Marinol) and smoked marihuana.

Only 43% said the available legal antiemetic drugs (including oral synthetic THC) 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 oral synthetic THC and roughly as safe (Doblin and Kleiman, 1991).

AIDS

The American AIDS epidemic first came to notice in 1981, and by now more than 150,000 Americans have died of the disease. Nearly 2 million are infected with the HIV virus, and perhaps as many as a quarter of a million are ill. Although the spread of AIDS has slowed among homosexuals, 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 inner city black and Hispanic intravenous drug abusers and their sexual partners. The period of incubation (between infection and the development of symptoms) is variable, but averages 8 to 10 years. It appears that almost all infected persons will eventually become ill. No cure is known. Opportunistic infections and neoplasms (cancerous growths) can be treated in standard ways, and the virus itself can be attacked with anti-viral drugs, of which the best known is zidovudine (AZT). Unfortunately, AZT, along with other drugs used in

the treatment of AIDS, sometimes causes severe nausea that heightens the danger of semi-starvation for patients who are already suffering from nausea and losing weight because of the illness.

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. The synthetic cannabinoid dronabinol (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.

Depression

Cannabis was first proposed as a treatment for depression by Jacques Joseph Moreau de Tours in 1845 (de Tours, 1857). During the next 100 years his proposal was supported and disputed in a number of medical papers. The most recent study on cannabis and depression was undertaken in 1973. Eight hospitalized patients were given either THC or a placebo for up to a week. The THC did not help them, and in four it produced discomfort and anxiety so serious it had to be withdrawn (Kotin, *et al*., 1973). But the patients were not prepared for the experience of an altered state of consciousness, and the brief duration of the trial must also be considered. Standard antidepressants often require three weeks or even longer to work. Today, among the minority of depressed patients who do not respond to any of the standard antidepressants or find the side effects unbearable, some have discovered that whole smoked marihuana is more useful than any legal drug (Grinspoon and Bakalar, *op. cit*., 1993). This evidence is anecdotal, and large-scale clinical studies will eventually be required.

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Marihuana has more in common with penicillin than safety, low cost, and medical versatility. There are also historical parallels. Just as World War II provided the impetus for research on penicillin as an antibiotic, the AIDS epidemic is now exerting some pressure on researchers to explore cannabis as a medicine. But it took more than 10 years to recognize the medical potential of penicillin, and its

systematic exploration was long delayed by lack of lack of interest and resources. For similar reasons, the urgently needed large double-blind clinical studies on cannabis have not yet begun. In this case progress has been delayed largely because the medical establishment and government authorities are stubbornly committed to wild exaggeration of marihuana's dangers when it is used for non-medical purposes. In fact, the potential dangers of marihuana
when taken for pleasure and its usefulness as a medicine are historically and practically interrelated issues: historically, because the arguments used to justify public and official disapproval of recreational use have had a strong influence on opinions about its medical potential; practically, because the more evidence accumulates that marihuana is relatively safe even when used as an intoxicant, the clearer it becomes that the medical requirement of safety is satisfied.

If any other drug had shown similar promise, public and professional interest would be intense. But the U.S. government, in its zeal to prosecute the War on Drugs, has been doing everything it can to reduce that interest and prevent the fulfillment of marihuana's medical promise (Grinspoon, *et al*., 1995). Cocaine and morphine (Schedule II drugs) are legally available as medicines; marihuana is not. In 1972 an effort began to put marihuana in Schedule II, a classification that would allow doctors to prescribe it. Finally, in 1988, after years of hearings in which scores of witnesses presented impressive evidence of marihuana's medical usefulness, an administrative law judge recommended that it should be transferred to Schedule II. The Drug Enforcement Administration rejected the recommendation and was upheld on appeal.

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 it is not as though cannabis were an entirely new agent with unknown properties. Studies conducted in the past ten years have confirmed a centuries-old promise. I believe that as restrictions on research are relaxed, and this promise is realized, cannabis will come to be recognized as a wonder drug of the '90s.

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