What Is the Drug?

Cannabis is a natural plant with various cannabinoids and with varying amounts of these compounds found in its leaves, leaf buds and flowering tops. Its illegality can be a serious concern for the user because there is no assurance of quality control. It could be contaminated with pesticides, mold, bacteria, or other adulterants such as PCP. To avoid the danger of getting contaminated medicine, some people choose to grow their own cannabis. As noted in Krampf's chapter, cannabis buyers clubs have been organized by patients to assist in supplying other patients with clean, non-contaminated marijuana.

The THC pill is not synonymous with marijuana or cannabis. The THC pill is a synthetic form of just one of the 60 cannabinoids found in the cannabis plant, the one believed to be the most psychoactive. It is a Schedule II drug and is available only by prescription.

What Are the Therapeutic Effects, Side Effects and Adverse Consequences of Cannabis?

Every medication available for prescription in the United States undergoes rigorous and often exhausting research evaluation before it is released to the general public in order to demonstrate that the medication has therapeutic benefit and that it is safe. Each medication is
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tested for therapeutic effects, side effects and adverse effects, and the appropriate dosing level is determined. Like any other medicine, cannabis or THC has many effects. And as with any other medicine, the patient should understand the potential risks and benefits of cannabis before using it so that the decision to use cannabis can be made by a careful evaluation of the risks and benefits.

THERAPEUTIC EFFECTS

An effect is therapeutic if it treats the problem or helps reach a goal. For example, cannabis may have the effect of appetite stimulation along with decreasing nausea, and therefore it may enhance weight gain. For cancer and AIDS patients who cannot maintain weight or suffer from the debilitating nausea and vomiting side effects of chemotherapy this is a major victory and would be-considered a therapeutic effect of cannabis. For a glaucoma patient using cannabis, its ability to lower intraocular pressure would be considered the therapeutic effect, and appetite stimulation may be considered a side effect. In general, patients will experience the therapeutic effect with their first trial use. This is of great benefit, because the patient can soon determine whether or not to continue to use it and need not waste time trying to determine the most effective dose if the medication is not helpful. The preceding chapters discussed many of the therapeutic effects of cannabis.

SIDE EFFECTS

Side effects are effects accompanying the indicated therapeutic effect and are more of a nuisance and not usually a cause for concern. As with many medications, side effects from marijuana may or may not occur depending on such variables as dose, absorption factors, the environment, and attitudinal mindset of the patient. Potential side effects of THC/cannabis include:

Euphoria: A feeling of well-being or elation that may be accompanied by talkativeness, spontaneous laughter, or quiet introspection. It is usually at its most intense about 20 minutes after inhaling marijuana. This "high" is not necessary in order to obtain other therapeutic benefits, and patients may often develop a tolerance to the "high" but not to the therapeutic effects. For many patients trying to cope with the stress of a life threatening illness such as AIDS or cancer, this side effect may be therapeutic as well.
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Drowsiness: Persons frequently complain of feeling sleepy after using marijuana. For this reason it is important for patients to avoid driving a car or operating dangerous equipment when using cannabis. Patients are easily aroused and this side effect is often dose related. As patients adjust to this medicine a dose can usually be achieved without causing drowsiness.

Conjunctival reddening of the eye: This "red eye" is due to a temporary dilation of the blood vessels of the lining of the eyeball. It is caused by systemic effects of THC, not cannabis smoke irritation.

Tachycardia or rapid heart rate: This is often dose related and due to the response of the sympathetic nervous system to the chemical constituents of THC. The "heart pounding" usually starts within 20 minutes and stops within 45 minutes after the THC dose (Kanakis et al. 1979). This may be a risk to persons with angina or other cardiac problems, and consequently should be used with caution under medical supervision.

Increased appetite: Commonly called "the munchies," an increased appetite often occurs within 10 to 60 minutes of taking marijuana. This can be a worrisome side effect for persons struggling to keep extra pounds off.

Dry Mouth: Patients are encouraged to have a beverage available to decrease this mild discomfort.

In addition to the above side effects, less common effects include an alteration in the perception of the passage of time in that it seems' slower, sensory or perceptual distortions, mood changes ranging from a very relaxed state to anxiety or panic, a raising or lowering of the blood pressure, and dizziness. Research by Perez-Reyes et al. indicates that smoking high potency cannabis or taking more than 35mg of oral THC may cause dizziness when standing up quickly and a slow heart beat (vasovagal syndrome) (1990).

ADVERSE EFFECTS
Cannabis in doses exceeding the therapeutic levels or in individuals who are specifically vulnerable to its effects may lead to the experience of an adverse effect. Adverse effects are those that may be detrimental to the patient. Depression, hallucinations, paranoia, depersonalization, and confusion have been reported by a small percentage of people during or after cannabis use. These effects generally only last as long as the effects of the cannabis and are best treated by reassuring the patient and by providing a supportive and calm environment. No medication is required to counteract the adverse effects, although administration of aspirin, ibuprofen, or other non-steroidal anti-inflammatory drugs may help (Perez-Reyes et al. 1991). However, in cases where these symptoms are exhibited, the patient should probably discontinue the use of cannabis or THC.

What Is the Correct Dose?

Dosage is the most complex and important factor in using a medication and is the most frequent cause of serious injury or death from medications. Correct dosage includes the correct amount of the drug as well as the route and frequency of administration. As stated previously, cannabis has a very wide margin of safety and it is virtually impossible to overdose on it. However, other risks can be reduced by determining the lowest effective dose.

INHALED CANNABIS

When medicine is inhaled, it is immediately absorbed into the blood stream through the enormous network of capillaries in the lungs, and in less than a minute it reaches the target area in the brain where it can produce the therapeutic effect. Studies on the psychoactive effects of inhaled cannabis indicate that they begin within five to ten minutes, peak in about an hour, and last for approximately three hours. The amount of delta-9-THC in cannabis determines the strength and potential for mind-altering effects.

When smoking cannabis the dose received can be altered within limits by changing how much smoke is inhaled, the time between inhalations, and the number of inhalations taken. Other factors that affect the actual amount of THC and other cannabinoids being inhaled include the strength of the cannabid smoked, the amount of unchanged THC present in the smoke inhaled (the amount not burned up by fire), the amount lost in sidestream smoke, the method of use (cigarette or pipe), and the amount of THC trapped in the mucosal lining of the mouth and airway on the way to the lungs (Huestis et al. 1992; Perez-Reyes 1990). It is believed that a
person receives less than 50 percent of the THC content of cannabis cigarettes since part is destroyed in the burning process (pyrolysis) and part is lost in the smoke (Lemberger et al. 1972). One study showed 20 to 30 percent of the THC was lost during pyrolysis and 40 to 50 percent was lost in sidestream smoke, allowing less than 40 percent of the THC to reach the lungs (Perez-Reyes 1990).

Breath-holding during cannabis inhalation has been a habitual practice of many cannabis smokers. Research indicates that breath-holding for ten seconds can increase the plasma THC level over no breath-holding, but there is no significant increase in the plasma level for breath-holding longer than ten seconds (Azorlosa et al. 1995). Another study suggests that cannabis smokers could still achieve adequate plasma levels while lowering their exposure to carbon monoxide and other possibly toxic smoke constituents by limiting breath-holding (Zacny and Chait 1990).

The potency of THC can range from less than 0.1 percent in non-psychoactive hemp-type cannabis (grown for its stalk), to over 10 percent in extremely potent cannabis (sinsemilla). The higher the percentage of THC, the higher the likelihood of increased psychoactive effects (euphoria or dysphoria). There are reports of higher potency cannabis having been developed and a more dangerous drug thus being on the market. These reports are not true. The reality is that persons growing cannabis have developed their knowledge and growing skills and have learned to grow sinsemilla (seedless female plants) that develop flowers rather than seeds. These flowering tops or buds have a higher THC content than the leaves (Mikuriya and Aldrich 1988). Smoking these flowers can provide the same amount of THC with much less consumption of smoke required. Robert Randall smokes ten marijuana cigarettes a day to control his intraocular pressure. If he could get more potent cannabis, he might only need to smoke a fraction of that amount and could thus decrease the potentially harmful side effects from smoking.

For some patients the higher THC content may not mean more therapeutic value. The various combinations of cannabinoids seem to be a significant factor in the therapeutic effectiveness. One study examined the effects of the three main cannabinoids: THC, cannabidiol or CBD (a reputed biochemical precursor of THC), and cannabinoil or CBN (the immediate degradation product of THC). Pure forms of these cannabinoids were injected into human subjects. For THC, the researchers found that 20 mcg per kilogram of body weight was the average minimum amount to induce a "high," and 50 mcg per kilogram was the average maximum amount. For CBN, the amounts were 200 and 270 mcg per kilogram respectively. No high was reported with CBD. However, other studies indicate that CBD can have a significant interaction with THC (Karniol et al. 1974; Perez-Reyes 1973). It appears that the CBN gnd CBD can increase the sedative effects of THC and block the excitant effects (the "high"). As the CBD content approaches that of THC, the "high" will be diminished in its intensity, but the effects are...
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prolonged. These findings indicate various plant hybrids may assist in identifying particular strains for specific therapeutic effects. Further research is needed to determine the most effective combinations for desired effects.

Autotitration is the key advantage to smoking cannabis. Because the effects are so rapid in onset, the patient can easily determine how much to inhale to achieve an effective dose. The few patients legally prescribed medicinal marijuana receive their cannabis in prescription form and are aware of the THC content. Patients who rely on illegal access to marijuana have no way of determining the potency but can easily determine if a new supply is stronger or weaker and can adjust their intake accordingly. Patients who choose to grow their own can have the reassurance that all cannabis from the same plant will be similar in potency. In any case, a patient should wait several minutes between inhalations of smoke in order to prevent taking more than necessary.

Cannabis is commonly smoked in cigarette form or "joints" (the self-rolled cigarettes) and with this method the user also inhales the chemicals contained in the burning paper. Patients may prefer to smoke cannabis in a pipe because it avoids inhalation of the chemicals in the papers.

The water pipe (hookah) or bong offer other methods to inhale cannabis. With the water pipe, cannabis smoke is cooled by water and the larger particles are filtered out before the smoke is inhaled. Water pipes facilitate the use of small amounts of higher potency cannabis. Bongs operate similarly, but are designed to deliver single inhalations of smoke per pipe bowl followed by a wash of fresh air to the lungs. There are numerous designs for water pipes and bongs, but the basic principle is the same. Both are classified as drug paraphernalia in many states and are illegal to purchase or possess. Only four states (Alaska, Iowa, North Dakota and South Carolina) are without some form of paraphernalia law (Burris et al. 1996).

Decreasing the amount of smoke inhaled is necessary because of the pulmonary risks associated with smoking. Despite the potential negative health consequences related to smoking cannabis, the patient and the healthcare provider should also realize that the cannabis-smoking patient inhales only a fraction of the smoke that a cigarette smoker does. Additional research directed toward limiting any health risks of smoking cannabis should be undertaken.

Hopefully, an aerosol or nebulizer method can be developed that would allow for the quick onset of action and the patient's ability to autotitrte but would also keep the burning smoke and
other chemicals from being inhaled. In the meantime, if patients use a pipe or water pipe, it should be cleaned regularly to decrease the tarry buildup and other contaminants that adhere to the mouthpiece and accumulate in the water. Rubbing alcohol (pure grain alcohol) is a good solvent to use in cleaning any smoking device.

**ORAL CANNABIS**

Most medicines ingested by mouth take at least 20 to 30 minutes to become absorbed. The effects are experienced more slowly, are more variable, are of longer duration, and the response cannot be altered minute by minute. With the THC pills, the psychological effects begin within 30 to 60 minutes, peak at approximately three hours, and usually last more than four hours (Lemberger et al. 1972).

Prior to the Marihuana Tax Act of 1937, various pharmaceutical companies marketed a tincture of cannabis—cannabis extract prepared in an alcohol base. Eli Lilly and Company's Tincture Cannabis indica contained: "Fl. ext. Cannabis indica, Lilly, 13/4 fl. ozs.; alcohol, 14% fl. ozs." Without great concern for overdose but with the intent to minimize side effects, the directions for use were: "Dose, 10 minims, increased til its effects are experienced" (10 minims equal 0.6 ml, usually taken by dropper).

Patients who do not want to smoke cannabis may take it orally in tea, brownies, or cookies. Jamaican women frequently make a ganja tea using fresh cannabis leaves. When baking cannabis, it has been found that sautéing the cannabis in butter before adding it to the batter decreases the haglike flavor and changes the consistency to make it more palatable as well as extracting it efficiently. Another method of ingestion may be the use of a cannabis butter.

The THC pill Marinol (dronabinol) comes in 2.5, 5, and 10 mg capsules. As with the oral cannabis, it is more difficult to titrate the dosage because of the delayed onset of action. Based on anecdotal comments from patients who have tried both inhaled cannabis and oral THC,
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there seem to be more complaints of dysphoria and or hallucinations with the pill.

OTHER ROUTES OF ADMINISTRATION

Dr. West discussed the ophthalmic preparation of cannabis, Canasol, that is being used in some countries for glaucoma. Because the desired effect is to decrease intraocular pressure, eyedrops delivering the medication directly to the area of intent can maximize this effect and minimize other effects.

Other routes of administration include rectal by suppositories and topical with salves and compresses. There is a salve preparation available that is recommended for minor burns and cuts.

FREQUENCY

Depending on the desired effect, a patient may need to use cannabis on a continual basis to maintain a therapeutic level as with glaucoma. For patients with a seizure disorder or frequent spasticity problems, a regular pattern of use (e.g., every four hours) may be preferred to prevent symptoms from occurring. Other patients may use cannabis on an "as needed" basis, such as before chemotherapy to control the nausea and vomiting. Cannabis may be used prior to meals if the desired effect is to increase the appetite.

Marinol has been approved for use as an antiemetic for chemotherapy-induced nausea and vomiting, and in March 1993 it was also approved as an appetite stimulant for AIDS patients with the wasting syndrome. The Physicians Desk Reference's (PDR) recommendation for Marinol administration as an antiemetic is: "an initial dose of 5 mg given one to three hours before treatment, then every two to four hours after treatment for a total of 4-6 doses per day." The patient should start at the lowest dosage and adjust the dose in small increments until the therapeutic effect is obtained. The recommended daily dose of Marinol as an appetite stimulant is: "two 2.5 mg. capsules; one before lunch and one before dinner. " Marinol is available by prescription in a one-month supply of sixty 2.5 mg capsules. The cost is $150 per month or greater; however, the manufacturer, Roxane Pharmaceuticals, offers an assistance program for indigent AIDS patients.'
What About Interactions with Other Drugs?

A drug interaction should always be considered when taking more than one medication or drug. A problem with patients using cannabis is that they may not report their use of it to their healthcare provider because of its illegality, and therefore their healthcare provider may not be aware of the possible interactions (Mathre 1985).

Cannabis and THC have been shown to alter the absorption and elimination of other drugs (Benowitz and Jones 1977, Paton and Pertwee 1972). Because of possible additive or synergistic action, cannabis should not be used in combination with alcohol, sedatives, or sleeping pills since that would increase sedation. For patients using theophylline, cannabis will increase the metabolic processing of that drug (Jusko et al. 1979).

Griffith's Complete Guide to Prescription and Nonprescription Drugs is a great reference for possible interactions of drugs. Under each medication listed, up-to-date information is provided about possible drug interactions, including mention of possible interactions with marijuana.

Am I Allergic to Cannabis?

This possibility should be considered with any drug. An allergic reaction may be as mild as an upset stomach, could manifest as a rash or it could be as serious as impaired breathing that requires emergency care.

Despite its widespread use throughout history, hypersensitivity or allergic reactions to cannabis have rarely been reported (Liskow et al. 1971, Kagen et al. 1983, Anibarro and Fontella 1996). Cannabis has been identified as the possible cause of some occupational respiratory diseases (Zuskin et al. 1990, Vidal et al. 1991).
If a person is aware of an allergy to cannabis, as with other medication allergies, this should be included in the patient's record and future use should be avoided. Without access to a known source of unadulterated cannabis a patient may suffer an allergic reaction to the additives. If chemicals are utilized in the growing process of the cannabis plant, patients may also be at risk for an allergic reaction to the chemical; therefore, organically grown cannabis is recommended.

Will I Develop Tolerance to the Effects?

Drug tolerance means that if a drug is used frequently and regularly over time increasing doses will be required to produce the same effects. In regard to the medical use of marijuana patients have found that tolerance to the therapeutic effects develops more slowly, if at all, than tolerance to the "high" and other side effects. Robert Randall has been successfully using the same amount of marijuana for more than 20 years to control his intraocular pressure. (For more detailed information see Chapter 15.)

Will I Develop Physical Dependence to Cannabis?

Physical dependence means that if a drug is used over time in a sufficiently high dose on a regular basis, the person will experience withdrawal symptoms if the drug is abruptly withheld. This will be covered in greater detail in the chapter on dependence and addiction. For patients using marijuana as a medicine, abrupt cessation of cannabis use will not cause any severe withdrawal symptoms, and they do not need to be concerned about this issue.

How Should Cannabis Be Stored

Once cannabis is harvested, the potency will deteriorate if the plant is not stored properly. Tetrahydrocannabinol oxidizes to cannabinol rapidly in samples stored at room temperature, and the concentration of THC may decrease at a rate of 10 percent per year (Starks 1977). It is best to leave the plants uncleared (with small stems and seeds) in storage rather than manicuring it or crushing it, which would increase exposure to air and thus accelerate the deterioration process.
Dampness is another factor that should be avoided because of the possibility of the cannabis getting moldy, especially with Aspergillus, specifically A. flavus or A. fumigatis. To prevent mold, the cannabis must be dried properly and should not be stored in plastic bags. For most persons with a healthy immune system, the body can resist infection and is not in danger from exposure to aspergillus. However, in AIDS patients and other patients with a compromised immune system, moldy cannabis might cause serious and possibly fatal lung infections if the spores are inhaled (Sutton et al. 1986). At the Boston University School of Medicine, it was determined that baking cannabis at 300°F (150°C) for 15 minutes would destroy the aspergillus fungi (Levitz and Diamond 1991). This procedure is recommended for immuno-compromised patients to avoid accidental inhalation of undetected mold.

Temperature and light are additional factors that can affect the potency. Cooler temperatures slow the deterioration process. Exposure to light should be limited. Cannabis stored over a one-year period had a decrease in THC of 36 percent in the light compared to a 13 percent decrease when stored in the dark. Dark glass bottles or metal tins are preferred containers. In summary, recommended storage is in an airtight, opaque container kept in a cool location. For long-term storage, the freezer may be preferred.

Administration of Marijuana During the Lynn Pierson Study

On the morning of the first marijuana treatment, the chemotherapy nurse notified Brazis (the research nurse,) of the patient's presence in the treatment room. The pharmacy was presented with a prescription for either marijuana cigarettes or THC capsules, depending on the previously discussed choice made by the patient. The marijuana for the study was provided by the National Institute on Drug Abuse. The cannabis was (and still is) grown at the University of Mississippi by the Research Institute of Pharmaceutical Sciences. The marijuana cigarettes were manufactured on a modified tobacco cigarette machine and were stored partially dehydrated and frozen at the Research Triangle Institute, North Carolina. The marijuana cigarettes came in 10-inch round tin cans each containing 50 or 100 cigarettes, each weighing 800 to 900 mg. Because of the storage method, NIDA recommended humidifying the cigarettes at room temperature prior to use. The cigarettes had been irradiated to assure that no fungus or other contaminant was present so as to avoid the respiratory consequences of inhaling moldy marijuana. A typical prescription for cigarettes read: “THc Cigarettes #12: Smoke one cigarette every 4 to 6 hours as needed for nausea and vomiting.”
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Dosage

The amount prescribed was individualized based on the patient's report of the intensity and duration of the vomiting. Some patients received medicine for up to ten days, while other patients used the THC capsules or marijuana before chemotherapy treatment. The patients were cautioned not to operate machinery or drive during their use of marijuana. In some patients, social interaction was appreciated while others preferred to be alone. The patients were informed that marijuana can diminish nausea without eliminating the vomiting.

Administration

Marijuana cigarettes were associated with the mechanics of smoking and personal values. The use of the water pipe was more helpful than cigarette inhalation. The patients were advised to avoid sidestream smoke and to inhale as much of the entire marijuana cigarette as possible, holding each inhalation for the count of ten. The smoking of the cigarette during the initial visit was instructed to be four to six hours at a rate of one to three inhalations at a time, sidestream smoke was kept to a minimum. The smoking of the cigarette was done approximately 30 minutes before chemotherapy treatment. Additional lead time was required for patients with chemotherapy assistance programs.

Dosage and Administration of Cannabis

The dosage and administration of cannabis is essential for maximizing the outcome of treatment and minimizing the incidence of side effects related to drug interaction. With this in mind, the patients were informed of the effects of marijuana on the body and mind, including the mechanics of smoking. The patients were instructed to inhale as much of an entire marijuana cigarette as possible, holding each inhalation for the count of ten. The smoking of the cigarette during the initial visit was instructed to be four to six hours at a rate of one to three inhalations at a time, sidestream smoke was kept to a minimum. The smoking of the cigarette was done approximately 30 minutes before chemotherapy treatment. Additional lead time was required for patients with chemotherapy assistance programs.

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