The use of mind altering drugs has become a major characteristic of American social behavior, and in our complex technological society is is unlikely that man will ever be able to eliminate his desire or need for "artificial paradises" as a means of coping with the stresses of daily existence. Unfortunately, when individuals use drugs, many also tend to abuse them with subsequent disruption of their health, economic or social functioning, thus posing a danger to themselves and to the society in which they live.

When a particular drug has a dramatic acute toxicity, or produces physical dependence with subsequent withdrawal, etc., the definition of the abuse potential of that drug is fairly simple. Marijuana, however, does not have dramatic acute toxicity nor does it produce physical dependence. As a result the determination of the abuse potential of marijuana is difficult and, because of certain social biases, quite controversial. The objective of this chapter is to define the acute and chronic toxicity of marijuana as the drug is used in the United States and hopefully then to provide an accurate analysis of its potential dangers to be weighed against any benefits to be derived from its use.

The basis of this analysis will be (1) extensive experience with large numbers of marijuana users, (2) research into the drug practices of a marijuana using subculture located in the Haight-Ashbury district of San Francisco ans surrounding Bay Area (3) discussion and observation of marijuana experiments conducted by qualified investigators in the field, (4) review of the current literature on marijuana, (5) personal experience with the drug in question. I consider the last two factors the least important factors in my analysis for the following reasons.

Much of the literature on marijuana is dated and often simply a rehash of old articles with little new research or information, (fortunately some recent work indicates a reversal of this negative
trend). Many of the conservative "experts" on marijuana derive most of their information from dated literature, and a majority of these individuals also threaten "uncontrolled panic reactions with a single dose" I never study marijuana users first hand or treat individuals with problems of marijuana abuse. Their opinions then must be suspect.

Many young marijuana liberals, however, loudly proclaim that "marijuana is harmless" despite the fact science has never found a chemical agent that is harmless when dosage is considered (for example one can die from water over-dosage). Their verbal and written opinions are based on their own experiences with marijuana and they are saying, in effect, that marijuana has caused them no problem, and, therefore, it is safe for everyone else. If it ignores the variables of personality and environment, opinions based entirely on personal experience are of little value.

My own analysis then, will be based primarily on clinical experience, personal research, and discussion with other qualified and objective investigators.

**Marijuana and Other Cannabis Preparations.**

Marijuana, as defined in the editor's note, is the flower and leaves of the female Cannabis Sativa plant. The active ingredient in marijuana is believed to be tetrahydracannabinol (THC) and cannabis preparations vary in strength depending on the concentration of THC. For example, in India there are three basic preparations of cannabis. The weakest preparation is called bhang and consists of the dried matured leaves and flowering shoots of the female plant. Indian bhang corresponds to American marijuana. This relationship has caused a great deal of confusion in the eyes of the American public. Many conservatives have pointed to the tremendous damage done by "marijuana" in India whereas the Indian literature actually states that most of the problem occurs with the stronger preparations, they feel bhang (our marijuana) causes little problem, and should be reserved for the upper classes in India.

Ganja, a more potent preparation is formed by treating the small leaves and resinous matter until a solid homogenous mass is formed, whereas charas is the pure gummy resin obtained directly from leaves and corresponds to "hashish." This latter product contains the highest concentration of THC.
Marijuana and hashish are the two products used in the United States and differ only in that the latter contains a greater concentration of THC. A pertinent comparison is beer and bourbon; the intoxicating agent in both is ethyl alcohol and one can become as intoxicated on beer as on bourbon but he must ingest much greater quantities of beer to gain equivalent effect.

Hashish has been estimated to be at least five to ten times more potent than marijuana, but such estimates suffer from problems of THC standardization. THC concentration in Cannabis varies with climate, soil, cultivation techniques and there is a slight degradation of THC with time.

In addition, route of administration produces variability of effect. In Eastern and Middle-Eastern countries cannabis is taken orally often in beverages. In the United States marijuana or "grass" is the primary cannabis derivative used and the major route of administration is by smoking, although many individuals drink marijuana tea or eat "grass" brownies. Smoking the drug allows the achievement of a psychoactive blood level much faster than if the drug was taken orally and allows the user better control on titration of his own drug endpoint. The old chiche and excuse of the martini drinker, "I got drunk because I drank on an empty stomach" does not apply to the marijuana smoker. However, Isbell 5 in his preliminary report on the effects of delta 9-THC indicated that this compound is 2.6 times as potent when smoked as when ingested orally. The increased potency of smoked delta 9-THC may represent a more efficient absorption of the compound through the lung as compared to the intestine or a heat-isomerization of -delta 9-THC to a more potent compound. The reason for this variation in potency is unknown at present.

**Motivation for Marijuana Use.**

Marijuana users in America have a variety of motivations for their drug use 20 including curiosity, group conformity, sedation and intoxication. For example, many people smoke the drug for relaxation in a manner similar to the American tradition of having a beer or cocktail at the end of a trying day.

In younger people, the predominant motivation for marijuana use is to get "high" or "stoned", the alcohol equivalent of being "drunk". Overtitration appears primarily to occur with the inexperienced or abusive marijuana smoker, a situation which parallels the situation with alcohol. The experienced marijuana user is able to achieve a consistent "high" described as a felling of adequacy, euphoria, well-being and satisfaction7. The experienced user prefers a congenial group setting rather than smoking marijuana alone, a situation which again parallels
alcohol and its associated cocktail party.

In other parts of the world cannabis is taken under a wider range of circumstances. For example in India and the Middle East, cannabis is still used rather widely 4, 8 for medical purposes. These indications of sedation, analgesia, etc., seem to be met by superior therapeutic agents in the United States and it is unlikely that the drug will be revived in current American medical practice. Cannabis is also used by laborers to alleviate fatigue. As stated by Chopra, 8 "A common practice amongst laborers engaged in building or excavation work is to have a few pulls on a ganja pipe or to drink a glass of bhang towards the evening. This produces a sense of well-being, relieves fatigue, stimulates the appetite, and induces a feeling of mild stimulation, which enables the worker to bear more cheerfully the strain and perhaps the monotony of daily routine of life".

Reference to the life-style of lower class cannabis users in India was analyzed in detail by Mr. Joseph Oteri, defense attorney in the classic Massachusetts marijuana case. "Commonwealth vs. Leis." 1 The reason for this detailed analysis was to critique the oft-quoted statement by foreign scientists that "marijuana causes brain damage."

Mr. Oteri presented convincing evidence and expert testimony that the clinical descriptions of marijuana induced brain damage were questionable and were reports of individuals who used charas (hashish) in large quantities over many years. He also presented evidence that the individuals studied were predominantly lower class with inadequate diets and miserable living circumstances. It is well known that chronic dietary deficiency can produce brain damage and in the above well publicized clinical studies the exact contribution of cannabis was uncertain. If one used marijuana regularly and had adequate diet it is highly unlikely that he would develop chronic and irreversible brain damage.

Cannabis also has a long history of religious use in India 4, 8 and in the religions of certain primitive African tribes9. Eastern mysticism is much more popular in the United States recently and "Gurus" of the psychedelic community (popularly known as "hippies") feel that marijuana is an indespensable agent in their meditation and worship. Current marijuana regulations have produced some interesting constitutional conflicts as in the case of Gridley Wright who claimed that his arrest on the charges of marijuana possession violated his right of religious freedom. This case was vividly described by Dr. Lewis Yablonsky in his excellent book 10.

**Acute Marijuana Toxicity**
Marijuana intoxication is a dose-related phenomenon as has been previously described. With adequate dosage, the drug can produce a state of intoxication characterized by euphoria, time and spatial distortion, and motor impairment. The La Guardia report 11 reported motor impairment with decreased hand and body steadiness although reaction time was only slightly altered despite significant perceptual alterations. These perceptual alterations are often described by contemporary youth as a Psychedelic experience.

 Conjunctivitis is a consistent finding with marijuana intoxication and is not a primary irritant effect of the smoke but occurs even when the drug is taken orally 12.

 In my clinical research the predominant acute toxic symptoms secondary to marijuana overdoseage were nausea and vomiting. It is interesting that of the 24 cases of marijuana intoxication with nausea and vomiting I have seen, 20 reported feeling a little "high" the next day, but none reported having a hangover. The following case illustrates this point.

 Case 1. A 27 year old female school teacher was an experienced marijuana smoker. One night while watching T.V. with friends, she decided to smoke some of her newly acquired "Acapulco Gold." Four "joints" and several "grass" brownies were shared among the three people and all became very "high". The patient became nauseous and vomited 5 times. She slept well and the next day was quite hungry, but felt well and did a full day's work.

 The marijuana-induced toxic psychosis is poorly defined despite numerous reports of "insanity" in scare literature distributed by conservative elements to the general public. It is known that heavy marijuana smoking can precipitate a psychotic reaction in individuals with severe personality disturbances 21 11• In this case the psychoactive drug is acting only as a "trigger".

 Primary marijuana psychosis is a very rare reaction.

 At San Francisco General Hospital 5000 acute drug intoxications were treated in 1967. Despite the high incidence of marijuana use in San Francisco, no "marijuana psychoses" were seen. In fifteen months of operation the Haight-Ashbury Clinic has seen approximately 30,000 patient-visits for a variety of medical and psychiatric problems. Our research indicated that at least 95% of the patients had used marijuana one or more times 13, and yet no case of primary marijuana psychosis was seen. There is no question that such an acute effect k theoretically
possible, but its occurrence is very rare.

I have seen three cases of marijuana-induced psychosis and the individuals (2 doctors and 1 newspaper reporter) involved were remarkably similar. They were all successful members of the establishment, in their middle thirties, and were using marijuana for the first time in "far out" environments. All had extreme paranoid reactions characterized by fear of arrest and discovery, and two of three were hospitalized in private hospitals under a "non-drug" psychiatric diagnosis.

It must be understood that any drug reaction is dependent on three variables: the chemical agent itself, the individual's personality, and the environment in which the drug is used. The above psychotic reactions represented the user's attitude toward experimenting with an illegal drug and their rigid personality structure rather than an indictment of the pharmacological properties of marijuana, and demonstrates only that "upright" Americans committed to the current dominant value system should not experiment with illegal drugs even though they might be quite capable of handling accepted intoxicants such as alcohol. Were the legality of the drugs reversed, then their experiences would also be reversed.

As with virtually any other psychoactive drug, marijuana can induce acute anxiety with some feelings of panic in the user. This type of reaction is uncommon and is often related to an improper set or attitude by the user, or pre-existing personality problems. The perceptual alterations produced by moderately high doses of marijuana occasionally produces a feeling of depersonalization in the user and his fear that this effect may last produces fear and anxiety. Individuals who are insecure or threatened by circumstances surrounding the drug experience, such as arrest, are more prone to this type of reaction. Prolonged reactions have been reported 14 but almost always are related to high dose use in individuals with unstable pre-drug personalities or individuals with unstable pre-drug personalities or individuals who have had experience with more potent psychoactive drugs such as L.S.D.

**Marijuana-induced "flash-backs"**

The spontaneous recurrence of the effects of lysergic acid diethylamide (LSD) have been reported and discussed on numerous occasions in the last few years since the use of this drug has become widespread.15, 16, 17, 18 Many lecturers on drugs have speculated that since marijuana is a "hallucinogen" (an extremely debateable point) then it too should cause flashbacks. Recently spontaneous recurrence of marijuana effects were reported by Keeler et
In the large marijuana-using population of Haight-Ashbury the recurrence of marijuana effects is almost unheard of except for an occasional ill-defined perceptual phenomena and reports of such occurrences in other areas seem doubtful at best. LSD O-r SIP flashbacks however, are quite common in Haight-Ashbury. There is no question that marijuana can serve as a trigger for an LSD "flashback" just as any psychoactive drug including alcohol can, but this is not a primary reaction. The following case demonstrates this.

Case 2.

A 29 year old white male came to San Francisco General Hospital complaining of recurrent hallucinations anf feelings of panic. These had been recurring for I month since he had ingested 100 micrograms of LSD with friends while riding in a car. He went to a friend's house and the fear reaction eventually subsided. Two days later he smoked a "joint" and had a flashback characterized by marked perceptual alterations with a panic that was similar to his LSD experience. One week later the patient drank two glasses of wine, and had a similar but less intense experience. Treatment consisted of reassurance, regular counseling sessions with a physician and the elimination of all psychoactive drugs. The "flashbacks" re-occured periodically, but with decreasing intensity, and finally ceased 8 months post-LSD experience.

Individuals in Haight-Ashbury have reported smoking as much "grass" as they possibly can to achieve "hallucinations" and a "psychedelic state." Meyers 6 compares this to the twilight zone of nitrous oxide intoxication and confirms that it is virtually impossible to achieve a fatal anesthetic level with marijuana smoking, although it is possible to produce death in animals with massive cannabis overdoseage via coma and respiratory failure

Chronic Marijuana Toxicity

The most common example of chronic drug toxicity in the United States is the alcoholic. Alcohol is a high caloric substance (7 calories per gm) and repeated alcohol intoxication produces not only primary drug toxicity, but also associated secondary nutritional deficiencies leading to cirrhosis of the liver, peripheral neuritis, and eventually organic brain damage.
Such a well defined toxic syndrome does not exist with marijuana, as it is used in the United States, primarily because cannabis is an appetite stimulant and the individual who becomes repeatedly intoxicated with marijuana continues to eat well thereby eliminating any nutritional organ damage.

In terms of social consequences, however, there does appear to be the marijuana equivalent of the alcoholic commonly referred to as a "pot head." The "pot heads" I have observed become "stoned" almost daily with marijuana and become anxious if "grass" is not available. This habituation or psychological dependence is disruptive in that they tend to ignore personal and social responsibilities such as personal hygiene, health, work, etc. It is interesting that an unusually high incidence of the "pot heads" reported using alcohol in excess at one time, but rarely use "booze" unless "grass" is not available. Certain younger individuals who regularly use marijuana also develop what I have called the amotivational syndrome in that they lose the desire to work or compete. Such cases come to the attention of a physician only if the patient becomes anxious over the loss of a drive he deems highly desirable or if pressures are exerted by important personal associations. The following 2 cases illustrate this point.

Case 3. A 24 year old white male "hippie" sought help at the Haight-Ashbury Clinic because of loss of his sexual drive. He had been a moderately successful businessman with wife, child, suburban home, etc. For various complex motivations he decided to "drop out" and as a result left his marriage and business to live the life of a "free man". He smoked "grass" intermittently since age 20 but in the last two years he smoked "grass" daily while living with his girl-friend and enjoying a very active sex life. He claimed to be very happy and anxiety-free, but in the last 6 months his interest in sex and life in general faded to a point where he became very worried. He had not had intercourse with his girl-friend in 3 weeks, and this had caused arguments, accusations of infidelity, etc. Physical examination revealed a normal male in good condition. He was persuaded to discontinue "grass" on a trial basis. His sex drive gradually returned and he felt "normal" the month after cessation of "grass".

Case 4. The parents of a 22 year old 2nd year medical student sought my advice because-TSTi.7- son was doing quite poorly in his studies and was considering dropping out of medical school. His first year in school had been quite successful, and the parents, whose boy had always wanted to be a doctor, were bewildered. Further discussion indicated that the boy had started smoking "grass" with his friends prior to his second year and had gotten sick of the "phony struggle for grades." After much debate the boy bowed to the wishes of his parents, moved home, stopped smoking grass, continued with his school, and seemed reasonably happy with his future career of medicine one year later. This decreased motivation has broader
social considerations which one analyzes the often repeated statement that marijuana is directly related to criminal activity. In fact most criminals in institutions that I have interviewed, indicate that if they planned a crime (bad checks, burglary, etc.) they avoided pot because they became sedated and lost the desire to perform a complicated illegal task. If any drug was commonly used, in association with their criminal activity it was a "pep pill" such as amphetamine.

Certain individuals use marijuana to escape reality and themselves, just as certain individuals abuse alcohol in the same manner.

It would appear that the ratio of marijuana users to abusers is approximately the same as alcohol abusers to users and implies that personality rather than pharmacological factors are the prime consideration.

**The "Stepping-Stone Theory "**

One of the most popular social indictments of cannabis is that it serves as a stepping-stone to the use of more dangerous drugs, particularly heroin. The advocates of this theory continuously present heroin addicts who in hopes of seeking favorable parol, say that they 1) are now cured, but 2) got on the "wrong track" because they use marijuana.

Our research and my clinical experience substantiates the contemporary view that there is nothing inherent in the pharmacology of marijuana which leads to more dangerous drugs. Young people seeking marijuana must buy these drugs from individuals who specialize in the sale of illegal drugs and therefore are often presented with the opportunity to purchase other more potent illegal drugs. Such a situation parallels prohibition with its bootleggers, and rationally this information actually can be used as data to support the argument for liberalization of the controls on marijuana.

There is no question that certain individuals abuse progressively stronger drugs. It is apparent, however, that these individuals are seeking a chemical solution for their own personality problems. They use one drug, be it alcohol or marijuana to excess, without long term resolution of their inner conflicts and then move to a more potent agent again using it compulsively until severe physical consequences ensue or they decide that they cannot handle drugs.
The "stepping-stone theory" is without question invalid. Any drug progression that occurs is a result of personality and environmental factors, and is not dependent on the pharmacological properties of marijuana.

Unfortunately, this fact is often ignored by the legislature who demonstrate by their acclaim that "marijuana leads to heroin." For example, many individuals arrested for marijuana possession have been assigned to Nalline Clinics as part of their probation. Nalline is a true narcotic which has the special property of being a narcotic antagonist. It in no way detects marijuana, LSD, or methamphetamine, and often the first exposure of the young marijuana user to 1) a narcotic by injection, and 2) long term heroin users, is in the Nalline Clinic waiting room. This destructive legislative and social action is motivated by the invalid theory "marijuana leads to heroin."

In summary then marijuana is used in the United States for approximately the same reasons as motivate alcohol use. Younger people however seem to prefer marijuana because of its lack of "hangover" and enhanced perceptual effects which stimulate a "mild psychedelic experience" a state considered desirable by the new generation.

Acute and chronic marijuana toxicity parallels that of alcohol with the exception that the latter drug produces well defined chronic organ damage.

If one assumes then that the rational regulation of a drug should be in proportion to its abuse potential, then one would expect the regulation of marijuana and alcohol to be approximately equal.

If regulation of one drug far exceeds the regulation of an equivalent agent, then one can only assume mis-information or bias on the part of the regulating institutions. It is the hope of this author that the under regulation of alcohol will be brought into proportion with its abuse potential, just as the over-regulation of marijuana will be altered consistent with its abuse potential.

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