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Marihuana: Current Assessment

Marihuana, which has been known for over 2000 years, has become a subject of major controversy in the last decade or so. Unfortunately, the scare stories attributed to the use of marihuana in the late 1930s [1] have been replaced by studies of recent origin, some of which are poorly controlled and from which questionable conclusions have been drawn [2,3]. The government has published an objective evaluation of the effects of this drug on health [4]. The interest in this drug may be measured by the number of recent articles which have appeared in this journal [5-8].

The Law

Marihuana has been legally defined as referring to all parts of the plant *Cannabis sativa* L. Congress designated one species, *Cannabis sativa*. When the law was enacted, the active principle, delta-9-tetrahydrocannabinol (THC), was unknown. Recently claims that still other species of *Cannabis* exist have been made. Botanists have been unable to agree whether there is more than one species of marihuana [7]. Although other plants may have some of the same diagnostic features as *Cannabis sativa* it has not been reported that they all contain THC or that they have the same pharmacological activity as *Cannabis sativa*. The THC content of more than 100 authenticated plants of *Cannabis sativa* varied from 0.04 to 6.1% [9]. In another study it was reported that 117 of 350 plants of *Cannabis sativa* examined contained no THC [10].

Another controversy arises over what constitutes identification of the drug. Although the variants or various species may be identified by an expert taxonomist when the whole mature plant is available, the identification is far more complicated when broken, powdered, or extracted drug is to be analyzed. The microscopic identification of the powdered plant material depends on the recognition of two types of hairs. Other plant materials have similar hairs [11]. The plant material is usually tested chemically using the Duquenois test. Other substances give positive responses to this test [12], and some samples of marihuana have given negative responses to this test [10]. Both thin-layer chromatography and gas chromatography have been used in the identification of the drug [13]. Ultimate identification might depend on infrared spectrophotometry, nuclear magnetic resonance, or gas chromatography/mass spectrometry [14].

Even if the combination of microscopic examination, the Duquenois reaction, and thin-layer chromatography were considered adequate for identification these would not

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indicate the amount of THC; THC and cannabidiol may be rather easily quantitated from extracts by gas chromatography [13].

The controversies concerning several species, and the activity of the drug, could be resolved by basing the law on the quantity of THC present.

Some states have made the possession of more than 100 g of marihuana a more serious offense. The law could be based on the weight of THC rather than marihuana. Using an average of 1% THC there would be 1 g of THC in the 100 g. The 1 g of THC would be contained in about 1600 g (3.5 lbs) of 0.06% THC marihuana or in about 16 g (½ oz) of 6% THC marihuana. It might also represent about 10 g of hashish, a concentrated form of marihuana. If the sample contained no THC it would be exempt from the law, as it should be.

Legal Sanctions

Over 30 million Americans have tried marihuana at least once. Over 10 million smoke marihuana on a regular basis [2]. In the five-year period from 1970 to 1974 it is estimated that over 1.5 million persons were arrested for marihuana-related offenses. About 93% of the arrests were for possession violations; 67% of those arrested possessed less than 1 oz (28 g) of marihuana. In spite of this it appears that marihuana use has increased.

In North Carolina in 1974 there were 10 193 drug arrests; 6313 were for possession of marihuana and 1229 for distributing marihuana. Therefore, 62% of the total drug arrests in the state were for possession of marihuana, 74% for possession and distributing. Only 6% of the arrests were for heroin and other opiate violations.

A recent report on herbal intoxication which describes the psychoactive effects from herbal cigarettes, teas, and capsules demonstrates the futility of trying to control substance abuse [15]. A total of 25 psychoactive substances were found in these products which were promoted as legal hallucinogens, euphorants, and marihuana substitutes.

Eight states, Oregon, Alaska, Maine, Colorado, California, Ohio, South Dakota, and Michigan, have decriminalized the possession of small amounts of marihuana. The offender is issued a citation and may be fined but does not get a criminal record. Congress is studying similar proposals for possible federal legislation. A survey of marihuana use in Oregon showed that there was no significant increase in use during the two years since the law has been in effect [16]. The Alaska Supreme Court stated the law prohibiting use in the home violates the right of privacy [17].

A recent study reported "that more severe penalties and higher perceived certainty of punishment do not have the effect of reducing the likelihood of subsequent cannabis use among a sample of persons who have been officially criminalized for the offense of simple possession" [18].

Qualifications of the Analyst

The microscopic identification of the powdered plant requires a person specially trained to recognize the diagnostic elements of *Cannabis* and not to mistake it for other similar plant material. The chemical examination also requires some special technique and training. The proficiency of a chemist who analyzes blood for alcohol is tested. He must be certified in many states. Those analyzing marihuana, which is more complex, should be certified and have their proficiency tested [19].

Identification of marihuana in court leaves a lot to be desired. In one instance, a police officer was offered as an expert [20]. The following have been offered by chemists: "I did not analyze all the material but by observation, one hundred percent of the brown vegetable material was marihuana. I determined the weight of the material to be 74.9

grams" [21]. A chemist testified that "green vegetable material" in his opinion was "High quality marihuana" according to microscopic and chemical tests [22].

It appears that the analyst weighs a mass of material which he looks at both grossly and microscopically, recognizes some plant hairs, gets the expected response to one or more chemical tests, states the weight, and gives his opinion that marihuana is present. The inference is that the material is all marihuana. It requires much more than what is presently done to determine the percentage of marihuana in powdered material. What does the percentage mean? It is not a measure of activity. When one of the leading experts with many years' experience with marihuana and other medicinal plants is reported to have identified as *Cannabis* an entirely different plant [23], is it not possible that chemical analysts might err in the microscopic identification of powdered plant material?

The quality of marihuana has not been defined. It is an extremely difficult and infinitely lengthy procedure for an expert pharmacognosist to analyze microscopically every minute fragment of about 75 g of powdered drug to state the percentage of marihuana present. The identification and quantitation of THC content could resolve the question scientifically. With one gas chromatograph an experienced chemist should be able to perform about 20 analyses per day.

Detection of Tetrahydrocannabinol in Biological Specimens

The detection and identification of tetrahydrocannabinol in milligram quantities such as is present in plant material is not difficult for a chemist with experience in the analysis of this drug. The amount present in blood is of the order of 5 to 100 ng/ml. Within about 10 min of smoking marihuana, the blood may reach a maximum of about 30 to 150 ng of THC/ml with the concentration decreasing to about 3 to 10 ng/ml in an hour. An excellent monograph has been prepared on the detection of cannabinoids in biological specimens [14]. Urine does not appear to be a good sample for assessing the drug's effect because the THC is not found in the urine, and 11-nor-9-carboxy THC has been detected 5 to 7 days after smoking marihuana [14]. Cannabinoids have been detected in urine using radioimmunoassay and Emit[®] homogenous enzyme immunoassay procedures. The determination of THC in blood by gas chromatography combined with mass fragmentography using deuterium-labeled analogs should allow for meaningful assessments of the effects of marihuana at various blood concentrations.

Operating a Motor Vehicle

Although degradation of the performance of a person under the influence of marihuana has not been adequately demonstrated it appears that operation of a motor vehicle might be ill-advised. Questions of space-time distortions and visual disturbances should be evaluated as to their possible effect on operation of a motor vehicle. One carefully controlled study offered the conclusion, "Chronic users under the influence of marihuana are less likely to accept risks than users not under the influence of marihuana" [24]. Another study reported that some drivers showed slight deterioration in driving performance after smoking marihuana cigarettes containing 5 to 8.4 mg of THC [25]. An operator killed in a motor vehicle crash was reported to have large concentrations of tetrahydrocannabinol in blood and urine [26]. Experiments which fully evaluate the effect of any drug on driving performance are difficult, if not impossible, to perform. A recent review of drugs and driving, including marihuana, is available [27].

Since there is no method of blood, breath, or urine analysis readily available to law enforcement officials and others, possible deterioration of driving performance is impossible to assess. Certainly no one should be arrested and charged with operating under

the influence of any drug unless the drug is found in the operator's blood, in a concentration which has been shown to cause deterioration of performance. It was surprising that a conviction for driving under the influence of drugs was allowed to stand on a law enforcement officer's observation and questioning of a driver [28]. No drug was found or admitted. The state supreme court stated that an experienced law enforcement officer could make such a determination. An expert diagnostician cannot ascertain that a person is under the influence of a drug without knowing the concentration of the drug in the blood and how that concentration affects an operator. When a person is driving erratically, he should be removed from the highway by being arrested for careless and reckless driving rather than for driving under the influence of drugs. The evidence should be available for the former charge and not the latter. Law enforcement officers and others should be made aware of the fact that they are unable to determine that poor performance is due to drugs or a specific drug except for alcohol.

Health Effects

The most commonly observed physical responses to marihuana are increase in pulse rate and reddening of the eyes. Dryness of the mouth and throat are also reported. The drug has shown promise of reducing intraocular pressure [29]. Marihuana tends to reduce aggressive behavior. It seems to impair short-term memory processes. Comparison of students who are nonusers, occasional, or chronic users revealed no statistical differences in academic performance, nor was there any evidence of reduced motivation.

Controversy exists concerning the following claims of harmfulness: decreased disease resistance, possible genetic damage, change in lung tissue, effect on electroencephalogram, depression of serum testosterone, tolerance, and withdrawal syndrome. No well-controlled study has confirmed claims of harm done by the drug. The lethal dose of THC has not been established, and no human deaths have been attributed directly to the toxic effects of smoking marihuana. The two or three deaths reported in the literature were certainly not conclusively proven to be due to the drug [30]. It is estimated that a dose 40 000 times the effective dose would be needed to kill; for alcohol, this is about 8 times. Based on the toxicity in rats [31] (LD_{50} is 40 mg THC/kg), a meaningless calculation would show that a 150-lb (68-kg) man would have to smoke more than 500 marihuana cigarettes containing 5 mg of THC per cigarette in an hour to absorb an equivalent amount of the drug. It is obvious that experiments in animals cannot be directly related to man, but the above example should illustrate the relative lack of toxicity of the drug.

In order to properly evaluate the safety of marihuana it should be compared to substances we are more familiar with. It certainly possesses none of the uncertainty which follows the injection of a drug, nor is it desirable to inject marihuana or THC. Deaths and withdrawal symptoms attributed to heroin, alcohol, and barbiturates do not occur with marihuana. Respiratory diseases and cancer associated with chronic cigarette smoking have not been reported. Cardiac effects of caffeine of coffee, tea, and soft drinks have not been attributed to marihuana. It is impossible to prove anything safe, but smoking marihuana appears to be safer than overindulgence with alcohol, tobacco, barbiturates, heroin, aspirin, and many other drugs. Many deaths have been attributed to the above drugs but practically none to marihuana.

At a recent meeting recognized experts gave their opinions on recent marihuana research [32]. They were critical of retrospective studies and the lack of large-scale, long-term epidemiological studies. The significance of the impairment of the T-cell (one type of white blood cell) mediated component of the human immune response is unclear. There is no evidence of the drug causing any mental illness, amotivational syndrome, or brain damage. The fact that the drug can alter DNA synthesis suggests the possibility

that it might affect the human genetic and reproductive processes. The drug should not be used by pregnant women. The significance that under certain conditions the drug reduces the level of human testosterone, a male sex hormone, is not clear.

Long-Term Use of Marihuana

Although the drug has been used for over 2000 years only recently has a scientific study been made of continued use. This study was made in Jamaica for the National Institute of Mental Health [33]. The smokers use ganja, a mixture of tobacco and marihuana. The average users smoked seven cigarettes with 3% THC per day for 17 years. The typical American user smokes one or two cigarettes a day with about 1% of THC. The Jamaican absorbs 10 to 25 times more THC than the American.

Rather than producing an amotivational syndrome, ganja smoking in Jamaica seemed to increase motivation. An elaborate series of studies led the researchers to conclude that the chronic use of potent *Cannabis* is not toxic to the human mind and body. Users and nonusers were compared with respect to blood pressure, electrocardiogram, chromosome breakage, electroencephalogram, signs of depression and neuroticism, liver functioning, respiratory functioning, hematology including number of white cells, motor coordination, and memory. The only significant difference detected between users and nonusers was that the users tended to exhibit hypoxia, a deficiency of oxygen, somewhat more than nonusers. There was no evidence of tolerance developing. Withdrawal syndrome did not appear during the week-long stay in the hospital. An as-yet unpublished study sponsored by the U.S. Army on the chronic and heavy use of marihuana reported similar findings to those of the above study. A comprehensive summary of the effects of marihuana has appeared recently [34]. A report of a recent conference on chronic *Cannabis* use has been published [35].

Discussion and Opinions

In retrospect it is easily understood how marihuana became a drug to be feared. As more people have used the drug and as more research has been done, much of the misinformation has been dispelled. Unfortunately, there still persists an attitude that the drug must be very harmful—if not immediately, then at some time in the future. No well-controlled research appears to exist that tends to support claims of any permanent damage, either physical or mental. Overdose fatalities are practically unknown. The long-term use has not produced any substantiated problems. There does not appear to be any research planned which will adequately demonstrate the dangers or safety of this drug. Our present knowledge of the drug does not support the rigid sanctions imposed on those who use the drug.

It would seem advantageous to provide a more scientific basis to our laws by basing them on the amount of tetrahydrocannabinol. This one change would make the “multiple species” argument invalid. It would also allow the chemically trained criminalist to apply the expertise for which he is qualified. Improved methods of detection of cannabinoids in biological specimens should allow for controlled studies relating the blood concentration and the drug effects.

It appears to be time to evaluate the laws concerning marihuana to see if they should be changed, particularly with respect to definition and penalties. The latest government position noted that the threat of criminal sanctions undoubtedly discourages some potential marihuana users but that “society pays a relatively high price for this form of deterrence: high in terms of stigmatizing casual users with criminal records; high in terms

of diverting limited criminal justice resources from other more serious matters; and high in terms of contributing to an atmosphere which nurtures disrespect for the law" [36].

Summary

Some of the controversies surrounding marihuana have been reported. The problems of multiple species and qualifications of the analyst could be resolved by basing the law on the identification and quantitation of tetrahydrocannabinol. Decriminalization of the use and the possession of the drug could help law enforcement officers, the courts, and the user. Recently reported methods for the determination of the drug and its metabolites in biological specimens should provide a basis for establishing the relationship between blood concentrations and drug effects. The short- and long-term effects of the drug are too subtle to cause much concern over any known or potential hazards.

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