

Psychological adverse effects of cannabis smoking: a tentative classification

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Summary: This paper stresses the need for an early definition and description of the "deviant" cannabis smoker in North America. Attention is called to the fact that on this continent heavy smokers have not yet been separated as "problem" users from other smokers.

A comprehensive review of possible psychological adverse effects of the drug is made. The following classification is suggested: a) Severe intoxications, b) Pathological intoxications, c) Acute cannabis psychoses, d) Subacute and chronic cannabis psychoses and e) Residual conditions.

North American behavioural scientists find themselves in the privileged position of being able to study, from its onset, a rapidly developing new drug habit. Indeed, only during the past decade has the use of cannabis on this continent expanded beyond the limits of selective minorities to involve larger sectors of the population and acquired the proportions of a social custom.

With an estimated 20 million regular users in the United States alone (1969)²¹ it is hardly relevant to devote any more effort in trying to elucidate who becomes a user, why he does so or how he does it. In other words, it would seem no longer pertinent to concentrate on studying the differences between users and non-users. Since it has proven useful for most other social drug-habits, it now appears necessary to attempt a classification of the different types of cannabis users in order to detect

those in need of assistance, particularly psychiatric.

Are there any "problem" users? That is, are there individuals whose involvement with the drug deviates from that of the majority of users? These questions are difficult to answer at this moment since the habit is still illegal and has not been integrated into the established institutional order. No official norms have been set for cannabis smoking and no definition has been put forward of what constitutes a normal or social smoker. In these circumstances the perception of the abnormal or deviant smoker is always biased or arbitrary.

Nevertheless, the literature on the subject is showing increasing interest in detecting individuals who show peculiarities in relation to cannabis.

Even though in North America problem smokers are not yet identified on the basis of quantity or frequency of cannabis use, in other areas of the world where the habit has been practised for a long time, these factors seem to make a difference. In Morocco for example, heavy smokers are considered deviant as are the alcoholics among social drinkers in our culture.³

The fact that the amount of smoking has not become an issue on this continent so far, may be due in part to the widespread belief that cannabis use does not involve a process of pharmacological addiction. However, Williams as early as 1946²² reported that individuals under experimental conditions showed an increase in their daily consumption with a parallel decrease in the euphoric response and the tachycardia which are characteristic effects of the drug. More recently, experiments with different animal

species have demonstrated beyond doubt that a high degree of physiological tolerance to Δ^9 -THC does develop with continuous exposure to the drug.^{7, 18, 23} It is predictable, then, that heavy cannabis smoking will become a subject of clinical interest in the near future because of its addictive connotations.

While in North America problem users have not as yet been defined on the basis of their pattern of cannabis consumption, there has nevertheless been a consistent effort to report and discuss the cases of users who exhibit so-called "adverse reactions" to the drug. There seems to be no general consensus as to what is meant by "adverse reaction"; therefore an effort to clarify this concept is warranted. Most smokers tend to define as "adverse" a cannabis experience which was unpleasant to them; but one could also include in this category all effects which are objectively unusual, unexpected or harmful regardless of the subjective feelings. A case in point is that of the "flashbacks" or "echo reactions" which, in their milder forms, are experienced by many users with pleasure, while most observers will consider them as adverse effects of the drug.

In order to establish a baseline of comparison it would seem appropriate to describe what should be interpreted as a "normal" cannabis experience before discussing further the adverse effects of the drug.

The immediate effects of cannabis smoking may be classified as subjective feelings and objective signs. Both are greatly influenced by the user's expectations and personality, the dose of the drug and the setting where the experience takes place. Understandably, it is among the subjective reports that one finds a higher degree of variability.

The way individuals react to cannabis and the symptomatology they experience are determined to a large extent by a process of learning, through which patterns prescribed by more experienced users are adopted. As H. S. Becker puts it, the novice smoker must learn to smoke effectively to recognize the effects of the drug and to define them as pleasurable.²

Many of the effects reported by smokers are related to the cultural context in which the drug is used. In Egypt, for instance, one of the ex-

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pected effects is an increase in sexual potency,²⁷ in India the alleviation of hunger,⁹ and in Morocco cannabis is thought to increase endurance, as can be inferred from the local proverb "A pipe of kif before breakfast gives a man the strength of a hundred camels in the courtyard"³. In North America cannabis smoking is part of a life style adopted in reaction to living patterns which are no longer satisfactory. Therefore the drug is generally reported to produce effects which are in contrast with the system most smokers disapprove. In reaction to the tension, alienation, materialistic competitiveness and disregard for spiritual and esthetic values that they see in such a system, cannabis users frequently claim to feel relaxed and communicative, to be more aware of themselves and others, to be able to express themselves more freely and to have a greater enjoyment for companionship, sex, food and sensory-perceptive experiences.

Clinically, the usual subjective effects of average doses of cannabis (between 50 and 100 $\mu\text{g.}/\text{kg.}$ of smoked $\Delta^9\text{-THC}$) include mild euphoria, altered sense of time, impaired memory with the individual losing the thread of his speech, and sensory and perceptual distortions through enhanced kinesthetic, auditory, visual, tactile, gustatory and olfactory sensitivity.²⁹

Objective measurements have both confirmed and contradicted such subjective effects. It has been observed, for example, that individuals under the effects of cannabis consistently make wrong estimates of the time elapsing during the performance of a task. They usually feel the time to pass more slowly than it actually does.³¹

Different degrees of impairment are detected when the subjects are given tests requiring retention and recall of information such as arithmetical calculations, recognizing previously observed associations in learning tests and in complex tasks in general.^{11, 31}

The reported changes in perceptive abilities have not been confirmed in studies aimed at testing increase in auditory, tactile and olfactory discrimination.^{5, 34}

Finally, measurements of psychomotor performance indicate that cannabis produces impairment in reaction time, particularly if the task is

complex, and a decrease in muscular strength combined with some body and hand unsteadiness.^{11, 18, 22}

The preceding description gives an account of the most frequently observed effects of cannabis. The so-called "adverse reactions" constitute states whose symptomatology differs in quantity and quality from the above. Taking a comprehensive view, the following classification of psychological disturbances associated with cannabis is suggested.

A. Severe intoxications

Wickler classifies the cannabinoids among the psychotomimetic drugs³² and Isbell³¹ has demonstrated that if $\Delta^9\text{-THC}$ is given in sufficient doses (200-250 $\mu\text{g.}/\text{kg.}$ smoking; three times as much when taken by mouth) it induces a psychotic state with marked distortions in sensory perception, depersonalization, derealization and both optical and auditory hallucinations.

In some cases impairment of the sensorium with mild delirium, some disorientation, slurred speech and slight ataxia have been observed. These effects last while the drug is still active in the organism and are followed by sedation and sleep when they subside.

The severe symptomatology described under this heading does not result from idiosyncratic, abnormal or unusual reactions to the drug; it is rather the manifestation of its stronger, dose-related pharmacological effects. These symptoms usually subside as the drug wears off, but occasionally this process may take longer than the average three to four hours after termination of smoking.

Most cannabis smokers are able to control the extent of the intoxication by regulating the pace of their smoking.⁶ Such control does not exist when the drug is ingested and some severe intoxications may result from taking the drug by mouth rather than smoking it.

The most widely used cannabis preparations in this continent are marijuana cigarettes containing a rather weak concentration of cannabinoids (approximately 1% of total weight). Local users may experience stronger or unexpected effects when consuming exotic samples with higher content of the active principles.

With the improved knowledge of the pharmacology and metabolism of cannabis there are grounds for

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Indications—Sustained moderate through severe hypertension.

Dosage Summary—Start usually with 250 mg. two or three times daily during the first 48 hours; thereafter adjust at intervals of not less than two days according to the patient's response. Maximal recommended daily dosage is 3.0 g. of methyldopa. In the presence of impaired renal function smaller doses may be needed.

Syncope in older patients has been related to an increased sensitivity in those patients with advanced arteriosclerotic vascular disease and may be avoided by reducing the dose. Tolerance may occur occasionally between the second and third month after initiating therapy. Effectiveness can frequently be restored by increasing the dose or adding a thiazide.

Contraindications—Active hepatic disease such as acute hepatitis and active cirrhosis; known sensitivity to methyldopa; cases of mild or labile hypertension responsive to mild sedation or thiazides alone; pheochromocytoma; pregnancy. Use cautiously if there is a history of liver disease or dysfunction.

Precautions—Acquired hemolytic anemia has occurred rarely. Hemoglobin and/or hematocrit determinations should be performed when anemia is suspected. If present, determine if hemolysis is present. Discontinue drug if hemolytic anemia is evident. Discontinuation and/or corticosteroid treatment has brought about prompt remission of anemia.

A positive direct Coombs test has been reported in some patients on continued therapy with methyldopa, the exact mechanism and significance of which is not established. Incidence has varied from 10 to 20%. If a positive test is to develop it usually does within 12 months following start of therapy. Reversal of positive test occurs within weeks to months after discontinuation of the drug. Prior knowledge of this reaction will aid in cross matching blood for transfusion. This may result in incompatible minor cross match. If indirect Coombs test is negative, transfusion with otherwise compatible blood may be carried out. If positive, advisability of transfusion should be determined by a hematologist or expert in transfusion problems.

Reversible leukopenia with primary effect on granulocytes has been seen rarely. Rare cases of clinical agranulocytosis have been reported. Granulocyte and leukocyte counts returned promptly to normal on discontinuance of drug.

Occasionally fever has occurred within the first three weeks of therapy, sometimes associated with eosinophilia or abnormalities in one or more liver function tests. Liver biopsies in several patients with liver dysfunction showed a microscopic focal necrosis compatible with drug hypersensitivity. Determine liver function, leukocyte and differential blood counts at intervals during the first six to eight weeks of therapy or whenever unexplained fever may occur. Discontinue if fever occurs in absence of infection.

Methyldopa may potentiate action of other antihypertensive drugs. Follow patients carefully to detect side reactions or unusual manifestations of drug idiosyncrasy.

Fluorescence in urine samples at same wave lengths as catecholamines may be reported as urinary catecholamines. This will interfere with the diagnosis of pheochromocytoma. Methyldopa will not serve as a diagnostic test for pheochromocytoma.

Usage in Pregnancy: Because clinical experience and follow-up studies in pregnancy have been limited, the use of methyldopa when pregnancy is present or suspected requires that the benefits of the drug be weighed against the possible hazards to the fetus.

Adverse reactions—**Cardiovascular:** Angina pectoris may be aggravated; reduce dosage if symptoms of orthostatic hypotension occur; bradycardia occurs occasionally. **Neurological:** Symptoms associated with effective lowering of blood pressure occasionally seen include dizziness, light-headedness, and symptoms of cerebrovascular insufficiency. Sedation, usually transient, seen during initial therapy or when dose is increased. Similarly, headache, asthenia, or weakness may be noted as early, but transient symptoms. Rarely reported: paresthesias, parkinsonism, psychic disturbances including nightmares, reversible mild psychosis or depression, and a single case of bilateral Bell's palsy. **Gastrointestinal:** Occasional reactions generally relieved by decrease in dosage: mild dryness of the mouth and gastrointestinal symptoms including distention, constipation, flatulency, and diarrhea; rarely, nausea and vomiting. **Hematological:** Positive direct Coombs test, acquired hemolytic anemia, leukopenia and rare cases of thrombocytopenia. **Toxic and Allergic:** Occasional drug related fever and abnormal liver function studies, and a rise in BUN. Rarely, mild and reversible jaundice, skin rash, sore tongue or "black tongue". **Endocrine and Metabolic:** Rarely, breast enlargement, lactation and impotence; weight gain and edema which may be relieved by administering a thiazide diuretic. If edema progresses or signs of pulmonary congestion appear, discontinue drug. **Miscellaneous:** Occasionally nasal stuffiness, mild arthralgia and myalgia; rarely, darkening of urine after voiding.

How Supplied—Film Coated Tablets ALDOMET* are yellow, film-coated, biconvex-shaped tablets, with the MSD symbol engraved on one side, and are supplied as follows:

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proposing other possible etiologies for these severe intoxications. The cannabinoids are metabolized in the liver through a process of hydroxylation and the active forms such as Δ^8 and Δ^9 then disappear from the blood stream within 15 minutes of an intravenous injection. It could be formulated that any condition affecting this rapid metabolism, such as impaired liver function, may result in stronger or longer-lasting intoxications.

B. Pathological intoxications

This category is proposed to include all those intense but short-lasting reactions which are emotional in nature rather than toxic. They occur as an adverse response to average and moderate doses of the drug. Individuals presenting them seem to recover completely as the cannabis experience comes to an end.

Included under this heading are some of the most frequently reported adverse reactions in the North American psychiatric literature: (a) panic and short-lasting paranoid states with fears of police arrest and betrayal by companions, fear of death, of losing one's mind, etc.; (b) acute depressive states with strong feelings of futility, detachment and alienation from friends and environment; and (c) severe depersonalization and derealization feelings with consequent panic.

These are the types of reaction described by Keeler¹⁹ in his earlier report on the adverse effects of cannabis and classified by Weil²⁰ as adverse acute reactions to marijuana in "persons without a history of mental disorder who have not taken other hallucinogenic drugs". However, both authors include in this group the acute form of psychotoxic confusional states that have been classified here in the category "severe intoxications".

It would seem important to distinguish clearly between these reactions because while the confusional states can be explained on purely pharmacological grounds, the panic, depressive and depersonalization reactions are likely to be more influenced by psychological and environmental factors. It is believed, for example, that anxiety and panic occur more frequently in the early stages of the habit when the individual has not yet learned to understand and predict the course of the intoxication. Some

initial neurovegetative effects such as tachycardia may be misinterpreted and feared.

It is also commonly assumed that paranoid reactions tend to occur in settings which are unfamiliar to the user, particularly if the drug is taken in the company of strangers. The fact that this practice is illegal also facilitates such reactions.

Most persons affected by acute depressive or dissociative reactions report having been emotionally upset before taking the drug; many experienced smokers consciously avoid taking cannabis in such circumstances because they presage an unpleasant experience.

Clearly then, personality factors, expectations and setting play an etiological role in these reactions. The term "pathological intoxications" is proposed here to stress their deviant, idiosyncratic nature. They do not result from the direct pharmacological effects of cannabis and the drug seems to operate only as a precipitating agent. Moreover, they last only the few hours the individual remains under the effect of the drug and should not be mistaken for the longer-lasting conditions to be described below as cannabis psychoses.

Unlike the pathological intoxications with ethyl alcohol¹⁴ these cannabis reactions usually leave the individual with a good recollection of the events and symptoms experienced. Owing to their benign course most such reactions do not come to the attention of the medical practitioners; they subside spontaneously or by the individual being "talked down" by understanding, supportive observers. Weil recommends that psychiatrists refrain from intervening in this situation in order to avoid the prolongation of symptoms that may result if the subject is defined as a psychiatric case. This is particularly important if he is admitted to a psychiatric unit, where his fears of becoming psychotic may be confirmed or reinforced.

C. Acute cannabis psychoses

This group should include all those psychotic and hallucinatory conditions which follow a cannabis experience. They are usually precipitated during the cannabis intoxication but, unlike the reactions described above, they remain active after the drug has been metabolized and may last as long as 15 days.

There are several reports in the recent psychiatric literature concerning this type of reaction. The examples include observations by Talbot and Teague²⁸ about cases observed among American soldiers in Vietnam, by Baker and Lucas¹ of hospital admissions in England and by Grossman in reference to American smokers who presented the reactions while in India.¹⁷ Defer and Diehl¹² have reported on a large case-sample gathered in Morocco and analyzed their phenomenology. These authors distinguish between *l'ivresse cannabique* (cannabis intoxication) and the *psychoses cannabiques aiguës* (acute cannabis psychoses). They emphasize the fact that the former last only a few hours whereas the latter take much longer to subside.

Not unexpectedly, this diagnostic category has evoked considerable controversy. There are some authors who even deny its existence, considering the role of cannabis to be secondary and insisting that these patients are psychotics in the first place.⁶ Others propose that the drug, with its disturbing effects on body image, self-perception and reality testing, may only serve as a final stressing factor which upsets the precarious balance in which the patients were functioning.¹⁶ Campbell put forward the hypothesis that individuals who develop cannabis psychosis have pathological EEGs with abnormal percentages of theta waves in the tracings.

Murphy²⁴ has correctly pointed out the need for a more careful follow-up of these alleged cannabis psychoses; he noted that several of the cases reported by Bromberg in 1934⁴ relapsed and schizophrenia was eventually diagnosed.

Finally, it is pertinent to repeat that as experienced an author as Weil believes that many of these psychotic conditions which last a few days result from medical mishandling of the more benign pathological intoxications which should have subsided in a few hours.

D. Subacute and chronic cannabis psychoses

Psychiatric publications originating in India⁸ and North Africa describe certain cannabis psychoses not yet observed or recognized on this continent. These are conditions believed to be caused by heavy, chronic consumption of the drug and have as a common denominator in their clinical

cal picture a rather severe deterioration of the higher cognitive functions.

Defer and Diehl¹² believe that the basic pathology in these cases is a progressive dementia with some paranoid manifestations (*syptomatologie pseudoparanoïde*). One of the most comprehensive accounts of the characteristics of these chronic psychoses has been made by Christozov based on 140 cases admitted to Berrechid Mental Hospital in Morocco.¹⁰ His phenomenological description includes:

a) *Behavioural and psychomotor manifestations*: Many of these patients appear lethargic and autistic but the hypoactivity alternates with periods of excitement and at times impulsive aggressive gestures. Their behaviour becomes incoherent and aimless, as frequently observed in chronic confusional states.

b) *Impairment of sensorium*: One of the most remarkable manifestations of these psychotic disorders is a severe disorientation as to time. Christozov believes that the traditional cultural disregard for time in Morocco may increase the severity of this symptom. Many subjects showed varied degrees of spatial disorientation as well. Auditory hallucinations are not infrequent and are believed to succeed the visual distortions experienced in the acute phases of these psychoses.

c) *Disturbances of the thought process*: The most striking features are the poverty of ideas with a tendency toward concrete thinking and poor capacity for synthesis. Many of these patients exhibit paranoid delusions of persecution and grandiose ideas. Here again, Christozov interprets the content of the delusional manifestations as being determined by local cultural traits, particularly among the male population.

d) *Impairment of the intellectual functions*: These patients appear to have lost much of their intellectual capacity and have poor concentration, memory and comprehension.

Many of the symptoms described by Christozov are also those of schizophrenic psychosis. In his report this author discusses the nosology of these two conditions and makes a differential diagnosis between them. In so doing he remarks that the diagnosis of schizophrenia should be discarded because the majority of these patients show a favourable response to treatment with complete

recovery. Based on this opinion, he proposes the name of "pseudo-dementia praecox" for the cannabis psychosis. Although his diagnostic criteria are probably acceptable to those who see schizophrenia as an irreversible process, this concept is likely to be rejected in North America.

Carrère and Pascalis in commenting on Defer and Diehl's paper,¹² point out that the withdrawn attitude observed in chronic cannabis abusers should be differentiated from schizophrenic autism because it is more a pleasant indifference than a detached perplexity.

Finally, some milder forms of these chronic cannabis conditions manifest themselves as brain syndromes with different degrees of euphoria. In Morocco these patients have been described as "kif-happy vagabonds".³¹ They seem to lead a sort of skid-row life, are not necessarily perceived as mental patients and are rarely admitted to hospital.

E. Residual conditions

Under this heading we include some psychological changes which have been attributed to the effects of regular cannabis use. One such condition is the "amotivational syndrome" described by MacGlothlin and West in 1968.²⁵ Many regular users have been observed to become apathetic, lose drive and sense of purpose, indulge in day-dreaming, have inward child-like thinking, operate on the basis of immediate, present-oriented responses rather than on long-term goal-directed behaviour, and evade activities which require sustained effort. Whether these manifestations are true effects of the drug, or merely a reflection of the attitudes consciously adopted within the frame of reference of a new philosophy of life, cannot be fully ascertained at this moment.

In the light of the pathology exhibited by heavy inveterate smokers in North Africa and the findings reported by Gershon¹⁵ and Rodin, Domino and Porzak²⁶ concerning the effects of cannabis on brain physiology, it would seem essential that psychiatrists make a very careful evaluation of these cases in order to detect early signs of organic impairment.

Other conditions that may be classified as residual manifestations are the echo reactions better known as

"flashback" experiences. In 1968 Keeler *et al*²⁰ reported on four cases of individuals who had experienced recurrence of visual and somatic sensations similar to those felt while under the effects of the drug, but without having smoked. These authors remark that only two of the four seem to have been disturbed by the phenomenon. It is now known that many individuals do experience recurrence of pleasurable cannabis effects during drug-free periods. Some claim to be able to bring on these feelings at will. However, since the elements involved here are eminently subjective impressions, it is very difficult to know what exactly is meant by an individual who reports feeling "high" without smoking. Keeler proposes as an explanation for these experiences the fact that habitual smokers develop, under the effects of the drug, an increased awareness for sensations which are normally ignored. Such increased sensitivity is progressively learned and does not necessarily disappear when the individual is not intoxicated.

Weil reports that cannabis precipitates flashbacks of LSD and the effects of other hallucinogenic agents in individuals who make use of those drugs as well. Echo reactions are usually benign and tend to fade with time if the drug is discontinued. However, in some individuals, particularly those with obsessive-compulsive or phobic personalities, they evoke a considerable amount of anxiety and may lead to hospitalization.

Résumé

Les effets psychologiques défavorables chez le fumeur de cannabis: tentative de classification

Le présent article souligne la nécessité de définir précocement et de décrire le fumeur "invétéré" de cannabis en Amérique du Nord. Il attire notamment l'attention sur le fait que, sur ce continent, on n'a pas encore séparé le gros fumeur des autres fumeurs en tant que usager "problème".

L'auteur passe en revue de façon complète les effets psychologiques défavorables possibles du médicament. Il propose la classification suivante: a) intoxications sévères, b) intoxications pathologiques, c) psychoses cannabiques aiguës, d) psychoses subaiguës et chroniques et e) états résiduels.

References

1. BAKER AA, LUCAS EG: Some hospital admissions associated with Cannabis. *Lancet* I: 148, 1969
2. BECKER HS: Becoming a marihuana user. *Am J Sociol* 59: 235, 1953
3. BELL D: Article on Morocco in *Week End Magazine* (Canada), March 4, 1972, p 11
4. BROMBERG W: Marihuana intoxications. A clinical study of *Cannabis sativa* intoxications. *Am J Psychiatr* 102: 825, 1934
5. CALDWELL DF, MYERS SA, DOMINO EF, et al: Auditory and visual threshold effects of marihuana in man. *Percept Motor Skills* 29: 755, 1969
6. *Interim Report of the Commission of Inquiry into the non-medical use of drugs.* Ottawa, Information Canada, 1970
7. CARLINI EA: Tolerance to chronic administration of *Cannabis sativa* (marihuana) in rats. *Pharmacology*, 1: 135, 1968
8. CHOPRA RN, CHOPRA GS, CHOPRA IC: *Cannabis sativa* in relation to mental disease and crime in India. *Indian J Med Res* 30: 155, 1942
9. CHOPRA IC, CHOPRA RN: The use of cannabis drugs in India. *Bull Narcot* 9, no 1: 4, 1957
10. CHRISTOZOV C: L'aspect marocain de l'intoxication cannabique d'après des études sur des malades mentaux chroniques. 2ème partie. *Maroc Méd* 44: 866, 1965
11. CLARK LD, HUGHES R, NAKASHIMA EN: Behavioural effects of Marihuana. Experimental studies. *Arch Gen Psychiat* (Chicago) 23: 193, 1970
12. DEFER B, DIEHL ML: Les psychoses cannabiques aigües (à propos de 560 observations). *Ann Medico Psychol* (Paris) II: 260, 1968
13. DEWEY WL, HARRIS LS, HOWES JF, et al: Pharmacological effects of some active constituents of Marihuana. *Pharmacologist* 11: 278, 1969
14. EY H, BERNARD P, BRISSET CH: *Manuel de Psychiatrie.* Paris, Masson et Cie, 1963, p 671
15. GERSON S: On the pharmacology of marihuana. *Behav Neuropsychiatry* 1: 9, 1970
16. GREENSPOON L: Marihuana. *Int J Psychiatry* 9: 488, 1970-71
17. GROSSMAN W: Adverse reactions associated with cannabis products in India. *Ann Intern Med* 70: 529, 1969
18. HOLLISTER LE, RICHARDS RK, GILLESPIE HK: Comparison of tetrahydrocannabinol and synhexyl in man. *Clin Pharmacol Ther* 9: 783, 1968
19. KEELER MH: Adverse reactions to marihuana. *Am J Psychiatry* 124: 128, 1967
20. KEELER MH, REIFLER CB, LIPTZIN MB: Spontaneous recurrence of marihuana effect. *Am J Psychiatry* 125: 140, 1968
21. KOLANSKY H, MOORE WT: Effects of marihuana on adolescents and young adults. *JAMA* 216: 486, 1971
22. MANNO JE, KIPLINGER GF, HAINE SE, et al: Comparative effects of smoking marihuana or placebo on human motor and mental performance. *Clin Pharmacol Ther* 11: 808, 1970
23. MORETON JE, DAVIS WM: Effects of Δ^9 -THC on locomotor activity and phases of sleep. *Pharmacologist* 12: 258, 1970
24. MURPHY HBM: The cannabis habit: a review of recent psychiatric literature. *Bull Narcot* 15, no 1: 15, 1963
25. MCGLOTHLIN WH, WEST LJ: The marihuana problem: an overview *Am J Psychiatry* 125: 370, 1968
26. RODIN EA, DOMINO EF, PORZAK JP: The marihuana-induced "social high": neurological and electroencephalographic concomitants. *JAMA* 213: 1300, 1970
27. SOUEIF MI: Hashish consumption in Egypt, with special reference to psychosocial aspects. *Bull Narcot* 19, no 2: 1, 1967
28. TALBOT JA, TEAGUE JW: Marihuana psychosis, acute toxic psychosis associated with the use of cannabis derivatives. *JAMA* 210: 299, 1969
29. TART CT: Marihuana intoxication: common experiences. *Nature (Lond)* 266: 701, 1970
30. WEIL AT: Adverse reactions to marihuana. *N Engl J Med* 282: 977, 1970
31. WHO Technical Report Series, no 478. *The use of Cannabis.* Geneva, 1971
32. WICKLER A: Clinical and social aspects of marihuana intoxication. *Arch Gen Psychiatry* 23: 320, 1970
33. WILLIAMS EG, HIMMELSBACH CK, WICKLER A, et al: Studies on marihuana and pyrahexyl compound. *Pub Health Rep* 61: 1059, 1946
34. WINICK C: The use of drugs by jazz musicians. *Soc Prob* 7: 240, 1960

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