

A CLINICAL AND METABOLIC STUDY OF ACUTE INTOXICATION WITH *CANNABIS SATIVA* AND ITS ROLE IN THE MODEL PSYCHOSES

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THIS paper describes an inquiry into the effects of giving oral doses of the narcotic drug variously known as hashish, marihuana and, in South Africa, dagga. The drug is a preparation from the plant *Cannabis sativa* whose narcotic effect has been known for centuries. The writer's interest in it was inspired by the work in recent years on the mental disturbances produced by the active principles of other plants, e.g. mescaline and lysergic acid. Because of the similarity of these changes to those occurring in conditions such as schizophrenia, some workers have suggested that these "model psychoses" could be used as a research tool in attempts to elucidate the mechanisms and causes of the naturally occurring psychoses. Although there has been a great deal of work on mescaline and lysergic acid, cannabis has not received much attention. This may be because its chemistry is still not fully worked out and preparations of the plant are difficult to standardize and vary in their potency.

Cannabis is widely though illegally grown in South Africa and there is no difficulty in getting supplies from the police for research purposes.

Because of possible dangers, such as addiction, in using the drug, research was confined to volunteers from the medical staff of Groote Schuur Hospital, the teaching hospital attached to the University of Cape Town. This also had the advantage that all volunteers, being medically trained, were reasonably equipped to describe their experiences under the drug.

As a background to the investigation a brief general history of the cannabis habit is given and a fuller one of the use of the plant in South Africa. The experiments and findings are described in some detail, using the words of the subjects as much as possible. Various physical changes that occurred are described as well as the results of special investigations such as blood-sugar curves and electro-encephalographic changes.

Finally the implications of the findings are discussed.

The work is limited to acute intoxication. Research on the chronic effects of cannabis addiction is badly needed. There is much divergence of opinion about the chronic effects, but this question, and the interesting sociological and legal aspects of the habit are inevitably beyond the scope of this inquiry.

Although the drug is known by various names, for the sake of consistency the name cannabis has been used as far as possible.

GENERAL HISTORY

One explanation for the name cannabis is given by Lewin (1931, p. 109). He says that the Assyrians used hemp as incense in the seventh or eighth century before Christ and called it "Qunubu" or "Qunnabu", a term apparently borrowed from an old East-Iranian word "Konaba", the same as the Scythian

name cannabis and as the word "Kanaba" which is derived from the primitive Germanic word "Hanapaz". Lewin suggests that these words are identical with the Greek term *κοναβος* meaning noise, and that it would seem to originate from the noisy fashion in which the hemp-smokers expressed their feelings.

The hemp plant, *Cannabis sativa*, source of the narcotic, is a native of Central Asia and is now grown in many parts of the world. It is an herbaceous annual that grows to a height of 4–8 feet or more. The leaves are long, slender and serrated and have about 5–7 lobes arising from the same point, rather like the fingers of a hand spread fanwise. Male and female flowers grow on separate plants. The seed is hard and bony. The plant is covered with glandulose hairs rich in a resinous exudate. The resin contains most of the active ingredient of the hemp, though the seeds also contain a small amount. Traditionally the flowering tops of the female plant have been regarded as the richest source of resin, but this is not now generally accepted. Narcotic potency varies with the heredity of the plant and with the climate—a hot dry atmosphere tends to increase the yield of resin and some people think that this is because the resin has a protective function.

The plant is known by many names. The Chinese call it Ma; the Indians give different names to it according to how it is prepared: bhang, composed of the leaves and sometimes the fruit of the plant, ganja, made from the flowering tops of female plants and twigs covered by resinous exudate, and charas, the most potent preparation, which consists of the resinous exudate secreted by the leaves, young twigs, bark of the stem and even the young fruit of the female plant (Chopra and Chopra, 1957, p. 5); in the Middle East it is called hashish (according to the *Shorter Oxford English Dictionary* the English word "assassin" comes from the Arabic hashisan, meaning hashish-eaters and, later, certain Moslem fanatics who were sent out to murder the Christian leaders in the time of the Crusades); in North Africa it is called kif; in Russia, anascha; in Turkey and Persia, esrar; in Spanish-speaking America, marihuana; in Brazil, macoha; in South Africa, dagga (by Europeans and Coloured people) and mbanzhe, mbangi, matakwane, intsangu, etc. (by Africans).

As a narcotic the plant has interested men for centuries—incidentally, it is also an excellent source of fibre, hence the name hemp.

From early times religions have made use of it. The Hindus regarded it as a holy plant and had many legends about its origin, such as that it was brought out of the ocean by the god Shiva and all the gods churned it in order to extract "nectar" from it. Much of the sanctity attached to the plant was due to the belief that it "clears the head and stimulates the brain to think".

Some of the Mohammedan sects regarded the plant as an embodiment of the spirit of the prophet Khizer Elijah, the patron saint of water (Khizer means green, the colour of the drink made from bhang) (Chopra and Chopra, 1957).

The lives of some tribes in the Congo centre on hemp, which is cultivated, smoked regularly and venerated. Whenever the tribe travels it takes the Riamba (huge calabash more than a yard in diameter which is used for smoking) with it. The man who commits a misdeed is condemned to smoke until he loses consciousness (Lewin, 1931, p. 114).

Apart from its use in religions it has been widely employed as a medicine. Its main therapeutic properties have been considered to be analgesic, sedative, anti-spasmodic and diuretic, though it has been recommended for a host of ailments both internal and external.

It was apparently introduced into Western medicine at the beginning of the 19th century by doctors attached to Napoleon's occupying forces in Egypt. They were sufficiently impressed by its sedative and analgesic properties to use it in the army, though the French generals were so appalled by the habit among the natives that they introduced several regulations forbidding its use.

Its use then became fairly widespread in Western Europe and it has been estimated that between 1840 and 1900 more than 100 medical articles were written recommending it for various ailments (Walton, 1938, p. 152).

Besides medical interest, it became fashionable among certain writers, artists and intellectuals to take cannabis as a "lark". Many of these people came to use it regularly and have left colourful accounts of its effects.

There were in the 19th century few alternatives to opium as a pain reliever, but by the beginning of the present century interest had shifted to new drugs, and sedatives such as chloral hydrate, paraldehyde and the barbiturates were being widely used. Cannabis preparations had always been difficult to standardize and if kept for long tended to deteriorate.

In addition, the chemistry of the active ingredients of cannabis had long eluded analysis.*

The difficulties of chemical studies of cannabis appear to have been enhanced by a series of unfortunate accidents to chemists engaged in such work. Walton (1938, p. 187) says that "Wood, Spivey and Easterfield, the Cambridge chemists, were not able to complete their program because of a series of tragic accidents. Wood barely escaped with his life when he took some cannabinal at the time he was preparing zinc ethyl. He lost consciousness, the zinc ethyl ignited and he was rescued from the burning room only with much difficulty. Easterfield was killed in a violent explosion while attempting to hydrogenate cannabinal. Spivey similarly perished while engaged in a synthetic study of the nitro-cannabinalactone."

The pharmacological action in animals is poorly understood. The main action is on the central nervous system and ataxia potency in animals closely parallels psychic potency in man. Samples of the crude material are such a mixture of different fractions that they vary considerably in their potency. Loewe (1950) is an authority on the chemistry and pharmacology of the crude extract and the synthetic preparations. He found it poorly soluble in water and it dissolved slowly even in ideal solvents such as acetone. Consequently it is absorbed slowly. Even after intravenous injection, 30–60 minutes may elapse before a peak effect is attained and the effect may persist for hours or even days. The margin of safety is enormous. Despite the wide use of the drug only two cases of death in human beings have been reported. Ewens (cited by Walton, 1938, p. 126), reported two cases from India in which a large overdose

* Goodman and Gilman (1955) state: "the isolation of the active principles proved most difficult. For many years it was erroneously believed that cannabinal, discovered in 1899, was the active principle of hemp. Cannabinal is a homogeneous, viscous oil obtained from purified 'red oil' derived from hemp extracts or resin. The chemical structure proved to be a dibenzopyran derivative. Cannabidiol was soon isolated from fresh hemp extracts and its structure identified. Cannabinal is the product of an inner condensation and reduction of cannabidiol. The former is virtually and the latter entirely inactive pharmacologically, but cannabidiol provides the basis for the synthesis in the laboratory of products of high potency which are probably isomers of the active principles of the red oil of hemp. Although reports of the isolation of natural active compounds and their derivatives have appeared it was not until 1942 that Wollner and his co-workers isolated and identified a natural tetrahydrocannabinal. This compound is quite active in animals and man, as is also a number of its synthetic congeners. The tetrahydrocannabinols are the intermediate products in the conversion by the hemp plant of cannabidiol to cannabinal. Approximately 80 derivatives of tetrahydrocannabinal have been synthesized and studied pharmacologically."

proved fatal. Ewens said "the effect was rapid coma with vomiting of green-coloured contents of the stomach, stertorous breathing, etc. with marked congestion of the conjunctivae and coldness of the body surface. At post-mortem there was a most curious congestion of all the internal organs of the body". Dogs have been killed with large doses of one of the synthetic cannabis preparations and the most striking autopsy finding was profuse intestinal haemorrhage; after intravenous injection the dogs developed fatal pulmonary oedema. (It is well known that both these findings sometimes result from acute cerebral disease in humans).

With more potent synthetic preparations of cannabis, death is associated with convulsions and appears more directly due to central nervous system damage.

Investigation into the chemistry of cannabis stimulated fresh clinical interest in the drug. In 1938 Walton wrote a comprehensive book on marihuana; in 1939 Bromberg described mental reactions seen during intoxication with the drug; in 1941-1942 Adams reported on the co-operative work of three laboratories—chemical, pharmacological and clinical; in 1942 Allentuck and Bowman described the psychiatric aspects of cannabis intoxication; in 1944 a team of workers, including doctors and police officers, issued a report on it in New York and the results of their experiments with 77 subjects, and in 1957 the Narcotics Division of United Nations Publications issued a full report on cannabis in India.

Occasional reports on the therapeutic use of cannabis have appeared in recent years. In 1947 Stockings described synhexyl, one of the synthetic cannabis preparations, as a "new euphoriant". He used it in 50 cases of "neurotic depression" and claimed that 36 showed definite improvement: their depression lifted, they had an increased zest for work and were more accessible to psychotherapy.

Parker and Wrigley (1950) tried synhexyl in 62 cases of melancholia and neurotic depression giving 10-20 mg. daily. They were not impressed by the drug after using the "double-blind" method, but despite this concluded their paper by saying that it is undoubtedly a euphoriant and further work should be done on it.

In 1954 Rolls and Stafford Clark described the successful use of cannabis in the treatment of a case of depersonalization. They included cannabis in the group of hallucinogens described by Osmond and Smythies (1954) and discussed its possible mode of action.

SOUTH AFRICA

Cannabis was in use for many years before Europeans settled in the country and was smoked by all the non-European races, i.e. Bushmen, Hottentots and Africans. It was probably brought to the Mozambique coast from India by Arab traders and the habit, once established, spread inland. The similarity of African names for the drug, e.g. mbangi, to the Hindi bhang, suggests this mode of entry into the country.

The term "dagga" is derived from the Hottentot "dachab"* and is applied

* Senator Vedder, who has lived in South West Africa for many years and is an authority on the customs and language of the native inhabitants, says that the term dagga originates from the Hottentot—dachab being the singular and dachagu the plural. The term can be explained in two ways. Firstly, dacha is an Arabic word meaning "to smoke". Secondly, in the Hottentot language "da" is a verb meaning "to tread down". If "cha" is added to a verb the word receives an additional meaning that you do it with pleasure and frequently, e.g.

not only to *Cannabis sativa* but also to *Leonotis leonurus* (Red or Wilde dagga) and *Leonotis leonotis* (klip-dagga). These two plants are reputed to have a mild narcotic effect (Gunn) but are not generally used for that purpose although they are apparently given to animals, e.g. racehorses, as a stimulant.

The plant has been used for many purposes in South Africa. Suto women smoke it to stupefy themselves during childbirth; they also grind up the seeds with bread or mealie pap and give it to children when they are being weaned (Watt and Breyer-Brankwijk, 1932). It has often been recommended as a local application for snake-bite and some "cancer curers" use the oil from a dagga pipe as an external application. It has also been recommended for malaria, anthrax and dysentery.

Apart from African folklore there are four studies by Europeans on the use of cannabis in South Africa. The position before 1913 has been described by Bourhill. According to him dagga smoking was widespread among rural Africans and did not constitute a problem. Only adult males were permitted to smoke. They did so in a leisurely manner and smoking was often accompanied by the "dagga games". These games were played by blowing saliva through thin reed pipes to create intricate patterns. When the smoke was inhaled through water (the customary way of smoking) excessive salivation (it was claimed) was induced. The old men of the tribes gave their fondness for these games as one of the main reasons for continuing dagga smoking.

Bourhill states that dagga smoking was not only permitted but actually encouraged among African mine-workers because "after a smoke the natives work hard and show very little fatigue".

The usual mine practice was to allow three smokes a day. Nevertheless, the impression was growing even at that time that dagga smoking was harmful to urban Africans. Bourhill's discussion of this view naively reflects social attitudes to Africans at that time. He accepted uncritically the current belief that Africans were unstable and inferior in intelligence.

ma means to give and macha to give gladly. Consequently, dacha might mean "to tread down gladly or frequently", i.e. the dagga smoker gladly becomes stupefied. Senator Vedder is of the opinion that both the Arabic and Hottentot languages have contributed to the name of the plant though many people might consider the Hottentot derivation given as rather too tortuous. Vedder tells a favourite story about dacha. Apparently in Karibib there was a Bergdama (one of the native people) who decided to surround his hut with a new kind of verandah. He placed barrels in a semi-circle round the hut and filled them with earth. On top of them he placed another layer of barrels so that the wall was more than the height of a man. In the top barrels he planted dacha plants. Many police passed but did not know what went on. When the plants had grown he cut them, plaited them, rolled them and fastened them with long thorns. Nobody disturbed him in this work. But a young Bergdama watched him and asked for an explanation. The old man said that the plant was dacha that could be smoked. The smoker would then enter into a wonderful sleep and see things that one did not normally see and he would receive a wonderful feeling of happiness and contentment. The young man asked for a pipeful of this wonderful stuff, filled his pipe and returned to his pondok to smoke it. But it did not take long before he put down his pipe, and very tired he sank into a deep sleep. When he awoke he was berserk.

In olden times the Bergdama used the plant for magic rites. They appointed one from their midst to smoke himself to sleep and his friends would watch him. If he smacked his lips they would say they could expect a year when they would find much wild honey, but if the smoker looked sad it was a foreboding of a bad year.

These people also used to dance a folk dance to an old song about dachab:

"The water bubbles O dachab
 You little seed which grows because of the water
 The bushy tail fed by the spring
 You cover the earth—you sit in my head
 The dachab from the river has got hold of me
 Show me a kudu O dachab
 So that my hunting will be successful", etc.

He paints a reasonably accurate picture of acute intoxication with cannabis, though it is doubtful whether auditory hallucinations are, as he claimed, part of the picture.

The second part of his paper dealt with "dagga insanity" among patients admitted to Pretoria Mental Asylum during the years 1908 to 1912. He claimed that 18 per cent. of all males admitted during this period were suffering from "dagga lunacy". In a review of 103 cases the average age was 27, the average period of detention in the asylum 255 days and relapses occurred in 41 of the 103 cases.

Bourhill's labelling of his cases as "dagga insanity" is not acceptable. He himself mentions the difficulty in excluding alcohol as a factor and there is no good reason why many of his cases might not have been schizophrenics who were also cannabis smokers. His emphasis on auditory hallucinations is much more suggestive of schizophrenia than cannabis intoxication.

In 1936 Watt and Breyer-Brankwijk cleared up much confusion about the plants to which the name "dagga" applied by showing that *Cannabis sativa* was "true" dagga with undoubted narcotic properties while the other plants called dagga belonged to the *Leonotis* family, i.e. klip-dagga, wilde dagga, etc. Only one species, *Leonotis leonurus*, had been investigated (Gunn) and was reported to be mildly anthelmintic, feebly narcotic and probably harmless when smoked.

Watt and Breyer-Brankwijk described some of the clinical effects of smoking *Cannabis sativa* and urged a controlled investigation into the relationship of the cannabis habit to the production of acute psychosis and of permanent mental deterioration.

The third paper appeared in 1938 as the result of this suggestion by Watt and Breyer-Brankwijk. It was based on an investigation by the medical staff of Pretoria Mental Hospital on 72 non-European patients (22 of whom had been diagnosed as "dagga psychosis"). The patients were observed while smoking cannabis and the results recorded.

The writers found that all cases showed marked mental dulling; 35 per cent. of the cases showed motor excitement; 45 per cent. reacted with depression and 20 per cent. "just became silly and fatuous". The authors themselves seem to have been doubtful about the information that could be gleaned from this experiment as all the patients were psychotics and some of the effects observed might well have been due to activation of the original psychosis.

The fourth paper, 1951, is a report by a committee appointed by the Government. It is not confined to the medical aspects and is, in fact, full of valuable information and gives a balanced history and assessment of the problem as a whole. The committee felt that the picture of acute dagga intoxication was fairly well known but that there was far too little information on the effects of chronic dagga smoking. The committee pointed out that since 1928, when the cultivation of dagga had been declared illegal, there had been an unceasing prosecution of those engaged in the trade. They found it impossible to give an accurate idea of the extent of dagga smoking in the Union of South Africa, but felt that the practice was widespread among Africans (both rural and urban) and less common among the Coloured people and Europeans. Of all persons prosecuted for dagga offences, Africans regularly constitute 75 per cent., although many of these are traffickers who do not themselves use the drug.

EXPERIMENTAL WORK

The investigation which is the subject of the present paper was designed to study the effect of giving a single oral dose of *Cannabis sativa* under controlled

conditions. All subjects were medically trained and the writer had known them for some time before deciding to use them in the experiment so that on the whole they were articulate and fairly stable people.

The work can be divided into five sections:

1. This deals with the effect of cannabis on 10 subjects (two female) in the 20–30 age group. Seven subjects were asked to participate and three volunteered spontaneously. They were all interns with no particular knowledge of psychiatry or chemical intoxications. During the experiment particular attention was paid to
 - (a) Subjective experiences and behaviour;
 - (b) Clinical changes;
 - (c) Certain special investigations, e.g. half-hourly blood-sugar estimations, urine output, electro-encephalographic recordings before and three hours after the cannabis had been taken.
2. The experiment was repeated on three subjects but on this occasion blood sugar estimations and electro-encephalographic recordings were not done.
3. The writer took cannabis but did not have blood-sugar estimations done.
4. One subject was inadvertently given an overdose and his reactions are described separately.
5. Four male cannabis addicts were interviewed.

TECHNIQUE

All the subjects knew that they were taking cannabis and took full responsibility for their actions.

They fasted from 10 p.m. the previous day and presented themselves in the ward at 8.30 a.m. On arrival an electro-encephalographic recording was done, blood was taken for blood-sugar estimation and the subject got into bed in pyjamas and a basal pulse rate was established. An oral dose of cannabis was taken without water. The dose varied between 4–7 grains according to body weight and temperament. An observer stayed with the subject more or less continuously (in all cases the writer and one other person acted as observers, relieving each other when necessary). The observers took notes throughout the experiment and sometimes took a tape-recording or took the pulse rate if the nurse did not arrive at the correct time. In addition, blood was taken from an arm vein every half-hour and urine output was measured before the experiment began and three hours after it had started.

A second electroencephalogram was done three hours after the cannabis had been taken and three to four hours afterwards the subject was given a meal and left to sleep and drowse through the rest of the day with occasional visits.

All but two (one of whom was the writer) of the ten subjects were kept in the ward overnight. The two who returned home were driven home, one at 10 p.m. and the writer at 5.30 p.m.

All subjects submitted a report within the next few days on what they remembered of the experience.

PREPARATION

One thousand grammes of powdered *Cannabis sativa* was extracted by the method given in the British P.C. (1934, p. 1229). The product yielded 110 grammes of concentrated resinous extract. Of this extract sufficient was taken

to make 1,000 pills, each containing 0.06 grammes of extract, using powdered liquorice root and powdered tragacanth as excipients. Each pill, therefore, contained one grain of *Cannabis sativa*.

A healthy female cat was given 6 grains of the extract of the *Cannabis sativa* made up into an emulsion with Pulv. Trag. Cr. Within two hours a change in its behaviour was noted in that it seemed disinclined to move and remained looking apathetic on the floor of its cage. When taken out and encouraged to drink it exhibited marked ataxia and had great difficulty in lapping, continually hitting its head against the side of the saucer, splashing the milk, etc. It remained apathetic for the rest of the day and made a perfect recovery on the following day.

I. (a) SUBJECTIVE EXPERIENCES AND BEHAVIOUR

General

The onset of the abnormalities of sensation was always abrupt and unmistakable. All subjects were somewhat apprehensive at the beginning of the experiment and anxious to report on every change. But once the drug really took effect there was no doubt about the reality and definiteness of the change.

A. after complaining hesitantly of various vague symptoms suddenly said, "This is it", and immediately lay down because of light-headedness and a feeling of unreality. He reported, "With me the first perceptual change was a change in the colour and outline of objects. Colours became striking and vivid—the curtains were a vivid green, the room looked freshly painted and the figures in the room looked as if they had been cut out of cardboard. There was no third dimension. They were flat with bright colours and sharp outlines, and were seen through a screen of moving black dots like a newsprint photograph, with moving dots instead of still ones."

B. also experienced an abrupt onset accompanied by marked physical changes. He said, "I had been waiting for the first symptom with some curiosity. I thought I noticed a mild weariness and an aching feeling, mostly in my neck and shoulders. I was just saying perhaps this was something definite when I was 'hit' by fairly violent somatic symptoms. There was now no longer any doubt that I felt abnormal. I felt less inhibited and was no longer reluctant to talk about myself. The somatic symptoms were waves of warmth which started in the centre of my abdomen and radiated up, fading out about mid-chest. This was associated with forceful, fast palpitations, dyspnoea, dry mouth and waves of throbbing frontal headache." He likened these physical symptoms to adrenaline release "qualitatively the same but quantitatively more violent—it was like having the visceral effects of panic and a mental sense of panic without cause and without alarming thoughts in my head".

The onset was usually accompanied by tachycardia which was often considerable, e.g. pulse rates of 130 were not unusual.

Another striking feature about the experience was that it came in waves and several of the subjects felt compelled to communicate this fact by drawing a line rising and falling. Each dip in the curve might last only a few moments. C. after describing the onset, said a few minutes later, "Well I'm blown—it's gone—like a colour film with the shutters coming down." Within a matter of minutes he said, "Here I go again—it's a floating away—like a balloon taking off—momentarily it's a positive exertion even to breathe, and yet it is lovely. What a silly thing to say—my emotions seem to have become dissociated from my speech but I feel I must keep on talking to keep human contact." This

subject also described the wave-like alteration in consciousness as “like seeing reality in glimpses as one drives past a row of palings”.

Other subjects interpreted the waves of abnormality as sleep. D., suddenly speaking after a few minutes of silence, said, “I was asleep then, wasn’t I?” B. would repeatedly fall silent for a moment or two then say: “I keep going off or going away from the room and the observers. I feel that if I keep banging myself I could keep in contact more easily. It reminds me a bit of driving in the early hours of the morning along a monotonous road when one is very tired.”

E. said, “I had phases of losing contact with reality and at times I did not know whether I was awake or dreaming, but when I surfaced everything was quite clear.”

These lapses lasted a few minutes but to the subjects they seemed an eternity. Their minds were not occupied with anything in particular at these times, except for those subjects who, on closing their eyes, saw visual images.

During these lapses the observer could always rouse the patient to give relevant replies to questions but the demeanour and intonation of the subjects suggested great languor and was in striking contrast to the briskness and alertness of the emergent phases. C. said, “Now I am in full possession of my senses—my mind is precision clear.”

The mood was usually one of detachment and mild amusement. The subjects, after emerging from one of these wave-like experiences, described what had happened without apparent anxiety.

Thought Disorder

Several subjects described their thought processes as “fragmented”. One subject, F., in whom this was accompanied by extreme anguish said, “There was no blunting of perception and no distortion, but before I could express a thought by word or action it was lost to me and displaced by another and often irrelevant thought. I thus had extreme difficulty in sorting out thought processes to a single idea goal.”

Several subjects felt they were thinking more efficiently than usual. C. said with deliberate emphasis, “There is no mental or physical feat of which I do not feel capable.” D. said, “I am enjoying talking because so many new associations occur to me—my talk is disconnected only because I immediately forget previous statements.” G. felt that he was acquiring deeper insights into his basic personality structure, that he had a new awareness of the meaning of things; yet in the next breath he said, “My thought processes are slow and I have difficulty in expressing myself—it’s like dysphasia—I’ve read a paragraph 4 to 5 times and it won’t stick.”

B. complained that he could not get the meaning of a simple cartoon he was looking at, and several subjects stared for many minutes at a book, puzzled because it had suddenly become meaningless.

One striking change was a loss of recent memory or rather a difficulty in recall. Because of this, conversation became bizarrely disconnected. If a subject was asked a question about a statement he had made a few seconds earlier he was often unable to answer because he had forgotten what he had just said. When reminded of it he immediately took up the thread of conversation, saying, “How odd—I remember it now, but before it was lost to me.” Direct questioning invariably elicited prompt and relevant replies and in most cases the 7 from 100 serial test was well done, but if subjects were left to themselves to pursue a train of thought this difficulty of immediate recall manifested itself.

Despite this the notes kept by the observer and the notes written by the subjects a day or so later corresponded very closely and in no instance was anything considered important forgotten.

Several subjects were struck by the dissociation between thought and action, e.g. F., when asked to sit up said, "I never thought I would be able to sit up—it is almost as though my muscles held me up without volition."

Delusions

Several subjects became suspicious during the experiment. H. refused on several occasions to close his eyes because he thought he was being hypnotized into seeing visual images. C. often paused before answering a question and admitted that he was examining it for hidden implications. He asked uneasily several times, "Is there someone hidden behind that screen?" I., at one time was convinced that a tape-recorder had been concealed in the room and talked into the imaginary recorder when left alone for a few minutes.

A. got very suspicious when someone came in to hand the observer the electrocardiogram of a patient—he was convinced that it belonged to him (an E.E.G. had been done on him), was abnormal and that this information was being withheld from him. He was eventually convinced by being handed the tracing with someone else's name on it.

J. became convinced that cannabis had unmasked a latent schizophrenia and when several people came in to talk to him he refused to answer any questions because he believed they had been called in to certify him. When the second EEG was done on him he was convinced that he was receiving electro-convulsive therapy in spite of the fact that three hours earlier he had been through exactly the same routine for an electro-encephalographic recording.

Temporal Orientation

All subjects experienced a disorder of temporal orientation and it gave a remarkable quality to the experience. Events occurring immediately after each other seemed separated by an eternity of time, e.g. B. said, "The puffs between cigarette smoking seemed an eternity", and D. said that a venipuncture which had taken under a minute seemed to take about fifteen minutes. Several subjects asked uneasily when someone had just left the room, "How long is it since he left?" and were astonished at the answer because they thought it was so much longer.

Subjects could never estimate the time correctly. They invariably made an error ahead, i.e. they always thought it was much later than it was. One subject thought it was afternoon and not morning and another said he would not have been very much surprised if it had been the next day.

Because of this temporal disorientation distances seemed much longer, e.g. when subjects were wheeled down the corridor they felt that the journey was immensely long.

Disturbances of Visual Perception

Four subjects experienced disturbances of visual perception. A. said that people looked as though they were cut out of cardboard. He later described the face of one of the observers as "like an alabaster tortoise", and another as "sharply delineated through a blue haze of cellophane with acne showing up as pink excrescences and the head two or three times bigger than normal".

H., while laughing hilariously, said to the observer, "Your eyes look like large oranges—as big as a beach umbrella."

B. described one of the observers as looking like "an Egyptian pharaoh in judgment" and the ceiling as having "an iridescence like mother-of-pearl", while some wire netting formed a "rather pleasing pattern—benzene rings or stained-glass windows with two lots of colours—emerald green and grass green and red and green".

D., watching the sun's reflection on the wall, said, "It looks like a hyena or a duck-billed platypus."

After-image

Many subjects seemed to experience a greater intensity and duration of after-images, especially when objects such as windows had been looked at just before eye-closure.

Visual Hallucinations

Six subjects experienced visual hallucinations but only when their eyes were closed and usually when they were experiencing a disturbance of consciousness. H. said, "Now I see gold with blue and red stripes—flickering lights and patterns like a cartoon. Now it is changing into a technicoloured cartoon with a silver ray going up into the sky". Later he said, "Whenever I shut my eyes I lose control and see my brain like a ballerina's dress going round and round in the middle of a glass cube. A. said, "I see a cross-pattern of people in old European costume—it changes so quickly—it has already changed a hundred times. Now I see a fat man in military costume running down some stairs. He is in a military uniform, has a snow-white beard and he is in a Roman tunic."

D. said, "I see church windows and mathematical shapes, mainly on the left. Now a meteor—a fiery ball that came and went."

C. said, "I see very beautiful, vivid colours like illustrated thoughts. Now there are little Chinese scenes like lace patterns—very formalized and lovely."

I. said, "I can see fixed prismatic colours racing over my head. Now intricate figures and symmetrical scenes—each half of the picture like the other as though carved out of ivory and lighted from behind. Now it has changed and I see a block of flats with a garage and stable gates and a man is leaning on the gate—it keeps changing and there are flickering bands of light going across like a forked flame."

G. had a variety of visual images. "There is a reddish glow when I close my eyes. I imagine a cat curling up—I don't like cats or scorpions—coloured lights. All based on a pattern—basic theme of glowing, with circles getting larger and larger—there seems to be a cat with long talons curled up crouching on top of me." About 20 minutes later he said, "Imagine a fellow draped like an Egyptian mummy—picture myself on a slab like a mummy—shaft of light" . . . "My teeth feel sore—feel full of holes—that damn circle keeps coming back . . . I rose out of that sarcophagus. Now there is a vague image of a ship in harbour—glowing light on the ship."

All the subjects emphasized the fleeting nature of visual images, the speed with which they changed and the inadequacy of language to describe them properly. If beautiful, they were indescribably so—the colours were of an intensity never experienced before and the patterns marvellously intricate and suffused with light. G. was the only subject who experienced unpleasant imagery,

but when asked if it frightened him he said, "I did not like them, especially the cat, but then I don't like cats but they never actually frightened me."

The general detachment concerning the images was exemplified by several observers who described them as looking like theatre scenes.

Disturbance of Perception of Body Image

B. said, "I had a series of recurring unpleasant feelings about the shape of my own body. One was that my ribs seemed big and thick and sticking out through shrunken flesh like an anatomy body. Another was that two fairly trivial scars on my body sustained in childhood seemed so enormous that they were almost the whole of me. A third disturbance was that my penis seemed deformed. I have the idea it seemed wooden with a clubbed end but it was not erect."

C. said, "My one eye feels bigger than the other—like a Picasso picture—my face is drawing out like a Greek mask and when the corners of the mask go up I feel happy."

H. said, "In the beginning I had a pleasantly warm feeling beginning in the umbilical area and extending down both legs and genitalia—not erotic but a delightfully soothing feeling. Later I soon realized that I was having a watered-down orgasm which was constantly present—a most delightful feeling. But at the same time I seemed to have lost all sensation from my bladder and penis and had no control over the sphincter muscles or erectors and can remember being acutely disturbed as to whether I was disgracing myself by passing urine, faeces or semen into the bed. I had no idea whether I was wet or not, except by looking to see." (We had great difficulty in getting urine from this patient—he felt quite incapable of passing urine because his urinary apparatus seemed dissociated from him.)

F. experienced three attacks of what he described as "a sort of vertigo. I feel I am travelling a spiral course in a forward and up and down direction and the spirals are gaily coloured and all this is accompanied by coloured vertiginous thoughts." Each of these attacks was accompanied by acute anxiety and only occurred when his eyes were closed. This subject also complained of a "fluid-like feeling in my mouth—like a pad—it seems to make it difficult for me to articulate. Yes, it is amorphous—How amorphous can one get." (This remark accompanied by much merriment.)

I. said, "My body feels as though it is in continual motion, rocking and spinning around through space. My teeth feel strange as though they are made of plastic."

A. complained bitterly of a "horrible vibration" through his body and of difficulty in moving his tongue because it seemed "structureless". He said, "From time to time I get a feeling of descent. I could see a mental image of myself folded like a jack-knife falling through space between triangles of vivid colours set at angles and depths at variance to each other."

Depersonalization

B., summing up, said, "The outstanding psychic experience was a loss of feeling real, an inability to know that I was really doing specific acts like talking, passing urine, etc."

F. said he had a curious double image of himself. "It is as though I am watching myself lying in a big transparent bubble with my face pressed close to the side."

C. and I. both likened the experience to watching a film of one's own performance.

H.'s difficulty in knowing what his body was doing has already been described.

Mood

Mild euphoria was present at some time in all subjects and often one of the first abnormalities noted was a sudden unexpected burst of laughter because the whole idea of the experiment seemed suddenly very funny, or because some mildly amusing occurrence had become uproariously amusing.

On these occasions subjects would be unable to restrain their mirth, which was usually infectious.

One subject became extremely distressed about his "fragmentation of thought" and begged in anguish to have the experiment terminated immediately because everything had suddenly become unreal and terrifying—"this is like schizophrenia—there is a blocking between emotion and thought and it frightens me." His agony lasted only a few seconds and during this period the observer felt quite unable to make contact with him. Within a few minutes he was euphoric and with a laugh said, "In a way I can understand why people take it—if you just let your thoughts drift without worrying about them having reality or meaning it is quite relaxing."

Two subjects felt that the whole experience was extraordinarily delightful. J. said, "It is such a lovely drifting voluptuous sensation", and C. said, as the experiment was coming to an end, "I've got such a let down feeling—it is like coming out of a golden dream." These two subjects were the only ones who felt they would gladly take the drug again.

A curious detachment was common. At times the observer would become quite disturbed about some unexpected occurrence, e.g. gross muscular contractions, inability to urinate, sustained tachycardia of 140, or expiratory dyspnoea, etc., but the subject, although aware of the occurrence, seemed insulated from anxiety about it. Some of the subjects mentioned headache as one of their symptoms, but when asked if it bothered them they laughed and seemed as detached as if it were someone else's headache. This detachment also extended to disorder of mental functioning, e.g. loss of recall, seemed amusing more than alarming. If they had difficulty with a test they usually shrugged lazily as if to say, "What does it matter anyway?" Four subjects showed anxiety, but even then it was mild, or very transient, except in F. This was well shown by J., who became convinced that cannabis had unmasked a latent schizophrenia and that the second EEG was really electroconvulsive therapy, but this delusion was accompanied by what he called "uneasiness" even though he had thought out all the implications of being psychotic, e.g. losing his job, the distress of his parents.

Although this is the most striking example, all subjects showed inappropriateness of affect at some stage. G., while complaining bitterly of painful muscular spasms, burst out laughing.

After several hours, when the effects of the drug were wearing off, most subjects felt apathetic, disinclined to talk and vaguely depressed.

(b) CLINICAL CHANGES

Physical Symptoms

An invariable complaint was marked dryness of mouth. This was often one of the first symptoms noted. All subjects complained of paraesthesiae

in the fingers and toes; five subjects also complained of paraesthesiae over the nose and round the mouth.

Several subjects described a "warm glowing feeling" which was experienced in the abdomen or pelvis.

Several subjects complained of intense praecordial discomfort.

Two subjects complained of expiratory dyspnoea.

Signs

A most interesting and striking feature was a uniform suffusion of the conjunctiva sometimes accompanied by oedema of the eyelids. This invariably appeared about one to two hours after ingestion of the drug and persisted for many hours. It was not accompanied by any subjective discomfort and did not wax and wane. All subjects developed a sinus tachycardia—in one case the pulse rate, initially 56, rose to 80, but in all the other cases the rate rose to between 120 and 140. An ECG was done on one case and the graph showed a sinus tachycardia. In most cases the tachycardia persisted for several hours before the pulse gradually returned to its original level.

There was occasionally some rise in blood pressure in the first hour or two but this was never excessive, mainly systolic, and never exceeded 160 mm. Hg.

All subjects developed moderate coldness of the extremities and in some cases fingers and toes looked pallid.

One subject (a blonde) developed patchy flushing of the skin over the face and upper trunk which persisted for some hours.

Five subjects complained of mild frontal headache.

Nausea was common, occurring about 3 hours after the start of the experiment and some subjects vomited. It was the writer's impression that this symptom was related to the moving of the subject to the laboratory for the second EEG recording. The impression was that any movement at this time aggravated vasomotor imbalance. Subjects frequently became very pale and cold, but after returning to bed and being warmed, or after vomiting, they improved rapidly.

No subjects complained of hunger during the first three hours although they had not been given anything to eat or drink since 10 p.m. When given food all ate with relish—five said, "Even hospital food tastes delicious."

Reaction to venipuncture was variable. J., after the third puncture, begged to be allowed to discontinue the blood-sugar estimations because they were "agonizing". F., after the third puncture, said, "It's amazing—the drug is an analgesic—I did not feel a thing though I watched all the proceedings." Most subjects thought that the needle pricks became more and more unpleasant, but quickly added that it may well have been a cumulative effect.

Abnormal Movements

Paucity of movement was usual and subjects ascribed this to the feeling of tranquillity and detachment. In many cases it was even an effort to speak and the observer had repeatedly to stimulate the subject by asking questions. Several subjects expressed their astonishment at the thought of anyone being impelled to violent or aggressive action by the drug.

G., however, exhibited the most astonishing muscular movements. These consisted of gross flexion-extension and abduction-adduction movements, principally of proximal muscles of the lower limbs and all muscles of the

upper limbs. The movements could be stopped momentarily if he were urged to do so but immediately began again and were accompanied by much discomfort and complaint of soreness. "This is real—this is motor cortex irritation not hysterical. No, it is not a convulsion—my knee is dancing a Scottish reel." There was a certain amount of facial grimacing at the same time and a curious struggle between laughter and tears. The movements continued virtually without cessation for about three hours and the subject was left with painful, aching limbs the following day.

A. periodically gave a sort of jump with arching of the back and said it happened when he got a "vibratory feeling" passing over his whole body.

F. complained of involuntary muscular twitching involving at different times proximal limb or abdominal muscles—visible to the naked eye but not gross enough to move a limb.

Muscular Co-ordination

Most subjects complained of slight difficulty in articulation but this was seldom objectively demonstrable. Crude tests such as the finger-nose test were usually well done, but picking up a small pin was difficult. The gait was not strikingly ataxic but subjects felt light-headed when walking and did not show any alacrity about getting out of bed for some hours after the drug had been taken, e.g. D. said, "About 8 hours after the start I thought I would have a bath but felt so unsteady when I got out of bed that I decided to sleep instead."

(c) SPECIAL INVESTIGATIONS

Electroencephalography

Parasagittal and temporal recordings were done before cannabis was taken and repeated three hours afterwards. Of ten recordings four were reported as showing no change and in six there was some change. The reports were as follows:

- E. The resting record shows a well-marked persistent 9 c.p.s. alpha rhythm in occipital and central areas.
After cannabis the only change is a slight tendency to diminished persistence with longer and more frequent intervals of fast activity. EEG—slight change towards less persistent alpha after 5 grains of cannabis.
- J. The resting record shows a well-marked, persistent and well-modulated 9 c.p.s. alpha rhythm which is present diffusely, except in the frontal areas where beta activity is seen.
After cannabis the occipital alpha remains largely unchanged except that it is not quite so persistent and there is some intervening fast activity with a little random alpha over the post-central areas. EEG shows some change after cannabis—tendency to replacement of non-occipital alpha by fast activity.
- G. The resting record shows a 9 c.p.s. alpha activity posteriorly, most persistent in the temporal areas and with a fair amount of fast activity in the parasagittal leads. The only change after 7 grains of cannabis was one very short episode of 6 c.p.s. activity that appeared in the posterior temporal areas.

- H. The initial recording shows a well-marked and almost persistent 10 c.p.s. alpha rhythm posteriorly, of rather low voltage; and low voltage beta activity anteriorly.
Three hours after taking 7 grains of cannabis the persistence of the posterior alpha activity is considerably less, it being interrupted by much irregular fast activity. The generally low amplitude remains unchanged.
- K. (Clinical record of this case was not included in the series.)
The record shows generally low voltage fast activity throughout; there is a minimal amount of posterior 11-12 c.p.s. alpha activity. After cannabis the only change is that there appears a moderate amount of bilaterally synchronous anterior temporal 6-7 c.p.s. activity.
- C. The resting record shows a well-marked and persistent 10 c.p.s. alpha rhythm posteriorly with beta activity anteriorly. Three hours after the ingestion of 6 grains of cannabis there is a slight quickening of the alpha rhythm to 11 c.p.s. and it is not so persistent and uninterrupted. The temporal leads show fast activity throughout—probably much muscle artefact.

Blood-Sugar Readings

Fasting blood-sugar estimations were done every half-hour for two and a half hours. These did not show any significant change. There was occasionally a tendency for the blood sugar to show some slight elevation about one hour after the cannabis had been taken but this was never outside the range of normal. (See graph.)

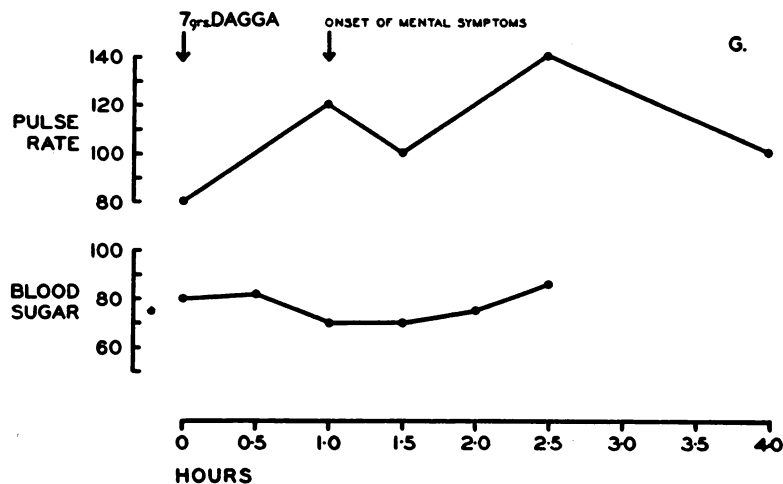


FIG. 1.

Urine Output

Because of the frequent references in the literature to a possible diuretic property of cannabis it was decided to measure urine output during a fixed period before cannabis was taken and for another fixed period after it had been taken. The following table gives the results in seven cases:

Subject	Before Cannabis was Taken		After Cannabis was Taken	
	Period of Time	Volume of Urine ml.	Period of Time	Volume of Urine ml.
A ..	2 hours	160	2½ hours	352
B ..	2 hours	224	1 hour	569
C ..	2½ hours	100	1½ hours	635
D ..	2 hours	192	50 minutes	352
I ..	2 hours	350	3 hours	400
J ..	1 hr. 45 mins.	150	3 hrs. 10 mins.	125
Writer ..	2 hours	250	3 hrs. 10 mins.	500

Because urine output appeared on the whole to show an increase after the ingestion of cannabis, more detailed study of two cases was done by Dr. Stewart Saunders. These showed a selective sodium and bicarbonate loss. This increase in sodium and bicarbonate is due to a tubular effect, there being no proportionate increase in the filtered load. Inhibition of carbonic anhydrase can also have this effect.

The evidence is sufficiently strong to suggest that further investigation of the diuretic properties of cannabis would be worth while.

The findings are tabulated below:

SUBJECT D.

Excretion of Chloride Before and After Cannabis given at End of Period ONE

Period	Time (Minutes)	Urine Volume (ml.)	pH	GFR(Ccr) (ml./min.)	Filtered Load Cl. (m.eq./min.)	Urine Cl. (m.eq./min.)
1 ..	124	771	7.25	84.8	9.47	0.2395
2 ..	121	660	7.8	93.2	10.21	0.4426
3 ..	115	550	8.1	92.4	10.33	0.3139

Excretion of Sodium:

Period	Time (Minutes)	Urine Volume (ml.)	pH	GFR(Ccr) (ml./min.)	Na ⁺ (m.eq./min.)	Urine Na ⁺ (m.eq./min.)
1 ..	124	771	7.25	84.8	11.66	0.1774
2 ..	121	660	7.80	93.2	13.51	0.7810
3 ..	115	550	8.10	92.4	9.61	0.7548

Excretion of Potassium:

Period	Time (Minutes)	Urine Volume (ml.)	pH	GFR(Ccr) (ml./min.)	K ⁺ (m.eq./min.)	Urine K ⁺ (m.eq./min.)
1 ..	124	771	7.25	84.8	0.424	0.1581
2 ..	121	660	7.80	93.2	0.475	0.1975
3 ..	115	550	8.10	92.4	0.453	0.1148

Bicarbonate:

Period	Time (Minutes)	Urine Volume (ml.)	pH	GFR (ml./min.)	Filtered Load m.mols./min.	Urine Conc. m.mols./min.
1 ..	124	771	7.25	84.8	2.4334	0.00435
2 ..	121	660	7.8	93.2	2.6003	0.168
3 ..	115	550	8.1	92.4	2.0882	0.1575

SUBJECT L.

Excretion of Chloride Before and After Cannabis given at End of Period TWO

Period	Time (Minutes)	Urine Volume (ml.)	pH	GFR(Ccr) (ml./min.)	Filtered Load Cl. (m.eq./min.)	Urine Cl. (m.eq./min.)
1	.. 60	42	5.7	80.2	8.52	0.069
2	.. 60	46	6.0	83.7	8.89	0.113
3	.. 60	50	6.3	78.1	8.83	0.130
4	.. 60	64	6.6	89.8	10.12	0.171
5	. 60	62		85.4	9.55	0.150

Excretion of Sodium:

	Na+	Na+
1 ..	11.15	0.076
2 ..	11.63	0.105
3 ..	11.30	0.128
4 ..	12.30	0.207
5 ..	11.61	0.212

Excretion of Potassium:

	K+	K+
1 ..	0.2887	0.035
2 ..	0.3013	0.053
3 ..	0.2812	0.036
4 ..	0.3233	0.058
5 ..	0.3577	0.080

Bicarbonate:

1 ..	2.254	0.0016
2 ..	2.351	0.0032
3 ..	2.280	0.0093
4 ..	2.028	0.0162
5 ..	2.6937	0.0274

2. The experiment was repeated on three subjects after an interval of several months. In each case the dose was reduced by one grain. It was striking that they all had the same experience the second time and one could, from their first experience, have predicted with accuracy the pattern of response on the second occasion. Several months had elapsed between the two experiments.

No blood-sugar estimations or electroencephalographic recordings were done on the second occasion and this may have accounted for the only difference observed, which was that the original tachycardia was much reduced and the main abnormality noted in heart rate was that it was more unstable than usual and accelerated rapidly on exertion.

3. The writer took 4 grains of cannabis and remained in bed in the ward until taken home by car in the late afternoon.

Before the cannabis was taken slight frontal headache and some apprehension was experienced. About 90 minutes after the drug had been taken some difficulty in articulation was experienced (this was not objectively demonstrable) and concurrently "I became aware of an astonishing difficulty in recall, so that I could not remember events that had just occurred. This inability of recall seemed to be associated with 'dips' in the level of consciousness when everything seemed rather unreal and hazy and in striking contrast to the periods when I emerged from the dip. It was like emerging from shadow into light. In addition, my concept of time was distorted so that it always seemed later than it really was and the journey down the corridor seemed eternally long.

"My mood change was striking. I experienced some euphoria but to me the really striking thing was detachment. This can be illustrated by the following

examples: I realized that my headache (frontal and occipital) was really quite severe and yet it did not really matter and at the time I compared it to the indifference to pain apparently experienced by patients who have been leucotomized for the pain of inoperable carcinoma; when being wheeled down the corridor in full view of my patients I felt that the situation would normally have embarrassed me and I was struck by my indifference; finally, after I had been taken home and was lying in bed, I could hear my children hilariously swamping the bathroom, which normally never fails to irritate me, and I was astonished at my indifference to it. Physical symptoms were not prominent. I experienced some paraesthesiae of hands and feet, was conscious of coldness and had a bad headache. My pulse rate remained more or less normal unless I exerted myself, when it immediately rose from 80 to 120. I developed slight conjunctival suffusion and had a diuresis. The effect of the drug lasted for 11 hours."

4. *Report of a Subject who took 48 grains of Cannabis*

About three-quarters of an hour after taking the drug the subject felt sleepy, with a heaviness of the eyes and a sense of rotation. About an hour after the drug had been taken he began to laugh uncontrollably and loudly and said that the whole idea of the experiment was killingly funny. For the next hour he laughed a great deal, spoke rapidly and excitedly and became fairly uninhibited in his behaviour, especially towards senior members of the staff whom he called by their first names. He addressed his chief, who had just been elected an F.R.C.P., by his first name and said, "You are very pleased with yourself about that F.R.C.P.—not that it was not richly deserved but really you are so self-satisfied about it." The matron of the hospital was also addressed with great familiarity and the superintendent and other members of the staff were criticized. His report on this aspect reads, "I can, of course, remember speaking a great deal, but time itself pressed on me. I was obsessed with time. There was such a lot to say and so little time and words seemed so insufficient. I remember feeling that I was behaving like a manic—with flight of ideas. I could not stick to a subject and revelled in the sheer pleasure of swinging the conversation round as it suited me. This was a time of intense activity and it all passed like a bright flash. Time and space seemed compressed into one bright minute during which all was gay talk, brilliant jokes and myself the care-free centre of it all."

At this time he experienced a "whirling of objects around a central axis which seemed placed in the middle of the ceiling", and he saw a vivid flash of colours which resembled a modern curtain set against a multi-coloured window. Objects seemed to stand out with "a lively 3-D effect" and the face of one of the observers seemed "exquisite, of very beautiful colour, and a lovely depth that made me want to sculpture his face". He was intensely hungry at this time.

After the first hour the euphoria began to wear off and he complained of various physical discomforts, e.g. intense cold in his feet which felt cold when touched and intense dryness of the mouth and nose. In addition, his hands and feet began to tingle and he complained of weakness of the extremities and several times asked anxiously whether this "peripheral neuritis" would persist. At about this time he wept when a venipuncture was done and said the needle prick was "agony".

He complained of difficulty in focusing his eyes and episodic mistiness of vision.

About three hours after the drug had been taken he became depressed and irritable, looked pale and vomited. He complained of a bitter taste in the

mouth, severe abdominal cramps "like an ileus" and moaned, "What have you done to me?"

He also complained that time was passing terribly slowly.

During the "manic" phase he had a tachycardia of 120 which persisted for 2½ hours. His pulse rate then came down to 80 and 8 hours later gradually settled to 70.

Five hours after the start of the experiment he looked so wretched and was in such abdominal discomfort that he was put on intravenous dextrose and given 50 mg. of largactil intramuscularly. Despite this he had a poor night and felt irritable and unwell and had periodic abdominal cramps for the next two days.

The report on his electroencephalograms reads: "The initial recording shows a well-marked 8 c.p.s. alpha rhythm posteriorly with irregular fast activity anteriorly and a small amount of anterior alpha. After drug ingestion there is a complete disappearance of the alpha activity and the whole record consists only of low voltage fast activity".

There was no change in blood sugar levels during the first 3 hours of the experiment.

(The abdominal cramps may be accounted for in part by the large amount of liquorice contained in the 48 pills.)

5. Interview with Coloured Male aged 32 Years

This labourer was completely illiterate and had spent most of his life working with horses in a hawking establishment. He made a good impression, was quick-witted and had an engaging friendliness. He said that he had been smoking dagga regularly (2–3 cigarettes) every night since the age of 15. "Once you smoke it it never lets you go. It makes your mind so that it can never fail. It makes you stronger, makes you laugh a lot and makes you like everybody. It makes me very energetic to my wife so that I even got twins. There is no crime in it—it is only with alcohol that it makes you do wrong things. It is best if you smoke it with other people but if alone you can think you hear the best band playing. Your imagination is so great that you can see someone you have not seen for a long time. But if there are other people with you you don't see or hear anything—you just enjoy yourself. If you smoke it and go to sleep immediately you feel terrible next morning. You must have a little enjoyment and exercise before you sleep and the next morning you feel fine."

He had no intention of giving up the habit and did not think it had harmed him in any way but, on the contrary, that it had enormously increased the savour of life.

Interview with a White Male aged 19 Years

This youth made a good impression. He had been in steady employment for 4 years, was neatly dressed, courteous and spoke intelligently. He said that he had been introduced to dagga smoking at a party 18 months previously and although he had started the habit as a lark he had found it so pleasant that he had, since that time, regularly smoked two packets of cannabis a night. He always mixed the drug with ordinary tobacco and rolled a cigarette with the mixture. He described the effect as a "sort of light-headedness—like having a few glasses of wine and yet different because it does not make you drunk. Two cigarettes give me a very pleasant feeling for about an hour—I feel like laughing and cracking jokes and somehow one has more courage than normally. Everyone seems to be my friend and it is much more fun to smoke in company than alone. If I am alone I just fall asleep."

He was conscious of tachycardia when smoking, increased desire for food, especially ice-cream because it relieved the dryness of his mouth, and he had also noticed that he passed more urine than usual. He was not interested in alcohol and said that if he were offered alcohol or cannabis he would unhesitatingly choose cannabis. He has gone for several months without it and has not experienced any withdrawal symptoms or any cravings for the drug. The reason why he started smoking again is that he finds the habit pleasant and it does him no harm and he never has a hang-over.

Interview with a White Male of 17 Years

This youth made a poor impression. He left school at 16 having failed to pass Standard 6. He came to the interview because he thought he would be asked to volunteer to smoke some under supervision—"and then you would see how wild I get". He started smoking cannabis one year ago. It was the custom in the gang of about 20 youths of which he was a member. The gang meets about twice a week and are sometimes accompanied by girl friends. They always smoke their cannabis, mixing it with ordinary tobacco, and make a party of the meeting. They take a few bottles of wine and a vast quantity of fish, chips and bread, "because we get terribly hungry". When smoking he feels "very happy, very strong and enjoys talking a lot. I always end up by fighting someone because I feel I can't lose and if I get hurt I don't feel the pain. Once I hurt my leg but did not even know about it until the next day when I saw it was so bad a wound that it had to be stitched."

Occasionally he feels very tranquil after smoking and just wants to lie in the sun and sleep, but usually he becomes restless and either walks aimlessly for miles or picks fights. He has recently acquired a pellet gun and takes it with him when he joins the gang. After smoking several cigarettes he climbs into a tree and takes aim at the other members of the gang. The confusion and fear aroused in them pleases him very much. He said that time had no meaning for him when he was smoking and far from having a hang-over he always felt very relaxed the next day and "could not worry about anything". He emphasized that the gang were not really wild—"we never do anything wrong, like breaking into houses".

Interview with a White Male aged 33 Years

This man claimed that he had smoked cannabis from the age of 14 to 32 but had given up the habit because he had been rescued from this "sin" by a minister of religion. He said that after cessation of the habit he had felt a craving for the drug for 6 months but had not suffered any physical withdrawal effects. (Another addict said that this man was still smoking cannabis.) He gave the impression of being unstable and humourless but had a remarkable capacity for self-observation.

He started off the interview by saying "dagga means women, murder and fight". He seemed to be particularly impressed by its effect as an aphrodisiac and stated that he was obsessed with the desire for women while smoking it. He claimed that his sexual vigour was so enhanced that he had on many occasions slept with 4 to 5 women in one night or had repeated intercourse with the same woman. After smoking he would follow women in the street "white or coloured—pretty or ugly—they all attracted me". If he was unable to strike up an acquaintance with the woman he would seek other women or masturbate. "A man has the energy to go on over and over and after one

time my nature was still high but if I slept even for 30 minutes all desire would leave me." Recently since he began to regard the habit as sinful he would sometimes get a strange feeling while looking at a woman, that "she would seem to change into something strange and horrible, e.g. a stone mountain or a devil". One not infrequent hallucinatory experience was seeing the "devil with long claws and feet looking as though he were going to jump at me and come down on me with his long claws. Then I would cry and pray to God to deliver me from the vice. The next moment I would be laughing madly because I knew it was not really there." He described several occasions when he experienced a marked change in visual perception—"say I was looking at your face, it might change like this—the eyes might start to look Chinese and the nose to broaden until the whole face looked like a mask and then it might make me want to laugh and laugh or if it were a man's face I might go and pick a fight with him. I never felt scared and a fight only ended when I won or was knocked out."

He claimed that his thinking was better when smoking cannabis. "My thoughts get faster and continuous—it is like a verse in your brain as though the devil is talking to me." He quoted a friend of his who when taken to court "always makes a better impression on the magistrate when he has been smoking dagga. He gives the impression of being better educated and cleverer than he really is, because if you think you are clever you seem to be cleverer." Despite the impression of accelerated thought and ideas "when one reads one sticks with one word and can't get any further". He mentioned that talking was particularly enjoyable and for this reason he always sought company when smoking. "Most smokers don't drink much with it—a man can sit the whole night with one small glass of wine in front of him as long as he has his dagga." He said that alcohol and dagga were completely different in their effect. "Dagga is 100 per cent. better—you walk up steady, you think a lot and you enjoy talking." An interesting observation was that he was much more reckless after drinking wine than after smoking cannabis. "Dagga makes you more scared in a way. I would never ride my bicycle or drive a car when I had been smoking because I knew the devil might mislead me and make me have an accident, but when drunk I would not mind doing these things."

He was also struck by the difficulty in estimating time. "If you walk for thirty minutes you think you have been walking for an hour and the same goes for talking."

He had also noted tachycardia and increased appetite, especially for curry and rice, and marked dryness of the mouth even after smoking through water.

He claimed that he could identify a dagga smoker at a glance by the "drooping, narrow, shining eyes".

He denied any hangover after smoking and said that the habit never interfered with his work.*

DISCUSSION

The results show quite a marked individual variation in response to cannabis. This seems to depend more on differences in the basic personality and temperament of the subjects than on difference in dosage. Apart from

* All the addicts smoked their cannabis and it is difficult to say how much of the drug was absorbed in this way.

The great advantage in smoking rather than ingesting cannabis is that the smoker can regulate the dosage so that with a little practice he can gauge with accuracy the amount that gives him the maximum satisfaction.

one subject who took 48 grains, the range of dosage was not wide, varying between 4–7 grains. In the three subjects in whom the experiment was repeated a very similar clinical picture was obtained on the second occasion despite a reduction of the original dosage by one grain. The impression given by the addicts who were interviewed was that they always reacted in the same way to the drug.

Despite this individual variation one could discern, in all cases, a common basic pattern of response. All subjects experienced a curious disturbance of consciousness, a disorder of time perception, difficulty in immediate recall allied to thought disorder and a change in affect usually in the direction of euphoria. Accompanying these mental changes, the constant physical changes were conjunctival suffusion, paraesthesiae, dryness of the mouth, tachycardia and diuresis.

The disturbance of consciousness is difficult to define. For the first few hours there was in all cases a waxing and waning of contact with reality, or, more correctly, a constriction of the field of awareness. Despite this the capacity for self-observation appeared to be heightened and all subjects responded relevantly if stimulated. Several of them who had no manifest disorder of perception vigorously denied any disturbance of consciousness, maintaining that they were at all times fully aware of their surroundings and the nature and purpose of the experiment. But to the observer there was undoubtedly a definite though often subtle and elusive change in the degree or direction of awareness in all cases.

The disorder of time perception was to all subjects an incredible phenomenon and gave to the experiment a curious, slightly unearthly quality. It always took the same form, i.e. during the first few hours estimated time was always later than actual time—moments of chronological time seemed an eternity. (The only exception to this was the subject who took 48 grains and felt initially that time was passing incredibly quickly while later it dragged with an agonizing slowness.)

There was no clear-cut disturbance of space perception though journeys seemed eternally long. This illusion seemed to be directly related to the time that the journey took.

The change in affect usually took the form of euphoria. The subject who took 48 grains was in a state of sustained hilarity accompanied by great activity for about 1½ hours. All the other subjects showed a less sustained euphoria, accompanied by excited talking. Although this was to some extent infectious it was clear to the observer that it was out of all proportion to the stimulus. The idea of the experiment would suddenly seem enormously amusing, and oddly enough the subject would often remark on its inappropriateness himself, e.g. in telling some story, with much giggling, he would say that it seemed absurd that it was so funny and yet laughter was irresistible. Occasionally the laughter was bizarrely inappropriate, e.g. one subject laughed as he complained of painful muscle spasms.

Another common mood change was detachment which often alternated with euphoria. It was as though the subject was somehow insulated from everything that was happening to him. This certainly contributed to some extent to the common feeling of double consciousness, i.e. that the subject was himself an observer. Anxiety was not uncommon but seldom gross. It was usually most intense as the drug began to take effect and seemed to be greatest in those subjects who tried to resist the experience. This was well shown by one subject who asked with every indication of intense anxiety for an antidote

to the drug, yet a few minutes later relaxed and said that he could understand people taking the drug for pleasure because once one "gave oneself up" to it it was pleasant.

Some degree of thought disorder was invariably present. In many cases this consisted predominantly of an inability to recall what had just happened so that the subject was often totally unable to sustain a conversation unless prompted about a recent remark by the observer. In some subjects the whole process of thinking seemed broken off abruptly, or they complained of "fragmentation" of thought and described thinking as having no beginning or end and such a tenuous reality that it was continually being shattered by other disconnected pieces of thoughts.

Mayer-Gross *et al.* (1954) stated that as long ago as the mid-nineteenth century Moreau had commented on the dissociation of ideas with cannabis and in 1932 Beringer had described three forms of thought disorder with cannabis. These were:

Fragmentation of perceptive wholes through fragmentation of thought processes. Disturbance of memory by which everything experienced is forgotten at once. Frequent and sudden interruptions of the stream of thought—the gaps only lasting a few seconds. Beringer compared these to epileptic "blanks", or the sudden disruption of the associative links in thinking of schizophrenics.

It is difficult to separate these thought disturbances from one another and they may well be closely interwoven. The sudden blockages of thought and apparent disruption of the pattern of thinking might be no more than consequences of the defect in the power of immediate recall.

The physical changes that occurred in all subjects were also of great interest.

The conjunctival suffusion, uniform and symptomless, was particularly notable. It has been mentioned by many writers and seems to appear at about the same time as the narcotic effect. It persists for many hours and disappears gradually. Chopra and Chopra (1957, p. 20) state that it can persist long after the narcotic effect has disappeared. They also stated that in most addicts a permanent congestion of the transverse ciliary vessels develops. One addict interviewed showed this congestion and his addiction had been of many years standing. A marked proneness to tachycardia on exertion or a sustained sinus tachycardia was shown by all subjects. Even allowing for excitement or tension or muscular activity there appeared to be a definite autonomic imbalance. Dryness of the mouth was universal and marked, almost like an atropine effect, but dilatation of the pupils, if it existed at all, was only slight.

Paraesthesiae in the extremities and peri-oral area was a marked feature in all cases, and in the case who took 48 grains it was accompanied by a subjective feeling of weakness of the extremities.

The more florid symptoms were a disorder of visual perception, the appearance of formed visual images, usually intricate, when the eyes were closed, bizarre disorder of body perception and a marked feeling of dissociation not only of self, so that the subject of the experiment often said he felt as though he were the observer of the experiment, but also of the various functions of self, so that action, volition, thought and effect became chaotically disorganized.

The abnormalities of movement, which in a mild form consisted of periodic contraction of isolated muscle groups, or occasional writhing movements and in a severe form were a continuous medley of movements, are noteworthy because they are so difficult to classify. Beringer observed a great variety of motor anomalies including hyperkinetic and hypokinetic states.

Walton (1938, p. 93) mentions a medical man, Burr, who took cannabis and "suffered a general convulsion which lasted three minutes; he felt well; his speech was not affected. The convulsion resembled an attack of hysteria . . . the convulsions appeared wilful in that he willed to convulse; he knew that he was throwing his arms about, that he was writhing like a snake, acting like a clown, making silly grimaces. But he could not will to do otherwise. He could restrain a convulsion for a few minutes, but soon the will to convulse overcame the will to inhibit." This description is very like the state seen in one subject on two separate occasions, though the use of the term "convulsion" is unfortunate. One is also reminded of the peculiar contortions of the Quakers. In other works there appears to be some neural dissociation but a precise explanation for this extraordinary state eludes one.

Diuresis was suggested by the volume changes in the urine in all subjects. In two cases where the electrolytes were done there was a selective sodium and bicarbonate loss.

The electroencephalographic changes were not specific. Six out of ten showed changes but they remained within the limits of normal. Of these four showed an increase in fast activity and one showed one very short episode of 6 c.p.s. activity in the posterior temporal areas while another developed a moderate amount of bilaterally synchronous 6-7 c.p.s. anterior temporal activity. In the subject who took 48 grains of cannabis the alpha rhythm disappeared completely and the whole record consisted only of low voltage fast activity.

There do not seem to have been many electroencephalographic studies done during cannabis intoxication. Wikler and Lloyd (1945) reported that electroencephalograms during marihuana smoking showed a marked increase in the number and amplitude of the fast waves but these appeared to be of muscular and not nervous origin. Williams gave *ad lib.* doses of pyrahexyl (a synthetic cannabis preparation) to six patients for 26-31 days and stated that during prolonged medication the dominant frequencies were markedly slowed.

The electroencephalographic tracings in this study certainly gave no indication of the site of action of cannabis and at most merely indicated a general cerebral disturbance. It is interesting that Loewe (1950) has described a powerful anti-epileptic effect in all the synthetic cannabinoids that he tested, but at the moment the significance and practical implications of his findings are not clear.

Any attempt to explain the pathogenesis of the symptoms and signs seen in acute cannabis intoxication is purely speculative. One could envisage the process as being a diffuse neuronal change affecting not only the cerebral tissue but also peripheral nerves. The change, being temporary, suggests some subtle and reversible change in neuronal enzyme systems. Rolls and Stafford-Clark (1954) have claimed that one property that all the hallucinogens have in common is their capacity to inhibit the action of amine oxidase. It is tempting to try to fit the conjunctival suffusion into the picture by suggesting that the change is primarily vascular and the suffusion a manifestation of cerebral hyperaemia. It is certainly such a striking and unusual feature that its elucidation may well yield some of the secrets of cannabis pharmacology.

Another possibility is that the principal action of cannabis is on the brainstem and thalamic structures. The chief argument in favour of this view would be the wave-like effect observed, which might suggest some disturbance of the "alerting" system between the reticular formation and the cortex. A clue

to the temporal disorientation is suggested by the work of Spiegel (1955) who has reported finding it in 23 of 39 cases who underwent thalamotomy for intractable pain. The autonomic changes might also be a result of brainstem disturbance. The apparent involvement of peripheral nerves is not so easy to fit into this theory but anterior horn cells can certainly be profoundly influenced by the reticular formation and there might conceivably be an effect on the afferent nerves.

An attempt to compare the cannabis intoxication with the naturally occurring psychoses leads to immediate difficulties. The lack of any precise diagnostic criteria for schizophrenia is one difficulty and another is the nature of the experimental situation. The mental abnormality seen was not the result of a slow insidious weakening of the ties with reality but an acute disturbance produced in apparently normal well-adjusted young people. Contact with them was maintained throughout the experiment and this fact deserves special emphasis. During the experiment many subjects said that the observer seemed their one link with reality. Solitude and a cutting-off of virtually all sensory input can lead to extraordinary effects as Hebb and his co-workers have shown even without the administration of a drug that has such profound psychic effects. The fact that the observer stayed with the subjects throughout the experiment may well have profoundly modified the results so that in all cases contact with reality was never completely lost, insight in most cases was retained and florid symptoms never became overwhelming.

Despite this there are several features that deserve comment. The subject who took 48 grains behaved very like a manic, with much laughter, talk and flight of ideas, distractibility, lack of inhibition, etc. The other subjects showed more of a schizophrenic picture, especially as regards the apparent fragmentation of thought and the bizarre distortions of perception, notably of body image.

CONCLUSION

It is not claimed that any of the results obtained in this study are new in the sense that they have never been described before. They have all been described at one time or another, in the voluminous literature on cannabis. But each age brings some difference in attitude to an age-old problem. At the moment the quest for chemical mechanisms in the psychoses is popular and much can probably be gained from research along these lines.

It is suggested that *Cannabis sativa* may prove a valuable research tool in work of this kind. Its great advantage is its extremely low toxicity and the fact that it can be administered orally. Once its chemistry is fully understood research with it should advance rapidly.

It may well prove to have important therapeutic value as well. There has always been sporadic interest in this aspect because of the euphoria it produces, but so far the wave-like effect has been a drawback. It might be a useful adjunct to psycho-therapy. Although one subject was emphatic about its value in giving him new insight into his basic personality most of the subjects did not emphasize this aspect and all of them, including the subject who took 48 grains, said that they had no difficulty in concealing matters that they did not wish to discuss. Obviously all subjects working together on the staff of a closed institution will have certain reservations about what they are prepared to disclose. This makes the situation different from that in a doctor-patient relationship.

Finally, an interesting sideline was the finding that cannabis is a reasonably

potent oral diuretic which causes a specific sodium bicarbonate loss. With the present search for oral diuretics of this type this may well turn out to have important therapeutic implications.

SUMMARY

- I. A clinical and metabolic study of acute intoxication with *Cannabis sativa* has been made. Special attention has been paid to its role as a research tool in the model psychoses.
- II. The general history of the drug has been briefly reviewed.
- III. The history of the drug habit in South Africa has been described.
- IV. Experimental work comprised the
 1. Administration of a single oral dose of *Cannabis sativa* to 10 medical volunteers and the observation of
 - (a) Subjective experiences and behaviour;
 - (b) Clinical changes;
 - (c) Special investigations, e.g. blood-sugar estimations, urine output, electroencephalographic tracings.
 2. The administration of a second oral dose of *Cannabis sativa* to 3 of the 10 subjects.
 3. The administration of the drug to the writer.
 4. The administration of an overdose to one subject.
 5. Interviews with four male cannabis addicts.
- V. The implications of the experimental work have been discussed.

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